

► **2022 | Midterm Checkup Report**
SciLifeLab Infrastructure



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Background and Instructions to Reviewers

Objectives

The Midterm Checkup is an internal follow-up on the SciLifeLab Infrastructure operations, focusing on recent development, performance according to terms and conditions for funding, deliverables, and future plans of the Platforms and Units. The aim of the Checkup is to channel general feedback, advices and recommendations from the SciLifeLab management/reviewers about current and future operations, and to get input for the budgeting process of infrastructure funding 2023 and 2024.

Reviewer Group

Reviewers are the SciLifeLab Management Group (Director Olli Kallioniemi, Co-Director Mia Phillipson, Infrastructure Director Annika Jenmalm Jensen, and Scientific Directors Janne Lehtiö (KI), Hjalmar Brismar (KTH), Christos Samakovlis (SU) and Staffan Svärd (UU)), and the Chair of the National SciLifeLab Committee, Gunilla Westergren-Thorsson.

The Midterm Checkup Report (this report)

The Midterm Checkup Report comprises the main material for the reviewers and is based on previous annual reporting from the Platforms and Units and the Midterm Checkup reporting (see below). The report includes user statistics and metrics, publication output, development and operational plans, budget for 2022, and Platform-wise requests for additional base funding 2023–2024 (see below).

Midterm Checkup Reporting

All Platforms and Units (except the DDD Units) were asked to write up a short report on operations 2021–2022, and plans for 2023–2024 and beyond, using the templates given on page 5 and 6, respectively. Deadline for reporting to SciLifeLab was set to September 2. The material submitted from the Platforms and Units is incorporated into this report.

Request for Additional Base Funding 2023 and 2024

The national budget to SciLifeLab will expand in 2023 (+10 MSEK vs 2022) and 2024 (+20 MSEK vs 2022), and some of this budget will be used to increase the base funding of individual infrastructure Platforms and Units. In the Midterm Checkup reporting, each Platform was asked to handle, prioritize and motivate any requests for increased base funding for operations 2023–2024 (see Platform Reporting template on page 5).

Platform Meetings with the Reviewers

During October 5–6, Zoom meetings with representatives from the Platforms (the Platform Management Groups/ Heads of Units) and the reviewers will be arranged. Platforms and Units will be given the opportunity to present their operations and have a direct dialogue with the management about the development plans and budget. A rough program for the platform meetings is presented on page 7.

Instructions to Reviewers

Written Feedback: Based on the material in this report and the interviews during the October 5–6 meetings, we ask the reviewers to submit written feedback to the individual Platforms and Units in the Midterm Checkup portal in Anubis (<https://anubis.scilifelab.se/call/INFRA22>). Please, try to balance any criticism with constructive input in your comments.

Base funding 2023–2024: We also ask the reviewers to indicate in Anubis which of the individual Platforms and Units should be prioritized for strengthened base funding 2023–2024 and provide a concurrent motivation for this. Bear in mind that the total additional base budget for the infrastructure is in the order of 5 MSEK for 2023 and 10–15 MSEK for 2024.

The review period is September 19–October 9, i.e. Anubis will be open for reviewers only during this period.

Platform Midterm Checkup Reporting Template

Organization and Management

i) *Organization. Provide a simple organogram picture of the current platform organization including external bodies (e.g. steering group, advisory board, user reference group etc). Briefly describe the roles of and interactions with the different bodies.*

ii) *Platform Management. Briefly describe the routines for and frequency of PMG meetings, other relevant platform forums, e.g. HU meetings etc., and interactions with other platforms.*

*Text: Use Times New Roman font size 11, 1.0 pt text space, and **maximum two A4 pages**, including the organogram.*

Development, Achievements and Plans

i) *Briefly describe the development of the platform 2021–now, and specifically highlight actions/decisions taken to address items listed in the Platform Specific Terms and Conditions for Funding document. Briefly, also report on achievements and any relevant KPIs for the platform (joint projects, scientific achievements, outreach efforts, training and education, platform retreats etc.)*

ii) *Briefly describe the development plans for the platform 2023–2024 and beyond.*

iii) *If you have specific questions or comments for the reviewers to consider during the Midterm Checkup, you may add these here*

*Text: Use Times New Roman font size 11, 1.0 pt text space, and **maximum two A4 pages**, including any figures.*

Request for additional funding 2023–2024 (optional)

The national budget to SciLifeLab will expand in 2023 (+10 MSEK vs 2022) and 2024 (+20 MSEK vs 2022), and some of this budget will be used to increase the base funding of individual infrastructure platforms and units. For your platform, suggest which technology areas or functionalities that are urgent to strengthen, and **motivate why this is critical for operations**. Specify in the budget table the receiver unit(s) and suggested level of funding for 2023 and 2024. Please, keep the request on a reasonable level as the actual funding available for direct support to infrastructure operations will be less than the 10 and 20 MSEK described above.*

**Suggestions can as well include increased budget to functionalities on other platforms or cross-platform capabilities*

*Text: Use Times New Roman font size 11, 1.0 pt text space, and **maximum one A4 page**, including budget table.*

Requests for expanded funding 2023–2024

Specify all costs in kSEK

Unit	SciLifeLab funding 2022 (kSEK)	Requested ScilifeLab funding 2023 (kSEK)	Requested SciLifeLab funding 2024 (kSEK)

Unit Midterm Checkup Reporting Template

Development, Achievements and Plans

- i) Briefly describe the development and major achievements (technology development, scientific achievements, new user groups, outreach efforts, training and education, contribution to cross-unit and cross-platform initiatives etc.) of the unit 2021–2022.
- ii) Briefly describe the development plans for the unit 2023–2024 and beyond
- iii) If you have specific questions or comments for the reviewers to consider during the Midterm Checkup, you may add these here.

*Text: Use Times New Roman font size 11, 1.0 pt text space, and **maximum two A4 pages**, including any figures.*

Program for Platform Meetings, October 5–6

Program Midterm Checkup 2022			
Wednesday, October 5		Thursday, October 6	
09:15–10:00	Drug Discovery and Development	09:15–10:15	Clinical Genomics
10:30–11:30	Genomics	10:45–11:45	Bioinformatics
12:30–13:30	Spatial and Single Cell Biology	12:45–13:30	Chemical Biology and Genome Engineering
14:00–14:45	Metabolomics	14:00–14:45	Cellular and Molecular Imaging
15:15–16:15	Clinical Proteomics and Immunology	15:15–16:00	Integrated Structural Biology

Infrastructure Organization, Funding, and Metrics for 2021

Organization

The SciLifeLab infrastructure is organized into ten platforms as shown in Figure 1.

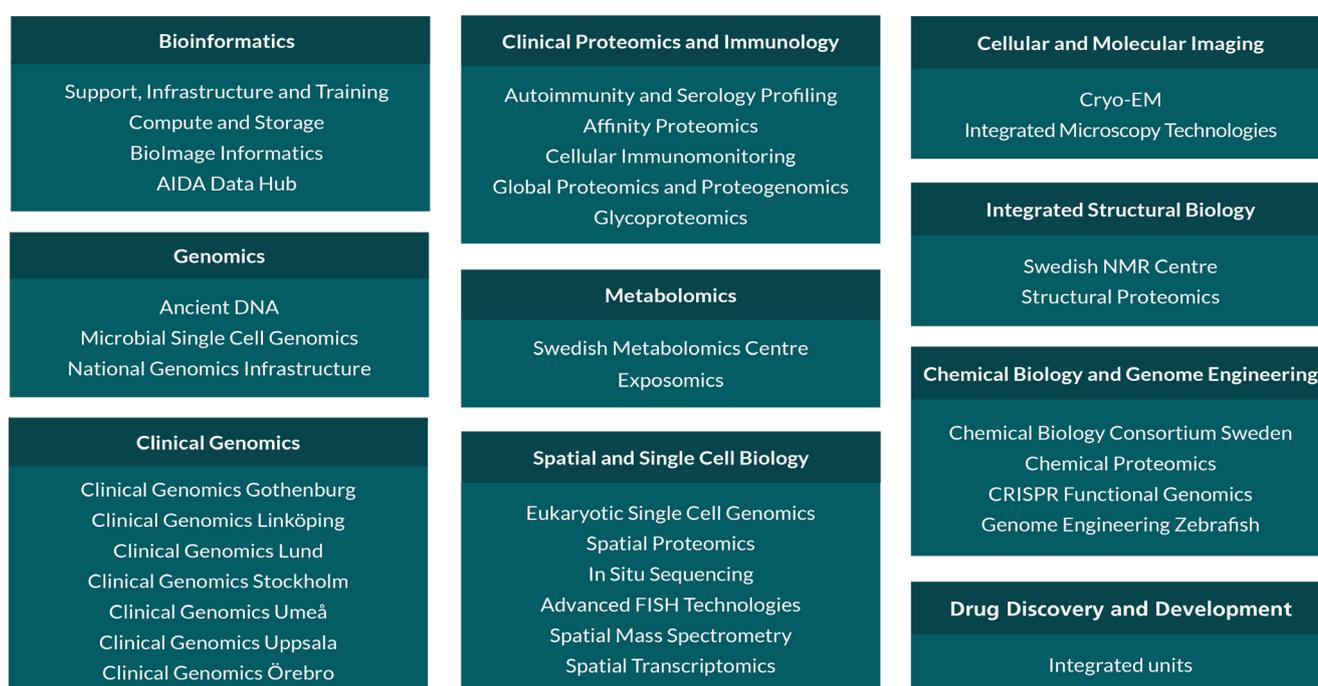


Figure 1: The organization of the SciLifeLab Infrastructure Platforms and Units.

Funding

In 2021, the total SciLifeLab funding to the infrastructure operations was 211 MSEK, and the support to annual depreciation costs for instrument investments amounted to 12 MSEK, see Figure 2. In addition to this, and income via user fees (amounting 320 MSEK in 2021), the infrastructure Units also received funding from their host universities, the Swedish research council (VR), KAW, healthcare and other sources. The total external funding in 2021, excluding user fees, was 295 MSEK. In Figure 3, the distribution of the total funding 2021 is presented across the individual infrastructure Units, displaying the large differences in size of funding and operations.

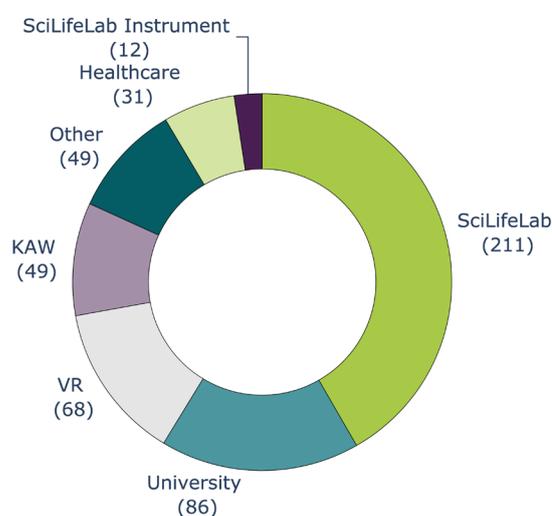


Figure 2: Total funding of the SciLifeLab Infrastructure 2021 (excluding user fees).

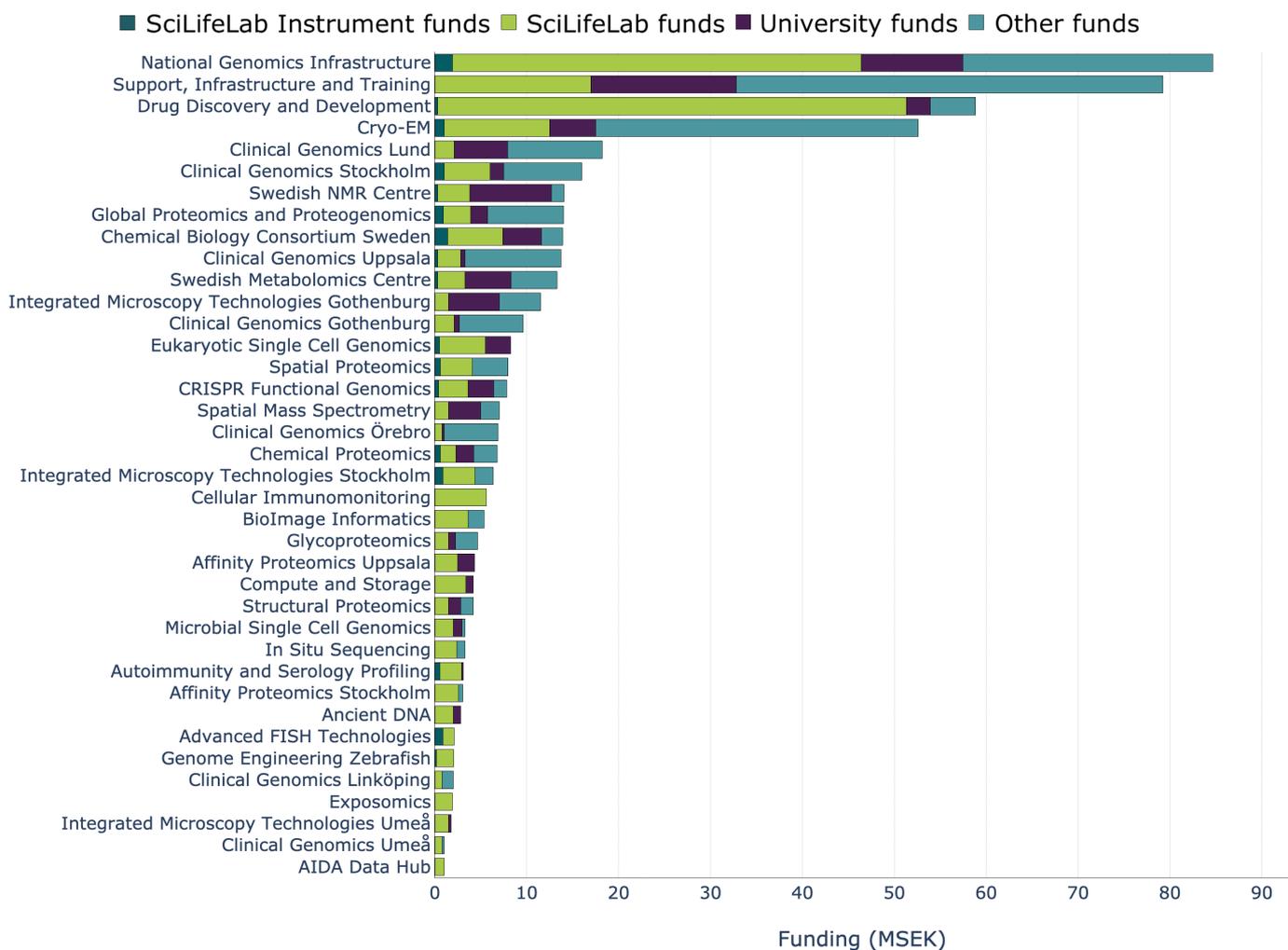


Figure 3: Total funding of the SciLifeLab Units 2021 (excluding user fees)

User fees

As mentioned above, the total income from user fees to the infrastructure amounted 320 MSEK for 2021. While Units are free to set-up their own individual models for charging users to fit the type of technology and service provided, user fees for academic researchers do typically cover costs for reagents and consumables plus part of costs for personnel, instruments and rents. Healthcare and industry users are usually charged full cost.

In Figure 4a, we have analyzed the total user fee income per FTE for each Unit for 2021. Not surprisingly, Units dealing with high reagent costs (e.g., Affinity Proteomics and NGI) and having a large share of healthcare users (Clinical Genomics Units) have the highest user fee income per FTE. We have also performed the analysis omitting the part of user fee income that covers reagents and consumables, see Figure 4b. The latter analysis should give reasonable measure on how successful individual Units are in charging users so that the fee also covers parts of the actual costs for operations.

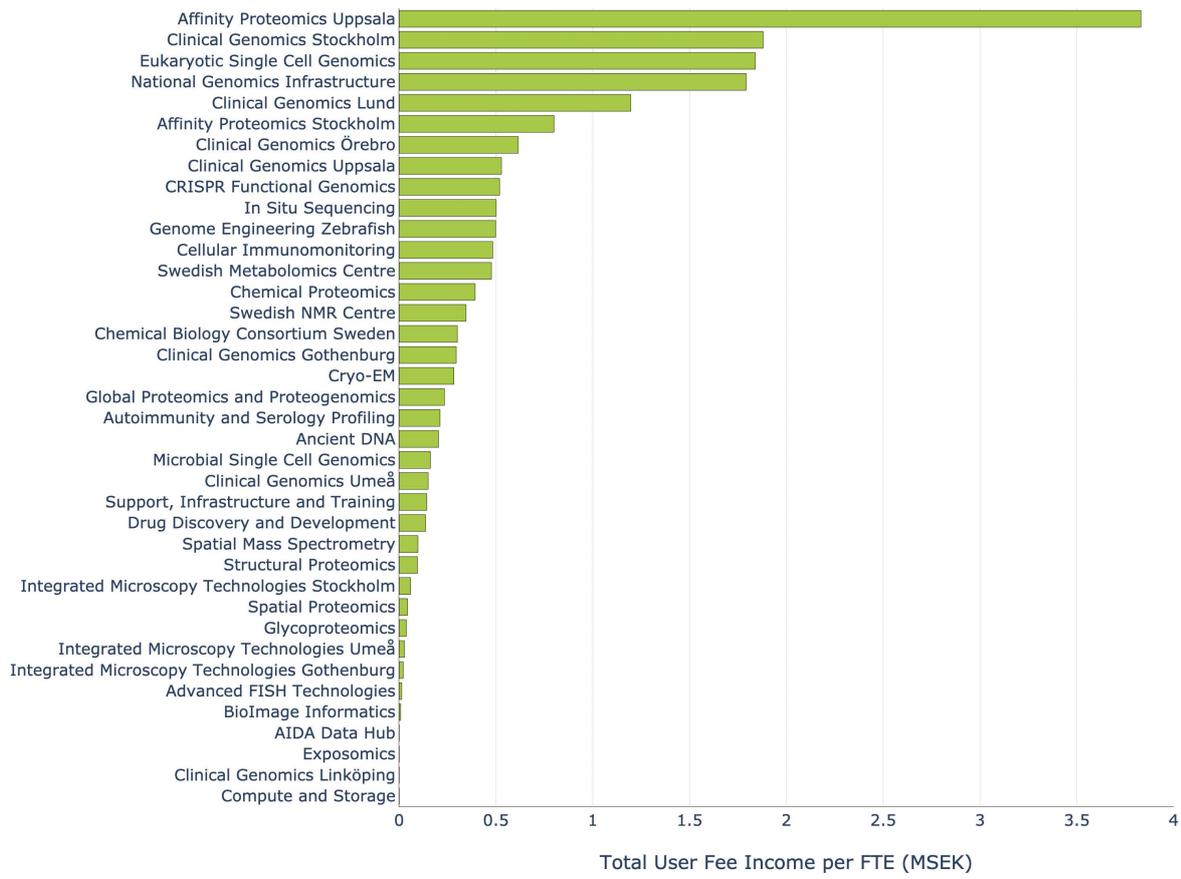


Figure 4a: Total user fee income per FTE for the infrastructure Units 2021 (MSEK)

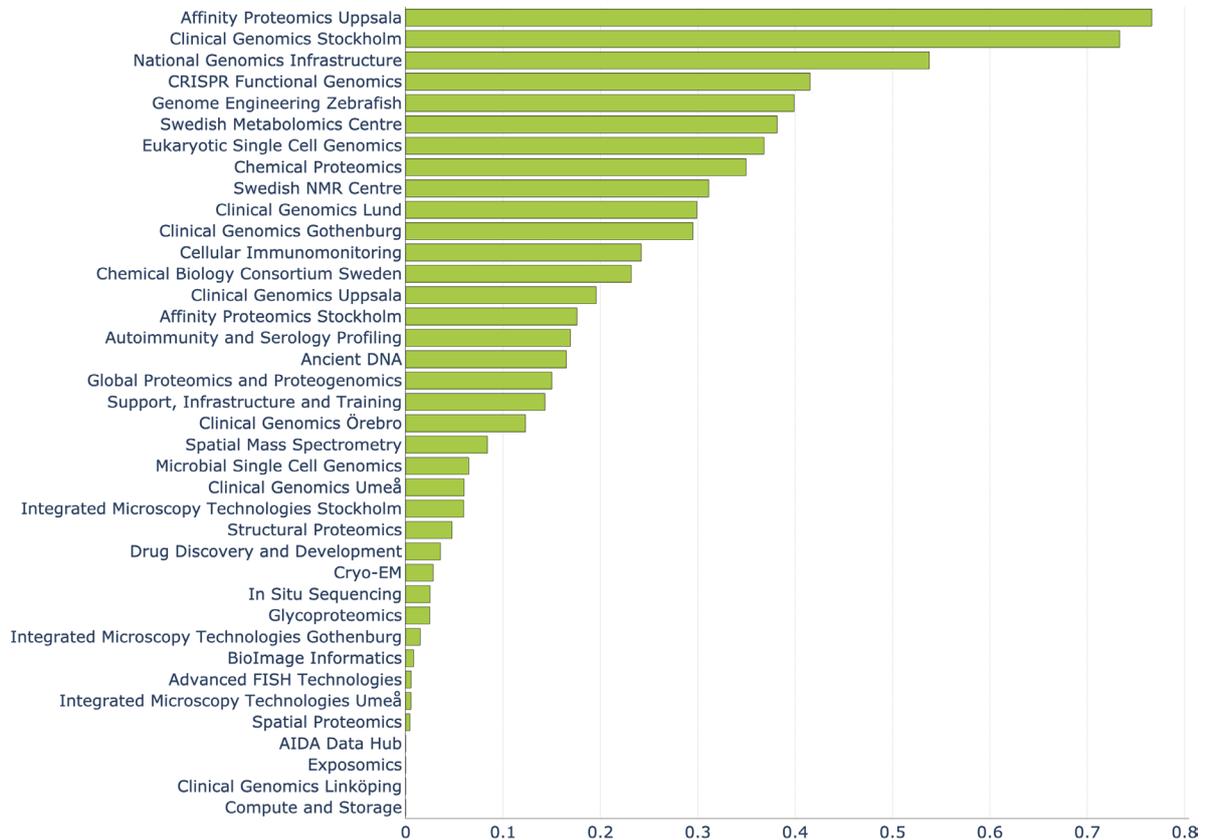


Figure 4b.: User fee income, excluding the part covering direct costs for reagents and consumables, per FTE for the infrastructure Units 2021 (MSEK)

Users

In 2021, the SciLifeLab infrastructure served in total 1,391 individual academic users, and the distribution of these based on the affiliation of the PI is shown in Figure 5.

The infrastructure also provides services to researchers in non-academic sectors (healthcare, industry, and governmental organizations) and allocate resources on internal technology development projects. Based on the total infrastructure FTE resources during 2021, 67% were spent on national academic user projects, 13% on internal technology development projects, 12% on healthcare projects, 5% on international academic user projects, 2% on industry projects, and 1% on projects with other governmental organizations, see Figure 6.

Distribution of users based on affiliation (including healthcare and industry sectors) across the infrastructure Units further is illustrated in Figure 7.

When analyzing the share of FTE resources spent on the above user categories and internal technology development for the individual infrastructure Units, large differences in profiles are observed, see Figure 8. For example, resources spent on user projects from the healthcare and industry sectors are quite unevenly distributed across the infrastructure Units, respectively.

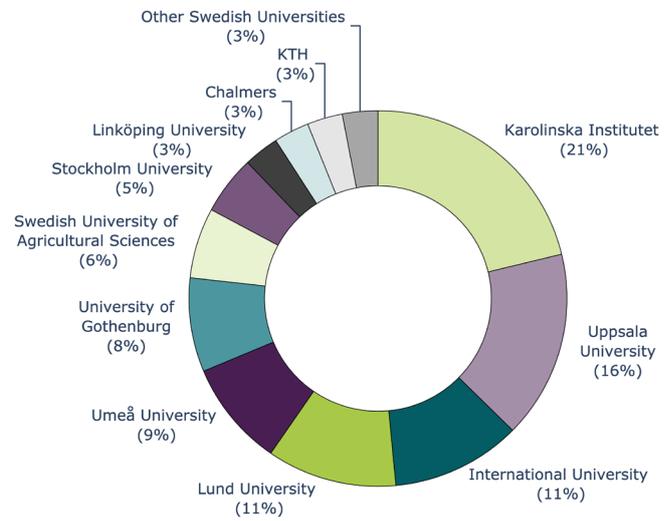


Figure 5: Distribution of academic users 2021 based on affiliation of the individual PIs.

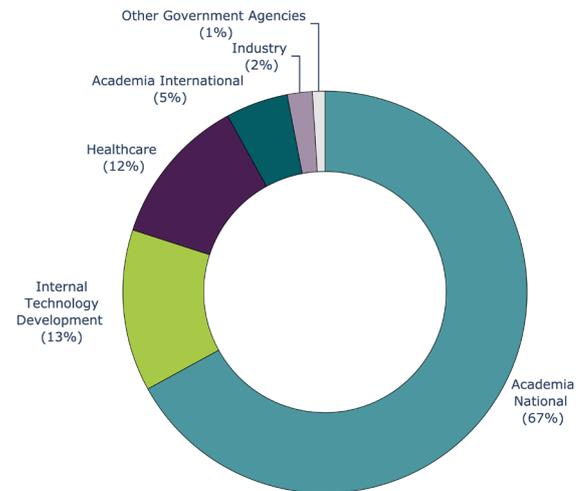


Figure 6: Distribution of total infrastructure FTE resources across user categories and internal technology development projects

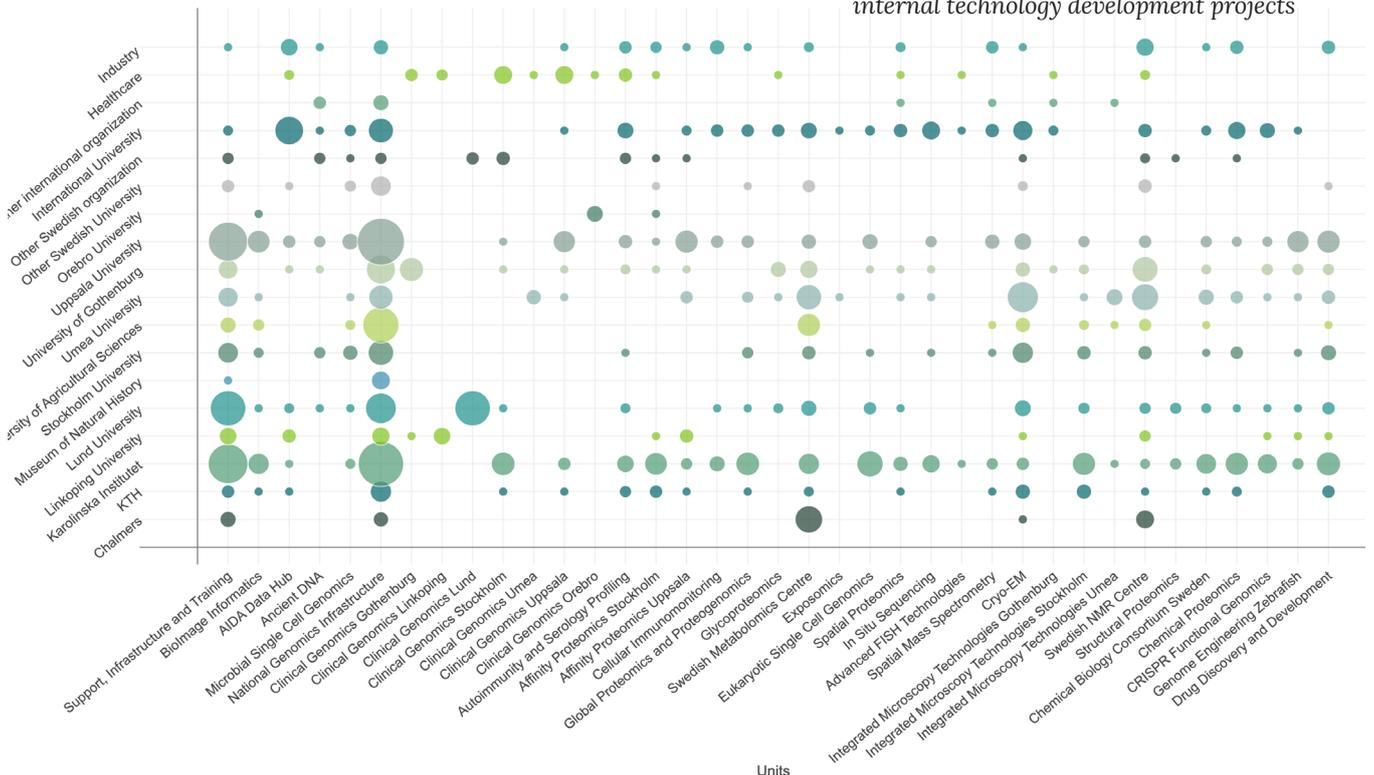


Figure 7: Distribution of users 2021 from universities, healthcare, industry, and governmental organizations across the SciLifeLab infrastructure Units. The size of the circles corresponds to the number of users.

■ Academia National ■ Academia Internat. ■ Internal Tech. Dev. ■ Industry ■ Healthcare ■ Other Gov. Agencies

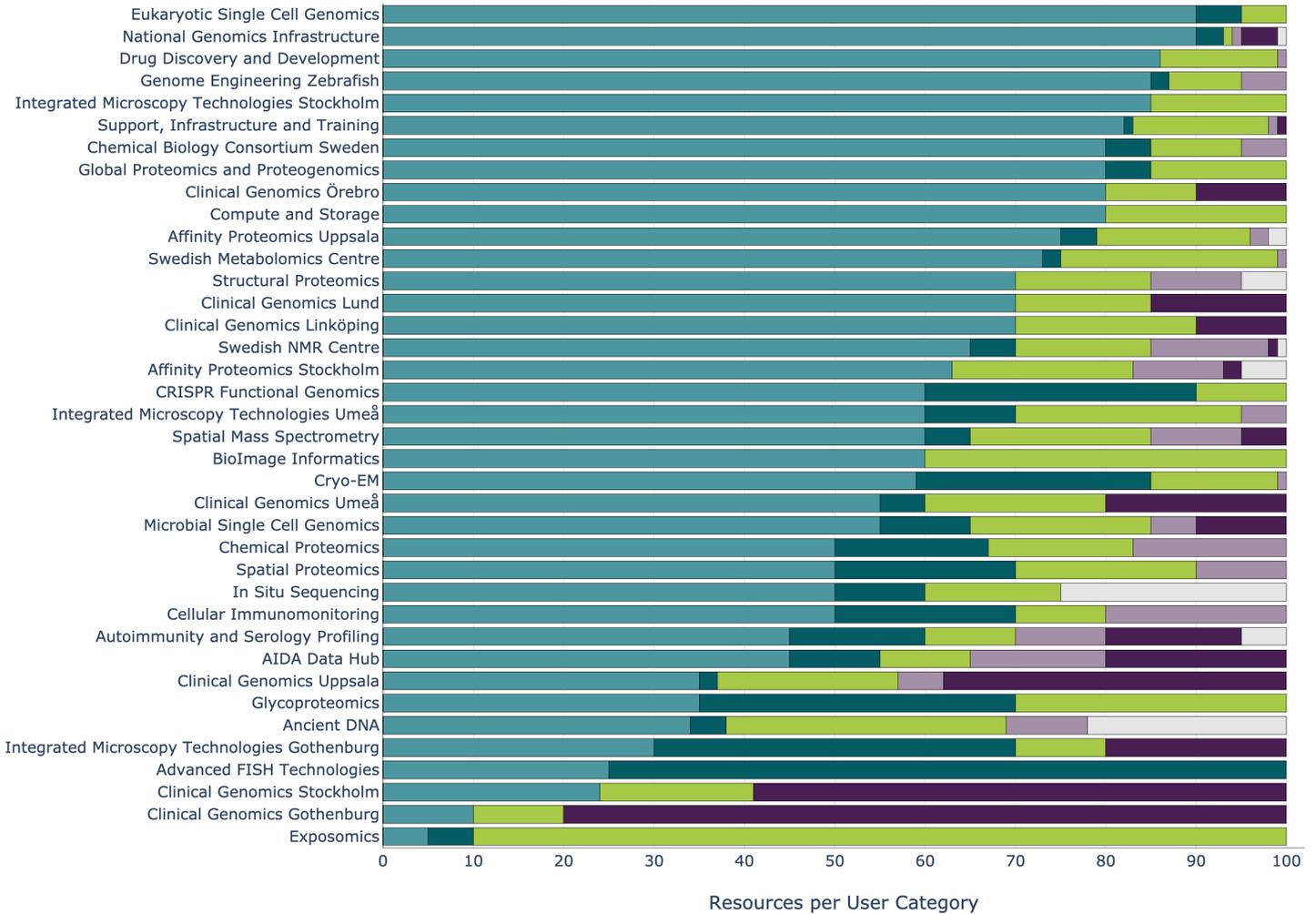


Figure 8: Percentage distribution of total annual FTE resources for each infrastructure Unit on user categories and internal technology development efforts for 2021.

Publications

The quantity and impact of scientific publications produced by the users of the SciLifeLab infrastructure are important metrics in monitoring the performance of Platforms and Units. The SciLifeLab Publication Database allows for the infrastructure Units to conveniently upload publications containing data generated through the use of the Units. Publications are in the database labelled either as service (infrastructure Unit mentioned in acknowledgement), collaborative (infrastructure staff in author’s list) or technology development (infrastructure staff as main/co-author). As seen in Figure 9, between 2016 and 2020, around 600 infrastructure publications were reported annually, while for 2021, there is a significant increase to 761 publications. This increase can most probably be explained by the expansion of the SciLifeLab infrastructure from 2021 with 8 new Units, and that many papers containing Covid-19 related research were rapidly published during the year.

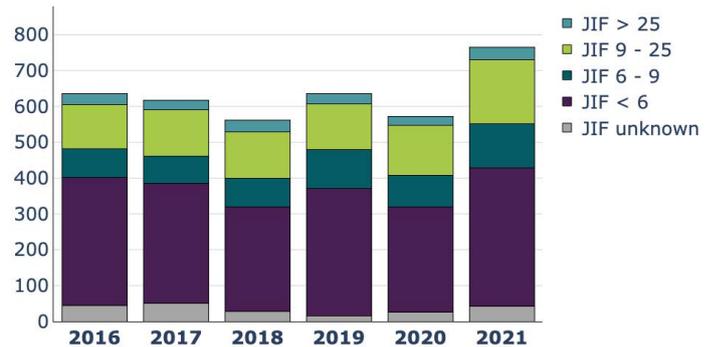


Figure 9: Infrastructure publications 2016–2021 with Journal Impact Factor (JIF) distribution

We also monitor the cross-Unit use of the infrastructure based on cross-Unit papers (i.e., papers where more than one infrastructure Unit has contributed with data and analysis to the user project), and the outcome for 2021 is visualized in *Figure 10*. While we are pleased to see the wide spectrum

of cross-Unit and cross-technology use of the infrastructure demonstrated in *Figure 10*, we would like to see an increase in the overall share of annual cross-Unit publications from the current level of ca 10%.

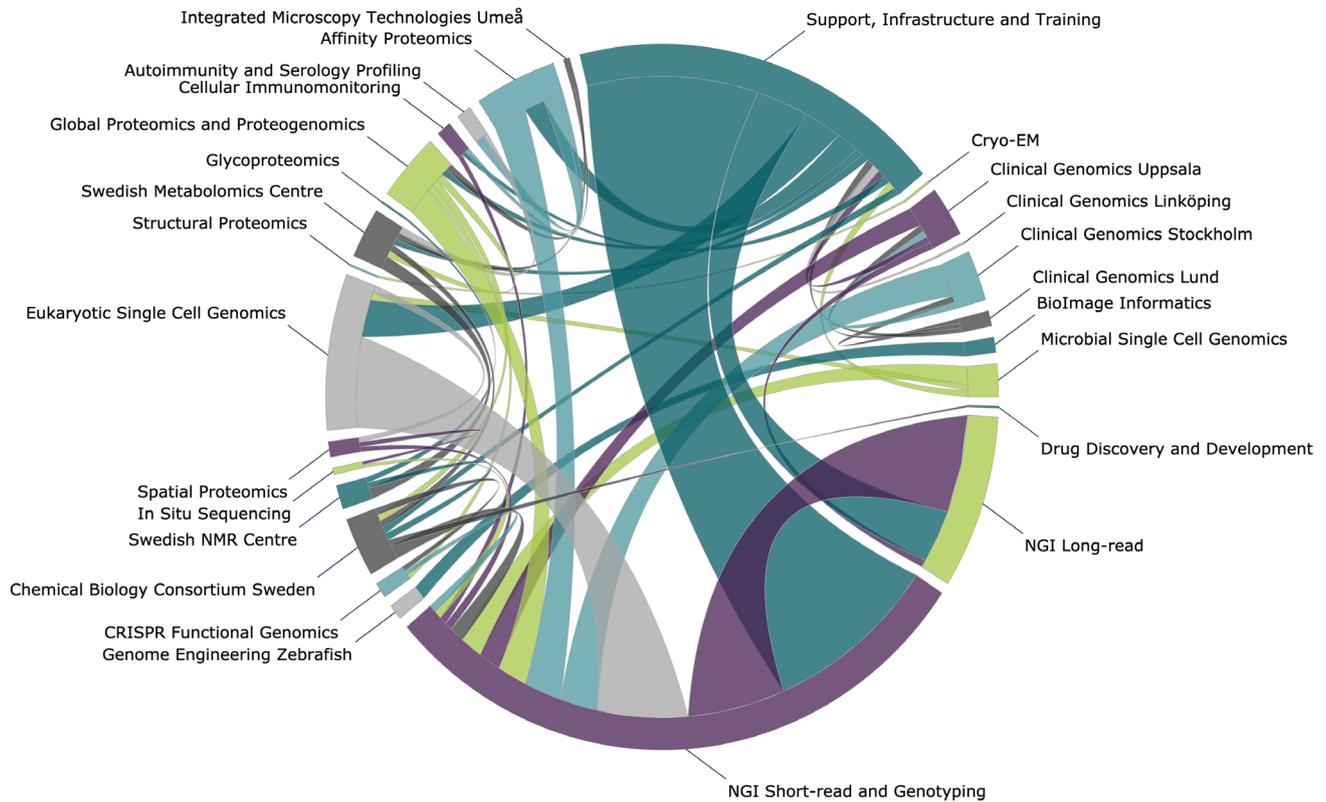


Figure 10: Circos plot illustrating cross-Unit use based on infrastructure cross-Unit publications 2021. Units are clustered Platform-wise, and the length of the circle segments corresponds to the total number of cross-Unit publications for each respective Unit. The ribbons represent publications where both the connected Units contributed with service, data or analysis.

► Drug Discovery and Development Platform

Platform Director: Per Arvidsson, KI

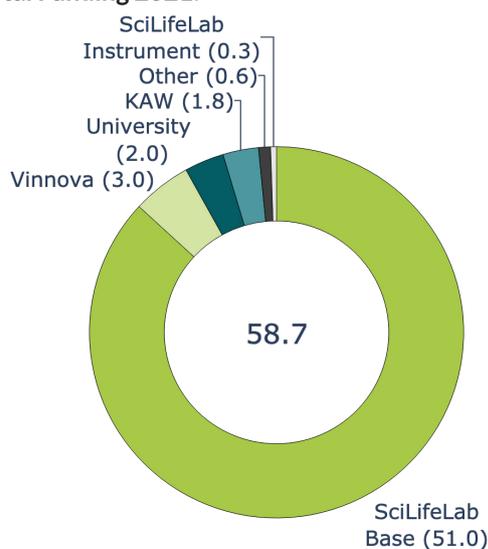
Co-Platform Director: Kristian Sandberg, UU

Platform Coordination Officer: Rebecka Klintonberg, UU

Platform and Units SciLifeLab Funding 2021:

Unit	(MSEK)
Drug Discovery and Development	51.0
Sum:	51.0

Total Funding 2021:



Platform Specific Terms and Conditions for Funding - Drug Discovery and Development

This document concerns the terms and conditions for SciLifeLab funding of the Drug Discovery and Development Platform and Units from 2021 and onwards and outlines the strategic direction MG wants the platform to take. The mid-term checkup in the middle of the 4-year funding period will focus on how well the Platform and Units have taken into account the items in this document.

1. Continue DDDs core objective **“Turn academic ideas into innovations”**

- Develop DDD into a national drug discovery innovation hub

2. Assure that DDD offers state of the art drug discovery technologies and training to Swedish researchers

- Optimize throughput of DDD related ideas and output of deliverables (prototype drugs based on small molecules, antibodies, oligonucleotides, and other modalities)
- Implement Oligonova HUB at Göteborg University as an integrated part of the DDD platform in a way that allows development of therapeutic oligonucleotide programs

3. In accordance with SciLifeLab Roadmap 2021-2030, build translational capabilities for drug discovery projects

- Work towards a closer collaboration with the Swedish innovation system in projects that aim to develop new therapeutics

4. Make use of DDDs legal agreement to promote public-public and public-private partnerships as a mean to increase overall budget and critical mass

- Consider interactions with external sites and strategic partnerships, such as with SGC-Stockholm node, EU-ESFRI programs, etc.

5. Ensure that SciLifeLab funds are used in the platform in a manner that will align with the priorities and goals of the entire SciLifeLab organization, specifically for DDD:

- Be responsible for SciLifeLab’s DDD capability
- Help build SciLifeLab’s translational capabilities (as defined in point 3 above)

6. Provide resources to engage in the SciLifeLab capabilities, integrating data and know-how from several different platforms

7. In collaboration with the CBGE platform, the Bioinformatics platform and Data Centre, continue to develop chemoinformatics and data-driven capabilities, such as open science and FAIR data bases for drug discovery and chemical biology related data

8. Consider the financial basis and long-term sustainability for drug discovery by alternative models of operations. In collaboration with MG and OO investigate the possibility to generate income by revenue share to expand the platform. Driven by SciLifeLab, this could eventually make a systems transformation concerning sustainable of infrastructures in Sweden.

Drug Discovery and Development

Drug Discovery and Development Platform (Web links for Platform: [Webpage](#), [Publications](#))

Basic Information

Platform directors: Per Arvidsson, Kristian Sandberg
SciLifeLab Platform since: 2014
Host university: KI, KTH, LU, SU, UU, GU
FTEs: 36.9
FTEs financed by SciLifeLab: 34.8

Funding in 2021 (kSEK)

SciLifeLab: 51000
SciLifeLab Instrument: 300
UU: 2008
KAW: 1900
Vinnova: 2000
Total: 57208

Resource Allocation 2021

Academia (national): 86%
Academia (international): -
Internal tech. dev.: 13%
Industry: 1%
Healthcare: -
Other gov. agencies: -

User Fees 2021

Total (kSEK): 5054
Reagents: 74%
Instrument: 26%
Salaries: -
Rent: -
Other: -

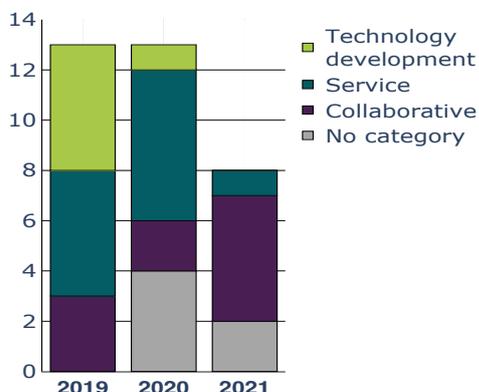
User Fees by Sector 2021

Academia (national): 97%
Academia (international): -
Industry: 3%
Healthcare: -
Other gov. agencies: -

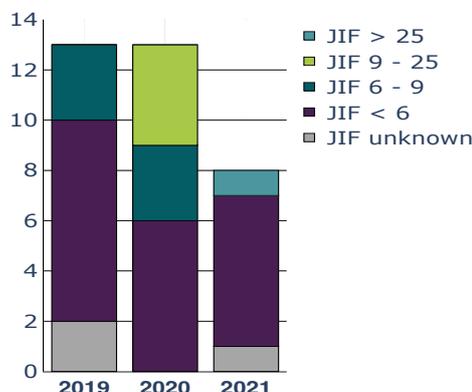
Services

Integrated drug discovery efforts to the Swedish academic research community. Industry standard infrastructure, expertise, and strategic support to help progress projects towards a pre-clinical proof-of-concept. The drug leads can be either a small molecule drug or a human antibody therapeutic.

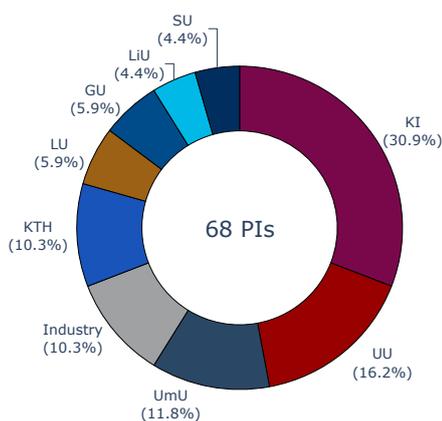
Publication by Category



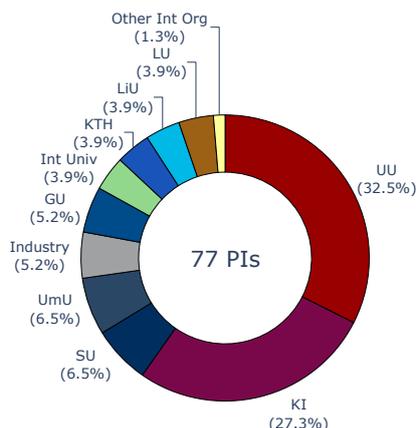
Publication by Journal Impact Factor



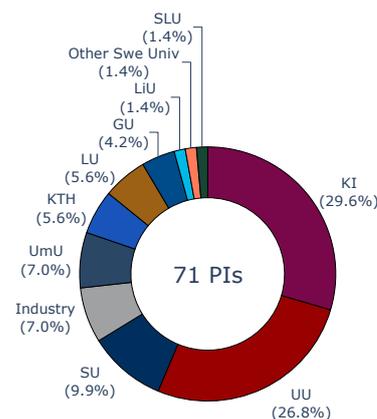
Users 2019



Users 2020



Users 2021



Organization and Management

Organization

SciLifeLab DDD is a distributed national research infrastructure within SciLifeLab hosted by Karolinska Institutet (KI), Stockholm University (SU), Uppsala

University (UU), the KTH Royal Technology Institute in Stockholm (KTH), Lund University (LU) and Gothenburg University (GU).

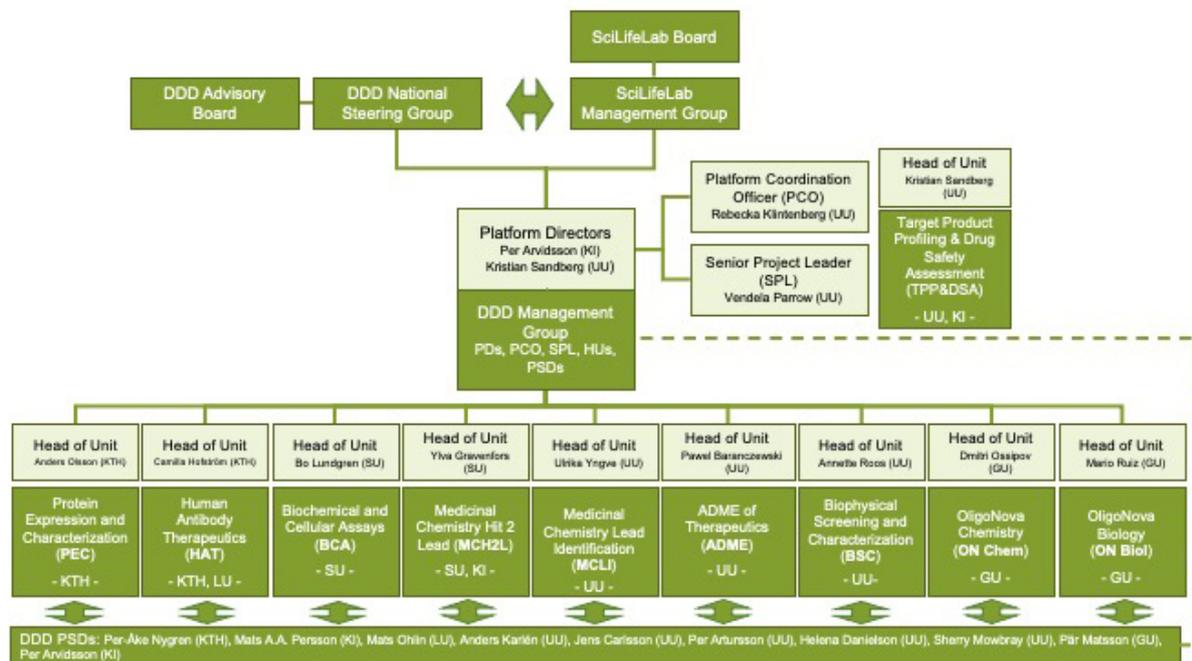


Figure 1

Organization of SciLifeLab Drug Discovery and Development platform. Acronyms are explained in the text below.

SciLifeLab DDD is a distributed national research UU hosts four units. TPP&DSA (co-hosted with KI) at the Dept. of Medicinal Chemistry (ILK) has the responsibility for platform and project coordination and assessment of liabilities driven by target, small molecules (SM) or Biologics. Support to principal investigators (PI's) and Innovation offices. TPP&DSA_UU harbors the SciLifeLab DDD office function which allows UU, via a delegation from other host universities, to sign agreements for all of DDD. The unit Medicinal Chemistry Lead Identification (MCLI) is also located to ILK. MCLI compare, design and synthesize lead molecules with a promising profile for proof-of-concept in vivo. MCLI also has competence and capacity for work with DNA encoded chemical libraries and access to radiochemistry and peptide chemistry. The ADME of Therapeutics (ADMEoT) unit at the Dept. of Pharmacy performs studies to determine absorption, distribution, metabolism, and excretion (ADME) of putative drugs and perform pharmaceutical profiling (irrespective of therapeutic modality) using PKPD and PBPK modeling based on bioanalytical data. The unit for Biochemical Screening and Characterization (BSC), co-hosted by the Dept. of Chemistry and Dept. Cell and Molecular Biology (ICM) at UU, identify and characterize ligands, structural

biology & fragment-based lead generation using methods for biophysical studies and structural analysis. SU hosts two units. The unit for Medicinal Chemistry Hit to Lead (MCH2L) at the Dept. Organic Chemistry compare, design and synthesize putative lead molecules with a promising profile for proof-of-concept in vivo. The MCH2L unit is co-localized with the Chemical Biology Consortium Sweden and collaborates to manage the SciLifeLab compound collection and to distribute compounds in assay ready plates from the SciLifeLab compound collection. Operations at MCH2L are tightly coordinated with MCLI at UU. The unit Biochemical and Cellular Assays (BCA) at the Dept. Biochemistry at SU develops and runs assays required to drive chemistry and to confirm functional binding of antibodies. KTH hosts two units. The unit for Protein Expression and Characterization (PEC) at the Dept. Protein Sciences produce, purify and characterize proteins from E. coli, insect and HEK cells. The unit for Human Antibody Therapeutics (HAT) at the Dept. Protein Sciences design human phage libraries, make selections and characterize therapeutic antibody candidates. Selections are also performed on DNA Encoded Chemical Libraries. KI employs the Platform Director for SciLifeLab DDD and co-host MCH2L and TPP&DSA. LU co-host the HAT unit at the Dept. of Immunotechnology,

unit for rapid engineered antibody development (U-READ) with design of human phage libraries, selections and characterization of therapeutic antibody candidates. Operations at U-READ (LU) are tightly coordinated with HAT at KTH. In 2022, two new units have been established at GU. The OligoNova hub for cell biology (ON_Cell) performs screens for antisense oligonucleotides and siRNA to find candidates for therapeutic development. The OligoNova hub for chemistry (ON_Chem) synthesizes, compares and designs antisense and siRNA oligonucleotides with a promising profile for proof-of-concept in vivo. ON_Chem is also responsible for managing the storage and distribution of oligonucleotides collection in assay ready plates.

The DDD Advisory Board meets annually and consists of Kjetil Taskén (University of Oslo, Norway - chair); Fiona Marshall (Global Head of Research, Merck, USA); Justin

Bryans (CSO Charles River Laboratories, UK); Lorenz M. Mayr (Vector BioPharma AG, Switzerland) and; Lovisa Afzelius (Flagship Pioneering, USA). The DDD National Steering Group consists of four representatives from academic research and three representatives from industry/innovation systems (Håkan Billig, GU – chair, Maria Jenmalm Jensen, Linköping University, Lars Ny, GU, Tomas Lundqvist, Malmö University; Lars Lannfelt, UU and BioArctic; Anna Sandström, AZ, and Outi Vaarala, Orion Pharma, Finland. The Steering Group meets six times per year and decides on project priorities and strategic directions for the platform. The platform directors (PDs) represent the entire platform and lead the work at DDD. The PDs meet regularly with the SciLifeLab Director and SciLifeLab Infrastructure Director. The PDs and the chair of the Steering Group meet the SciLifeLab Board annually.

Management

The platform management group meets weekly (hybrid meetings) and consists of the PDs, the Platform Coordination Officer (PCO), the Senior Project Leader (SPL), the Head of Units (HoU) and ad hoc the Platform Scientific Directors (PSDs). DDD Project Leaders manage projects run at the platform and are coached by the SPL and individually sponsored by the PDs. Projects are prioritized bi-annually by the Steering Group. Projects run at DDD are extremely interactive and each project involves the majority of units at DDD but also units at other platforms and national infrastructures e.g. CBGE, NGI, NBIs, MAX4 etc. Interactions with the various innovation systems in Sweden are maintained during project scouting, in the project work and in meetings with a national reference group from the innovation systems, approximately four times per year.

Annual operational plans are prepared in the fourth quarter and presented, together with the proposed distribution of available funds, to the steering group for approval.

Annually, DDD arranges two symposia that are sponsored by SciLifeLab. In addition, approximately eight public virtual presentations on the theme “Drug Discovery Seminars” are arranged and announced via SciLifeLab events. News are distributed via an account for DDD on LinkedIn and the website on SciLifeLab. For internal communication has DDD a Slack channel and arranges “State of the Platform” virtual meetings every month. In addition, DDD arranges one off-site meeting for the platform every year and bi-annually kick-off meetings to which the whole platform are invited.

Development, Achievements and Plans

Development of DDD 2021 - now

Since January 2021, the following major achievements have been made at DDD:

- 4 new Biotechs have spun out from programs supported by DDD:
 - Sara Mangsbo, UU – Strike Pharma AB
 - Marene Landström, UmU – MetaCurum Biotech AB
 - Thomas Helleday, KI – One-carbon Therapeutics AB
 - Marika Nestor, UU – Akiram Therapeutics AB
- 2 alumni projects have been listed on Nasdaq First Growth Market
 - Lipum AB (UmU)
- Elicera Therapeutics AB (UU)
- DDD are actively engaged in the VR-funded antibiotics drug research project ENABLE2 and in the IMI funded project EUBOpen
- DDD are actively engaged in three projects for pandemic preparedness (ADAC, spike binders, Mpro inhibitors)
- A new modality, therapeutic oligonucleotides, is offered from DDD thanks to the built up of two new units at GU: ON_Biol and ON_Chem. Two projects for the development of oligonucleotide therapeutics will start December 1st, 2022.
- One symposium with >700 participants (CryEM in Drug Discovery) and 16 public seminars

- Inauguration of the OligoNova Hub at AZ BioVenture Hub in Mölndal, April 25 th -26th
- The unit for In Vitro and Systems Pharmacology (IVSP) at UU is closed October 1st 2022. The former Head of Unit, Vendela Parrow is recruited to DDD in a new position as Senior Project Leader and will take a special responsibility to develop project leadership skills and interactions with the innovation systems
- LU and GU have joined the DDD office agreement that authorize UU to sign contracts with external parties on behalf of DDD
- Selections in up to 73 DNA Encoded Chemical Libraries (DECL) containing >108 unique binding moieties combined with virtual screening and machine learning is now offered to swedish academic scientists thanks to collaborations between DDD and other SciLifeLab platforms (NGI), academic scientists (Ulf Landegren, UU; Ola Spjuth, UU; Jens Carlsson, UU; Oscar Verho, UU) and procurement/collaborations with biotech companies (WuXi Apptec; XChem; Hitgen)
- Establishment of technologies for the development of protein degraders (protacs) in collaboration with academic scientists Mikael Altun, KI and Helena Danielsson, UU and industrial partners Recipharm OnTarget Chemistry. Regular discussion on this topic is also done with AstraZeneca, RISE, Beactica Therapeutics, and Healthcap.
- The Vinnova funded project “InnoPharma” was launched in 2021 with the aim to develop DDD as the national hub for seamless collaboration within the swedish innovation systems for drug discovery. As a pilot, recommendations and best practice developed in this project will be implemented at DDD and within innovation offices/incubators during 2023-2024
- In collaboration with the DDD platform advisory board, a long term strategic plan for DDD was launched (see further below)
- Key performance indicators will be decided by the Steering Group in September 2022. These KPI's are divided into “external” KPI:s that focus on sustainability, portfolio, equal tremes, societal impact, external communication, partnerships and adaptation to new technologies. Another set of “internal” KPI's focus on efficiency, quality, continous improvement, resources, competence and internal communication. Data from selected KPI's can be used for communication purposes, “story telling” and can be tailormade for the specific occasion. A final draft of these KPI's can be found in the Anubis review portal. Actions derived from output data from KPI's and their links to the strategic objectives will affect the annualoperational plans.

The achievements listed above meets the DDD specific terms and conditions for funding. For example, the management at DDD is monitoring projects and has established criteria for progression applying checkpoint criteria. In the KPI's are FAIR principles highlighted as an important guideline for data sharing and quality assurance.

Alternative models for the financial basis and long-term sustainability for drug discovery is under continous discussions with Vinnova and potential private investors, both to finance DDD operations but also to support principal investigators working together with DDD. Models that entail revenue shares to expand DDD operations requires substantial changes in legislation at a national and European level as long as DDD is organized within univiersities.

Development plans for DDD 2023-2024 and beyond

A long-term strategic plan for DDD was developed in discussions with the DDD platform advisory board and was launched in January 2022 (see doc in Anubis review potal). The advisory board points out the following:

- DDD main competitive advantage is the close alliance with Swedish academic scientists
- The teacher's exemption law is a very important competitive advantage for innovations emerging from Swedish academic research. Universities and innovation agencies should jointly use the teacher's exemption law and find incentives to apply these to the DDD platform operations
- Future therapies will increasingly be based on novel technologies, not new targets. DDD should not include disease focus within the platform, rather stay focused on technologies
- Stay focused on a few modalities – do not spread resources too thin
- The ability to form strategic partnerships with industry is essential

DDD will continue to prioritize larger academic programs in four therapeutic modalities: small molecules, antibodies, oligonucleotides and “new modalities”. In support of this, more emphasis will be placed on how to implement state of the art technologies for these modalities. Focus areas for technology implementation are 1) machine learning; 2) oligonucleotides; 3) display and selection technologies and; 4) development of proximity-inducing agents (PIA). DDD should, together with the innovation systems, develop common practice how to advance and capitalize academic drug discovery projects into clinical studies and practice. In line with these ambitions, professor Jens Carlsson, UU,

was appointed PSD with special responsibility to develop and integrate computational methods at DDD for efficient hit/lead exploration. Furthermore, applications have been

Specific comments

It should be noted that DDD has very limited funding to allocate resources to technology implementation. If efficiency of project work increases (meaning that output from DDD can be maintained with less resources) could an increased part of the funding be allocated to technology implementation. SciLifeLab policies states that no more than 20% of available resources can be spent on development/implementation of new technologies. This limit may be increased to e.g. 30%. Another interesting opportunity is to launch an entrepreneurial postDoc program as suggested in the InnoPharma project. Such a program could also increase the DDD network at Swedish universities and identify new talents. DDD can contribute applications in our projects as a testbed, provide knowhow and coaching as well as, together with the innovation systems, provide education in drug discovery. Earmarked support to DDD from research

made to e.g. vetenskapsrådet (VR) to establish DDD as the academic national hub for novel drug discovery technologies for oligonucleotides and PIA.

funding organisations like vetenskapsrådet (VR), Stiftelsen för strategisk forskning (SFS) or cancerfonden would be beneficial.

The innovation systems (innovation offices, incubators) are increasingly seeking support from DDD for project evaluation and experimental support. Unfortunately, available resources at DDD cannot fully meet up to these requests. Additional funding from Vinnova would be warranted and might also be helpful for company formation of academic projects – in parallel to work done at DDD. Unfortunately, Vinnova lacks the required commission from the government (Ministry of Enterprise and Innovation) to give earmarked and joint support to PI's having projects at DDD. An alternative solution could be increased funding to DDD to provide this type of services to the innovation system as a new service.

Request for additional funding 2023–2024

Beside the initiative on oligonucleotides, DDD has begun investing in two focus areas for technology implementation where we see an immediate need and requests from users by using 3.8 FTE (18.6%) of available resources at DDD. This should merit an increased investment also from the SciLifeLab perspective:

Artificial Intelligence (AI) in drug discovery is a focus area for DDD technology implementation and requires integration of activities at DDD, CBCS, NBIS and SciLifeLab Data Center. DDD has realized that we should rely on commercial solutions for ADME and SAR predictions, rather than build own models based on our limited in-house data. Most importantly, we want to prioritize to implement AI in the design of new molecules since the number of chemists at DDD is limited and cost for in-house synthesis is high. The emergence of huge make-on-demand chemical libraries and DNA-encoded chemical libraries (DECL) with several billions of compounds per libraries also limits the possibility for conventional in silico screening strategies. A number of AI-based methods like deep reinforcement learning and neural networks have shown promise in making in silico screening of these libraries more efficient and a supporting infrastructure at SciLifeLab for this type of hybrid screening technologies combining wet lab data with in silico predictions is required. Our highest priority is therefore to implement AI in the workflows for ligand- and structure-based virtual screening in emerging technologies for drug discovery ongoing at DDD and CBCS (e.g. DECL, oligonucleotide screening, phage display libraries expressing protein/peptide that binds antigens and cell painting for morphological profiling and screening). The

initial focus for implementing AI-supported workflows is on small-molecule discovery and design, i.e. mining output from DECL- and virtual screens. Similar AI-technologies should also work for selections in phage-display libraries and oligonucleotide screens. In parallel we will start to use commercial softwares with machine-learning components, e.g. SciFinder synthetic route planning, ADMET Predictor, to name a few. Given the increased emphasis on structure-based drug discovery in the DDD strategy, we should carefully monitor the impact AlphaFold2 will have in this area. We have identified two groups that have the competence and interest needed for establishing an AI workflow at DDD. We are collaborating and have been co-applicant for SciLifeLab funded TDP grants with Ola Spjuth (UU) and Bengt Persson (NBIS)/Jens Carlsson (UU), respectively. Future opportunities in this rapidly developing area will likely be identified within the DDLS ecosystem. However, full exploitation of these opportunities requires a parallel build-up of competence and capacity at SciLifeLab.

Many new therapies are based on PIAs and operates by new therapeutic principles, such as targeted protein degradation (TPD). PIA is therefore identified as a focus area for DDD technology implementation. PIA projects are receiving increased attention from researchers in both biomedicine, chemistry, and biology. We also know from experience that any TPD or PIA project will demand coordination of numerous expert functions within SciLifeLab, and other the national infrastructures, beyond what is possible at the SciLifeLab units today. We therefore submitted a VR infra application for creating a new SciLifeLab capability for proximity inducing

agents and targeted protein degradation hosted by the DDD platform, in order to facilitate user support from multiple units (1 FTE + co-funding for up to six projects/technology implementations). Irrespectively of the funding outcome from VR, this initiative motivates additional funding along the recommendations from the 2021 IAB (international advisory board) report, i.e. to “provide a pan-platform user consultation mechanism, so projects that need support by multiple technologies, in different facilities and platforms can be well planned and effectively supported”.

As for information:

DDD has earmarked funding from the Government. Additional

support to other SciLifeLab platforms as suggested above would facilitate x-platform collaborations. Unfortunately, a substantial part of the DDD budget for 2022 comes from the ENABLE2 project (4.5 MSEK) and EUBOpen (1.2 MSEK). Continued funding of these projects are unsure. Reduced costs (2.4 MSEK) because of the phase out of the IVSP facility at UU will, in part, compensate for the possible loss of the ENABLE2 and EUBOpen projects. Reduction of operations is probably required if the ENABLE2 and EUBOpen projects are discontinued. This will reduce the capacity and competence at DDD and will affect also other projects run at DDD.

Drug Discovery and Development Platform Budget 2022

The DDD budget file for 2022 can be downloaded in the Anubis reviewing portal (<https://anubis.scilifelab.se/call/INFRA22>)

► Genomics Platform

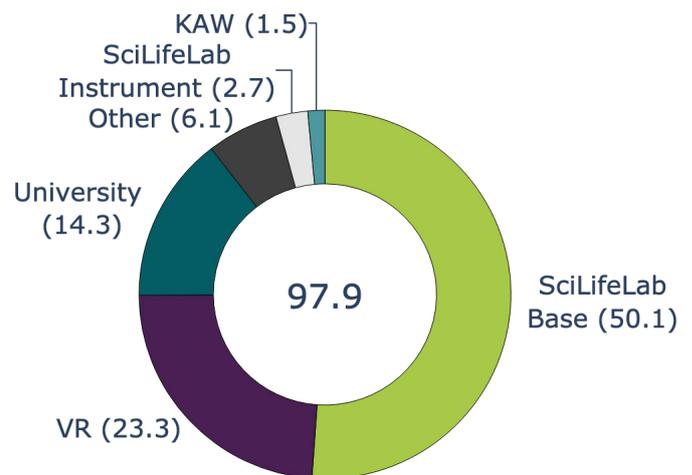
Platform Director: Tuuli Lappalainen, KTH

Co-Platform Director: Lars Feuk, UU

Platform Coordination Officer: Magnus Lundgren, UU

Platform and Units SciLifeLab Funding 2021:

Unit	(MSEK)
Ancient DNA	2.0
Microbial Single Cell Genomics	2.0
National Genomics Infrastructure	44.5
PD, PCO, Platform Strategic Budget	1.6
Sum:	50.1



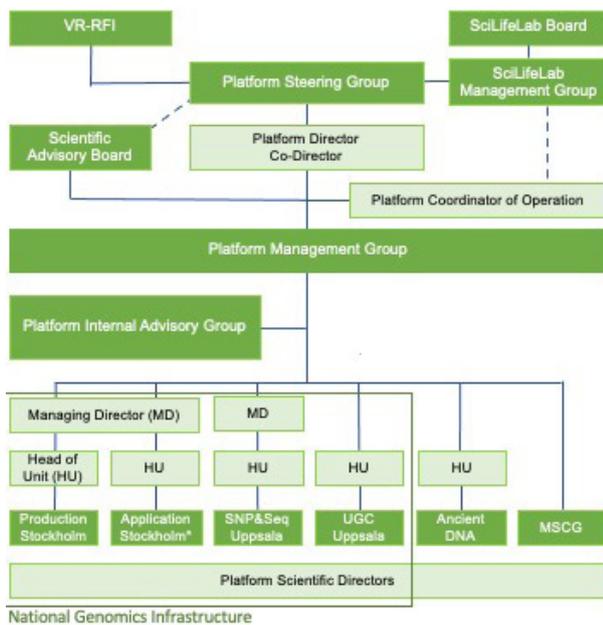
Platform Specific Terms and Conditions for Funding - Genomics

This document concerns the terms and conditions for SciLifeLab funding of the Genomics Platform and Units from 2021 and onwards and outlines the strategic direction MG wants the platform to take. The mid-term checkup in the middle of the 4-year funding period will focus on how well the Platform and Units have taken into account the items in this document.

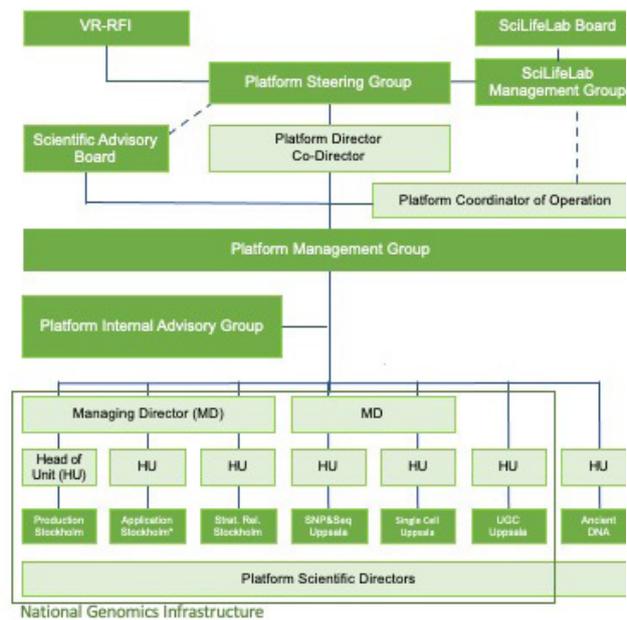
- Use SciLifeLab funding to the Genomics Platform for providing nationally important technologies and services within genomics, including services from the National Genomics Infrastructure (NGI), Ancient DNA and Microbial Single Cell Genomics units
- Focus on providing services that are in high demand by the Swedish research community and not commonly available from other providers, such as comprehensive support for study design and quality control, customization of services, long reads, epigenetics, and integrated multi-omics analysis.
- Ensure that SciLifeLab funds are used in the platform in a manner that aligns with the priorities and goals of the entire SciLifeLab organization
- Together with the SciLifeLab management provide a clear platform governance and steering structure according to the *SciLifeLab Infrastructure General Terms and Conditions for Funding*
- Provide access to high quality genomics services to other SciLifeLab platforms
- Contribute to cross-platform SciLifeLab capabilities in Precision Medicine, Planetary Biology, Pandemic Laboratory Preparedness, and others
- Coordinate, develop and provide services within single cell sequencing and spatial biology together with the Spatial and Single Cell Biology platform
- Collaborate with the Clinical Genomics platform with regard to e.g. technology development and evaluation, sample handling, and data and automation pipelines.
- Coordinate and integrate NGI functions between Stockholm and Uppsala
- Take part in large-scale national research efforts as a partner and collaborator, contractor, or service provider
- Promote that recipients of platform services handle their data in accordance to FAIR principles, and direct them to other resources for assistance when appropriate
- Plan and develop efforts as a key partner and data producer within the DDLS program
- Collaborate with the Bioinformatics platform and Data Centre in a way that aligns with the technology- and data driven operations at SciLifeLab
- Inform the Swedish research community about established and novel genomics technologies. Engage with the research community to inquire about the needs regarding technology and training about genomic technologies
- Support the generation of high-quality genomics data enabling publication in internationally competitive journals
- Be actively involved in developing national SciLifeLab nodes at each non-host university, primarily built around the Clinical Genomics, Bioinformatics, Spatial and Single Cell Biology and Genomics platforms, along with DDLS activities and WCMM centers

Organization

Organization during 2022



Organization 2023 onwards



* Includes a new single cell team

The Genomics Platform consists of the large VR and SciLifeLab-funded National Genomics Infrastructure (NGI) unit, and the smaller Ancient DNA unit. There are two ongoing mergers that will be completed during 2023: 1) Microbial Single Cell Genomics, formerly an independent unit in the Genomics Platform, is being merged to form a single-cell team as part of SNP&SEQ, 2) Eukaryotic Single Cell Genomics, formerly/presently an independent unit in the Spatial and Single Cell Platform, is being merged into the Applications subunit of NGI Stockholm. Furthermore, the Platform has an ongoing recruitment for Head of the Strategic Relations subunit. Pending funding for a Head of Unit, the single cell activities in Uppsala may form a new subunit, as depicted in the organogram to the right above.

The platform has the following decision-making structure, as defined in our General Terms and Conditions:

- The Steering Group makes major decisions and provides guidance to the PMG. It is appointed by both VR (for NGI) and by SciLifeLab, and has seven members that represent different universities. The steering group meets every six weeks including once per year in person.
- The Platform Management Group makes executive decisions of platform-wide matters and prepares strategy and major decisions for the Steering Group. The PMG consists of seven people with representation of all units and major activities of the platform. The PMG meets biweekly, including regularly in person, and has an active shared Slack channel. The minutes of the PMG meetings are made available to the staff through NextCloud.

- The Platform Director (Tuuli Lappalainen) and Co-Director (Lars Feuk) have a 1-1 meeting twice per month
- Each unit and subunit has a Head of Unit with responsibility for the budget and the staff. In fall 2022, the Heads will start to have regular meetings to complement PMG meetings at a more operational level

The platform has the following advisory bodies:

- Platform Internal Advisory Group (PIAG) includes the members of PMG, Heads of Units, and Platform Scientific Directors. It meets four times a year to discuss major developments and minutes from the meetings are made available through NextCloud
- International Scientific Advisory Board, appointed in 2022, consists of six leaders in genomics research and infrastructure in Europe. The SAB will meet annually, with the first in-person meeting planned for September 2022

The platform has following forums and meetings to engage with other platforms:

- The platform director and co-director have regular meetings every 2-3 months with the leaderships of Clinical Genomics Platform and NBIS, and also meets semi-regularly with the leadership of the Single Cell and Spatial Platform
- The platform has a regular R&D meeting with representation from Bioinformatics/NBIS, Clinical Genomics, and Single Cell and Spatial Platforms. Furthermore, multiple R&D groups of the genomics platform include members from other platforms to

discuss specific technologies or applications

- The platform is part of multiple collaborative projects with other platforms and other SciLifeLab functions, including Data Centre, Bioinformatics/NBIS, Single Cell and Spatial Platform, Clinical Proteomics and

Immunology

- The platform coordination officer attends regular meetings to communicate information to and from the SciLifeLab operations office and management

Development, Achievements and Plans

Platform development 2021 - now

Since the formation of the Genomics Platform and appointment of the new Director and Co-director in 2021, significant changes have been made both at the organizational and operational levels. The organizational structure, executive bodies and leadership positions have been defined (as described above) and approved by the steering group and by SciLifeLab management.

There have also been changes at the unit level within the platform, especially with regard to single cell activities. A process to integrate the Microbial Single Cell Genomics (MSCG) with the NGI Uppsala single cell activities was initiated in 2021. This was necessary both to harmonize and enhance single cell services in Uppsala, but also to address the lack of Head of Unit at MSCG. This integration process is planned to be formally completed by the end of 2022. In Stockholm, the single cell activities have previously been run at the Eukaryotic Single Cell Genomics (ESCG) unit, as part of the Spatial and Single Cell Biology Platform. In the spring of 2022, major changes at ESCG led to the joint proposal by the Spatial and Single Cell Biology and Genomics Platforms that ESCG would be integrated with the activities at NGI Stockholm. This process has now been initiated, where ESCG will be a team within the NGI Stockholm Applications unit headed by Anja Mezger, as part of the Genomics Platform. We anticipate completing the integration process at the end of 2022.

With the re-organization of single cell operations, single cell activities with a sequencing based read-out will be part of NGI, with two sister teams in Uppsala and Stockholm. This is an important and positive development for several reasons: a) the single cell activities will be integrated with the existing NGI operations, including LIMS systems, order portal, quality assurance work etc. b) long-term strategic decisions in the single cell area can be taken in a coordinated fashion with a national perspective in mind c) applications offered to users can be better coordinated between Uppsala and Stockholm, with the nodes specializing in certain niche applications, and d) national coordination with other platforms and local core facilities will be simplified and more efficient, as evidenced by NGI initiating and leading a recent Swedish Research Council grant application on single cell coordination.

The Specific Terms and Conditions outline the strategic directions and vision that SciLifeLab management have for the Genomics Platform. While several of the conditions

define the general ongoing operations of the platform, there are a few specific points where significant progress has been made and that are worth highlighting in this report. In addition to coordination with the Spatial and Single Cell Biology platform (described above), we are also encouraged to enhance collaboration with the Clinical Genomics platform. During 2021, we initiated regular meetings between the leadership of the Genomics and Clinical Genomics Platforms. The discussions have provided important understanding of how the respective platforms operate, and have also led to formal collaborations. The two platforms have initiated a joint project, with funding from Genomic Medicine Sweden, to evaluate two different long-read sequencing applications for use on clinical samples. This is a nation-wide project involving all Genome Medicine Centers and associated Clinical Genomics Units. In addition, Clinical Genomics Lund are now partners on an application for an Access to Infrastructure Grant from the Swedish Research Council, focusing on coordinating single cell activities within and between platforms, including exploration of the clinical application of single cell read-out.

Other notable achievements and activities during 2021-2022:

- Formation of new International Advisory Board with first meeting
- Joint development of new Data Delivery System together with Data Centre
- New internal cluster for data analysis and storage acquired and installed
- NGI spearheaded a new joint-capability lab with Affinity Proteomics Uppsala to offer high-throughput protein analysis based on Olink's proximity extension assay (PEA) in combination with NGS readout.
- First platform-wide retreat in 2021, with another planned for Sept. 2022
- Significant role in the Horizon -funded European Reference Genome Atlas (ERGA) Project
- Coordination with NBIS to offer "sample to annotated assembly" to users
- Engagement in capabilities, with NGI staff appointed Scientific Lead in Planetary Biology, participation in a funded Pandemic Preparedness effort, and meetings

with the Precision Medicine leaders.

- A rapidly growing number of Ancient DNA projects, including participation in the Swedish National Infrastructure for Digital Archaeology

- In 2021, >100,000 samples from 1,268 projects were analyzed and >750 meetings were held with users to discuss their projects.

Development plans for Genomics 2023–2024 and beyond

With the formation of the platform in 2021 and the significant re-organizations that have taken place during 2021–2022, there is a need for stability in the Genomics Platform organization during the next few years. The new integrations need to be completed not only on paper, but also in terms of staff integration and internal coordination of services and operations. One major internal goal for the next two year period is therefore to fully integrate the new activities in NGI operations and to coordinate and harmonize which applications to offer and where to set them up. These efforts go hand in hand with the overall ongoing integration of historically separate NGI units in Stockholm and Uppsala into a joint organization where the different parts work together seamlessly.

It will be important to further engage and formalize interactions with the Spatial and Single Cell Biology Platform to ensure that the two platforms work together towards offering the best applications for SciLifeLab users in the areas of single cell and spatial biology, and that the close collaboration with the Platform Scientific Directors with single cell expertise continue to be involved in and advise on development of applications.

An area of development over the next two year period will be to formalize interactions with the national hubs across Sweden. While discussions have now been initiated with Lund University and Göteborg University, the form and extent of interaction with local hubs still remain to

be defined. We will also initiate similar discussions with representatives from Linköping and Umeå, as well as local genomics core facility representatives across Sweden. These discussions will take place in parallel to, or in coordination with, continued regular interactions with NBIS and Clinical Genomics, who already have a nation-wide presence.

In the next few years we expect to see important changes and increased competition in the sequencing technology arena. New companies are launching products that are directly competing with existing Illumina instruments in terms of cost and throughput, while long-read sequencing is gaining ground for many applications. For NGI, this means that there will for the first time in several years be entirely new short-read sequencing technologies to evaluate. Setting up entirely new instruments from new providers at NGI will require significant development efforts in terms of library preparation, data handling, quality assurance and documentation, cost model changes and outreach.

We will continue working to ensure that Ancient DNA is able to benefit from routines and infrastructures set up at NGI. Ancient DNA will have access to existing tools such as the order portal, analysis cluster and data delivery systems. Across the platform, we will continue working towards increased integration of new and old units and nodes, improved cross-unit communication and exchange and joint R&D efforts.

Specific Comments or questions for the reviewers to consider

As a major platform, we have a large and diverse staff, and we continue to be competitive in recruitment and retainment. However, we foresee that the ongoing process

of universities and SciLifeLab building better career paths and advancement opportunities for staff scientists will be an important way to develop our staff further.

Request for additional funding 2023–2024

As a result of the current re-organization and mergers in the Genomics Platform, we see a need for funding for key staff positions in order to strengthen subunit leadership and to ensure efficient handling of administrative duties within the platform. Specifically we request funding for:

1) Administrative assistance

The administrative workload for the Genomics Platform has grown over the past two years, resulting in platform leadership and PCO taking time from strategic work to perform routine administrative tasks. We therefore request funding for an administrative assistant to schedule meetings, manage documents, assist with outreach events, support

internal communication, prepare meeting minutes etc. for the entire platform (2023 - 800kSEK, 2024 - 816kSEK)

2) Head of Single Cell Uppsala subunit

The merger of the Microbial Single Cell Genomics (MSCG) unit with SNP&SEQ has strengthened the overall single cell activities in Uppsala. It would strengthen the activities further if a new subunit would be formed, with a formally appointed Head to manage operations and staff. We therefore request 50% funding for a Head position. Funding to cover the rest of this salary has been applied for in the VR “Access to infrastructure” recently submitted. (2023 - 442kSEK, 2024 - 450kSEK)

3) *Co-Director engagement*

The size and organization of the Genomics platform requires both a Director and Co-Director who are very actively engaged in platform management and operations. Currently the Director is supported by SciLifeLab at 10%, while no support is specified for the Co-director. We think an active Co-Director is needed for the platform and should be compensated. We therefore request funding for 10% salary for the Co-Director position (2023 - 180kSEK, 2024 - 185kSEK).

4) *Head of Strategic Relations*

NGI Stockholm is now recruiting a new Head of Strategic Relations. This person will lead a group identifying and pursuing collaborative technology development with industry and academia partners. Our vision is that this should be a platform-wide mission supported by joint platform funding. To start that transition towards a platform funded position we ask for 50% salary support for this position for 2023 (650kSEK) and 100% salary for 2024 (1,300kSEK).

5) *Increase in ancient DNA service breadth and capacity*

The Center for Palaeogenetics (CPG) in Stockholm is a world-leading research environment in ancient DNA. SciLifeLab funding for 50 % of an Ancient DNA unit research engineer at CPG allows converting their development and experience in analysis into services for the research community. We also see a continuously increasing number of users and projects at the Ancient DNA unit and funding for a 50% position would meet the need for increase in capacity (470 kSEK per year for 2023 and 2024).

6) *Increasing annual costs*

With a large number of employees we see a significant budget impact from increase in salary expenses over a 4-year funding cycle. Annual salary costs at the platform are around 70 MSEK, translating to increased costs of 1.5-2 MSEK per year for salaries alone. We also see increased charges for rent and overhead. Yet base funding typically remains constant over the funding cycle. We therefore request funding to cover inflation related cost increase for 2024 (1,300kSEK).

Requests for expanded funding 2023–2024

Specify all costs in kSEK

Unit	SciLifeLab funding 2022 (kSEK)	Requested ScilifeLab funding2023 (kSEK)	Requested SciLifeLab funding 2024 (kSEK)
NGI Uppsala (SNP&SEQ)	13,900	14,342	14,350
MSCG /SCG Uppsala	2,000	2,000 *transfer to SNP&SEQ after merger complete	2,000*transfer to SNP&SEQ after merger complete
NGI Stockholm	21,900	22,700	22,716
NGI Uppsala (UGC)	8,700	8,880	8,885
Ancient DNA	2,000	2,470	2,470
Joint platform funding	1,200	1,850	3,800

National Genomics Infrastructure

Genomics Platform (Web links for Unit: [Webpage](#), [Publications](#))

Basic Information

Head(s) of Unit: Tuuli Lappalainen (Director), Susanne Hellstedt Kerje, Ulrika Liljedahl, Anja Mezger, Ellen Sherwood

PSD(s): Carsten Daub, Lars Feuk, Jessica Nordlund, Ellen Sherwood

SciLifeLab Unit since: 2013

Host university: KI, KTH, SU, UU

FTEs: 77.7

FTEs financed by SciLifeLab: 44.5

Funding in 2021 (kSEK)

SciLifeLab: 44500

SciLifeLab Instrument: 1900

Universities (KI, KTH, SU, UU): 11037

VR: 22292

KAW: 1600

EU: 2850

Other: 500

Total: 84679

Resource Allocation 2021

Academia (national): 90%

Academia (international): 3%

Internal tech. dev.: 1%

Industry: 1%

Healthcare: 4%

Other gov. agencies: 1%

User Fees 2021

Total (kSEK): 139298

Reagents: 70%

Instrument: 8%

Salaries: 5%

Rent: 2%

Other: 15%

User Fees by Sector 2021

Academia (national): 95%

Academia (international): 2%

Industry: 1%

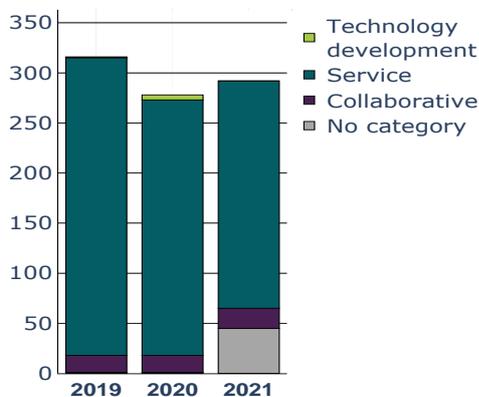
Healthcare: 1%

Other gov. agencies: 1%

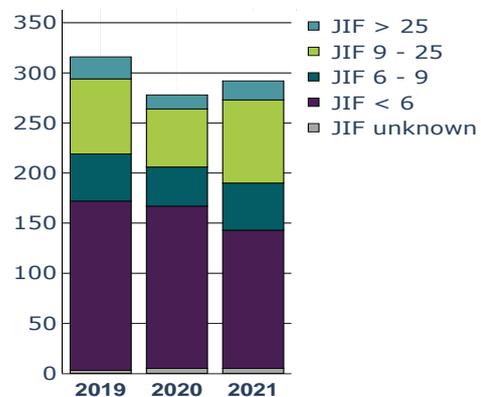
Services

- Sequencing using Illumina, PacBio, Oxford Nanopore, and Ion instruments
- SNP genotyping and methylation analysis using Illumina arrays
- Proteomics using the Olink Explore assay
- Spatial transcriptomics using the 10x Genomics Visium assay
- Single cell analysis using the 10x Genomics Chromium instrument
- HMW DNA extractions
- Bioinformatics QC and initial analysis

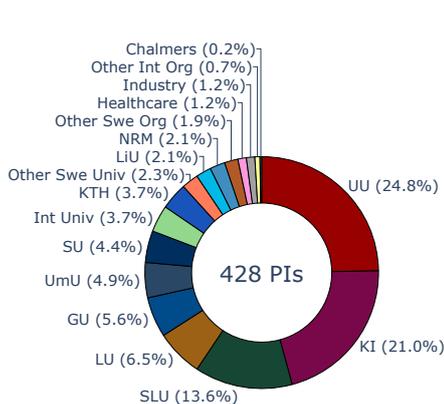
Publication by Category



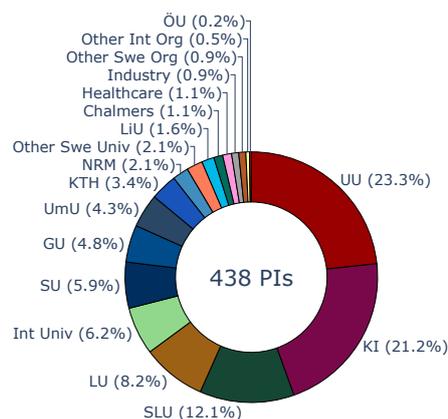
Publication by Journal Impact Factor



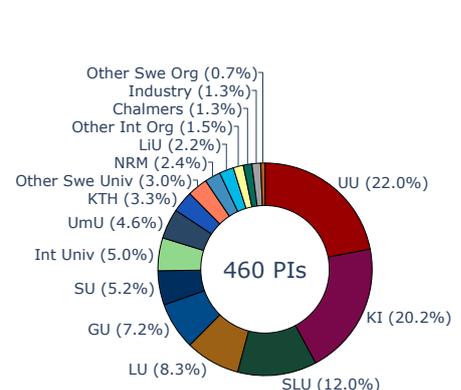
Users 2019



Users 2020



Users 2021





Unit:	National Genomics Infrastructure, NGI
Platform:	Genomics

Development, Achievements and Plans

i) Briefly describe the development and major achievements (technology development, scientific achievements, new user groups, outreach efforts, training and education, contribution to cross-unit and cross-platform initiatives etc.) of the unit 2021–2022.

ii) Briefly describe the development plans for the unit 2023–2024 and beyond

iii) If you have specific questions or comments for the reviewers to consider during the Midterm Checkup, you may add these here.

Spatial transcriptomics and single-cell activities are presented in separate reports.

Technology development, scientific achievements, and new user groups 2021-2022

NGI maintains the position as one of the leading genomics infrastructures in Europe via continuous evaluation, validation and implementation of new services. Below are examples of recent activities:

- The SciLifeLab Explore Lab was established in 2021 as a joint effort with the Affinity Proteomics Unit in Uppsala, making high-throughput protein analysis using Olink's proximity extension assay available.
- The EU Horizon Bioscan-ERGA-EBP-project funded in 2021 has propelled an effort to offer a "De novo sequencing package" including relevant lab technologies (long and short read) and advanced data analysis in collaboration with NBIS.
- We developed a single cell whole genome bisulfite sequencing (scWGBS) protocol, published earlier this year (Raine et al, 2022, Sci Rep 12(1) 5772). This project was funded in part via our ongoing effort in the EU H2020 project EASI Genomics.
- We have implemented several protocols of particular interest, including i) A waste-water covid enrichment protocol, ii) OmniC services with adaptation to non-mammalian species, iii) Amplicon-seq has been established in a highly multiplexed capacity.
- Targeted long-read sequencing is under evaluation together with Clinical Genomics in Uppsala with TDP funding. This sequencing approach enables studies of human structural variation and repeat expansions and is of great value for sequencing of clinical samples.

NGI continues to see a large and highly diverse user base in the projects executed, with 1231 projects from 499 users in 2021 and a similar forecast for 2022. NGI's users represented more than 30 different organizations, primarily Swedish academia, but also different governmental agencies and international universities. During 2021 and the first months of 2022, 412 publications using data produced at NGI have been published, 46 of them being collaborative or internal development projects. The technology development efforts described above have brought in new and increased users from fields including proteomics (Explore Lab), de novo (De novo package), and environmental biology (amplicon and RAD-seq). We have also noted an increase in sequencing for other SciLifeLab Platforms and in international users

Outreach, training and education

NGI regularly organizes webinars, seminars and lab tours. The largest event arranged by NGI, the highly appreciated, internationally attended Long-Read Sequencing Meeting (LRUA 2022) will be back this fall after a break during the pandemic, now co-organized with Clinical Genomics. NGI

takes part in SciLifeLab outreach events, such as the outreach week, and the KI Science Park day, open house and site visits. NGI frequently participates as lecturers in courses at master, doctoral and postdoctoral level at our host departments or as invited speakers at other sites. The lectures at our host departments are most often combined with a site visit.

Contribution to cross-unit and cross-platform initiatives

The Genomics Platform is a fully integrated platform with a management group with representatives from all units, working groups in various topics of interest spanning the entire platform, and annual all-staff meetings.

NGI is involved in multiple cross-platform initiatives: we have joint services together with the Proteomics Platform exemplified by the Explore lab, we develop the novo pipeline and have joint drop in sessions for user support with Bioinformatics Platform, we have quarterly management meetings and technology development groups with representatives from the Clinical Genomics and Bioinformatics Platforms, and we also have a cross platform unit with Spatial and Single Cell Biology.

Development plans 2023-2024 and beyond

Single cell activities will be a major part of the development activities at NGI, after merging the MSCG activities in the Uppsala node and ESCG activities in the Stockholm node (See MSCG & ESCG reports for additional details).

NGI aims to be at the forefront of NGS sequencing and to continue to provide a broad portfolio of the most cost effective and complementary sequencing technologies. There are several new and upcoming sequencing instruments on the horizon to be released in 2023. We plan to assess these new technologies and secure funding for the new capital investments required. However, a major challenge will be to attract funding at the right time.

The research community is transitioning from analysis of single analytes (DNA, RNA, protein) to projects where multi-omic analysis is desired. We will work towards extending our multi-omics capabilities by establishing “multi-omics packages” where know-how, robust and reproducible laboratory procedures, and joint-analysis pipelines (in a continued effort with the nf-core project) will be established. Some examples include combined spatial transcriptomics and mass spectrometry assays, combined single-cell gene expression and chromatin accessibility, and combined assays for DNA, RNA and protein analysis.

Monitoring of large populations, for example in projects aiming to study how species and ecosystems are changing over time is one area where cost-effective methods are not readily available. New SNP arrays (Illumina), improved multiplexed amplicon sequencing, as well as our in house developed upSPLAT approach have potential to provide genomics service for this important niche. The TDP funded upSPLAT project aims to develop a cheap and scalable library preparation method for large sample series from microbial communities and population cohorts, and involves a close collaboration with MSCG.

Finally, with the new SciLifeLab hubs throughout Sweden, we are looking forward to establishing new connections, collaborations and joint efforts to further enable genomics services to users throughout Sweden.

Specific questions or comments for the reviewers to consider during Midterm Checkup

For an organization of NGI's size, costs increase due to inflation (including rent) and annual salary increases not being reflected in the funding over the grant period leads to skewed budget planning. As costs of personnel, rent, service agreements, etc increase every year, the size of operations must therefore be reduced over the funding period. We would like to have a discussion with SciLifeLab, preferably together with the host Universities on how to make more sustainable four-year budgets for NGI.

National Genomics Infrastructure

Budget 2022

Costs	2022
Personnel cost	76 115 589
Other personnel costs	2 840 000
Depreciation	20 421 900
Service and license costs	10 943 884
Other operating costs	89 687 500
Premises costs	8 695 000
Other costs	1 343 000
Sum costs (kSEK):	210 046 873

Revenues	2022
Funding from SciLifeLab	44 500 000
Funding from VR	20 000 000
Funding from KTH	500 000
Funding from CZI	500 000
Funding from KAW	1 600 000
Funding from UU SFO	1 000 000
Funding from UU/KTH/SU/KI SFO	7 536 667
Funding from SciLifeLab Infrastructure Instrument Call	2 742 000
Funding from SciLifeLab Infrastructure TDP	1 500 000
Funding from VR EBP	1 000 000
Funding from SciLifeLab Uppsala	2 000 000
Swedish Research Council access to infrastructure	1 800 000
EU H2020, EASI Genomics	1 100 000
EU H2020, EATRIS Plus	800 000
User fees	121 170 000
Sum revenues (kSEK):	207 748 667

Microbial Single Cell Genomics

Genomics Platform (Web link for Unit: [Publications](#))

Basic Information

Head(s) of Unit: Johan Ankarklev (acting)

PSD(s): Johan Ankarklev, Fabien Burki

SciLifeLab Unit since: 2015

Host university: UU

FTEs: 2.0

FTEs financed by SciLifeLab: 2.0

Funding in 2021 (kSEK)

SciLifeLab: 2000

UU: 968

KAW: 300

Total: 3268

Resource Allocation 2021

Academia (national): 55%

Academia (international): 10%

Internal tech. dev.: 20%

Industry: 5%

Healthcare: 10%

Other gov. agencies: -

User Fees 2021

Total (kSEK): 324

Reagents: 60%

Instrument: 20%

Salaries: 20%

Rent: -

Other: -

User Fees by Sector 2021

Academia (national): 60%

Academia (international): 21%

Industry: 5%

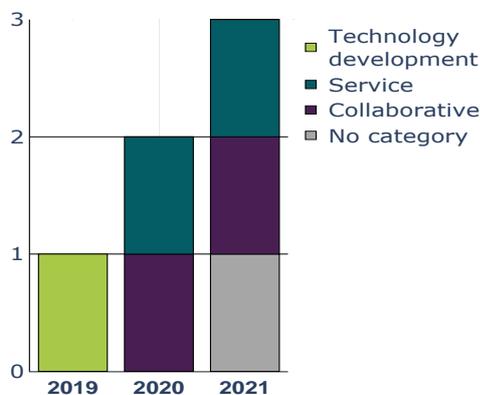
Healthcare: 14%

Other gov. agencies: -

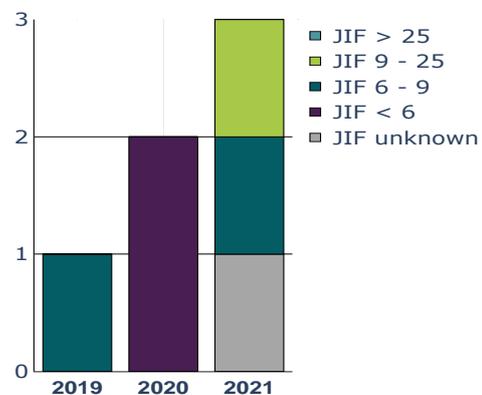
Services

- Single-cell sorting in microwell plates using FACS or the C1 Single-Cell Auto Prep system
- Lysis and WGA of individual cells using MDA
- PCR screening of amplified single cell genomes for marker genes
- Design of single-cell experiments, WGS, genome assembly and bioinformatics support
- BSL3 facility for sample handling of live pathogens
- 10X chromium controller

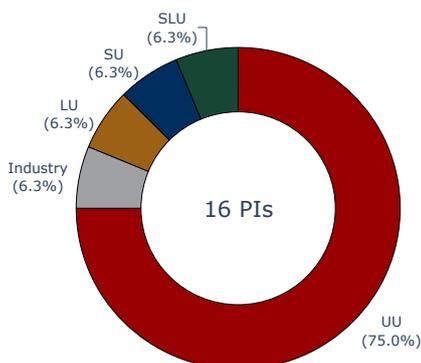
Publication by Category



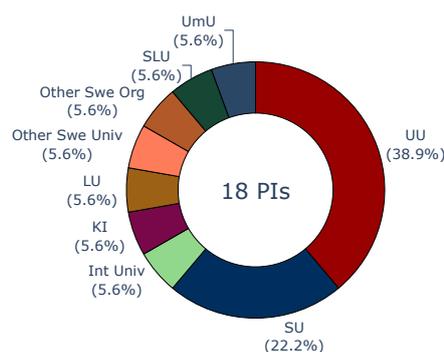
Publication by Journal Impact Factor



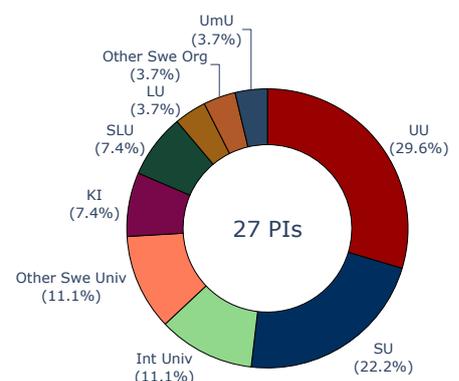
Users 2019



Users 2020



Users 2021





Unit:	Microbial Single Cell Genomics
Platform:	Genomics
Development, Achievements and Plans	
<p>MSCG has in the last few years enabled single-cell genomics to two distinct user groups, including <i>microbial diversity</i> and <i>infection biology</i>.</p> <p><u>Microbial Diversity:</u> Since its start, MSCG's main activity and services have been linked to projects involving microbial diversity and evolution. The projects often comprise challenging and difficult sample types and organisms, which are not well-characterized (e.g., environmental samples). In light of the complex nature of these samples, a large part of MSCG's effort and expertise is focused on optimizing cell sorting and lysis in order to enable single-cell genomic and transcriptomic applications to samples beyond standard protocols.</p> <p><u>Infection Biology</u> More recently, MSCG established a service niche in infection biology. MSCG's ambition is to potentiate complex genomic applications for infection biology research both at the clinical and basic biological level, as well as expanding the services to assist in projects studying disease transmitting insect vectors. MSCG has performed multiple projects involving eukaryotic pathogens of human and veterinary importance, such as malaria, <i>Toxoplasma</i>, <i>Cryptosporidium</i> and <i>Giardia</i>, as well as studies on both vertebrate hosts and insect vectors (mosquitoes and flies). Due to MSCG's extensive expertise in infection biology and BioSafety, MSCG assisted in establishing COVID-19 routines for projects coming into the Genomics Platform and identified and implemented alternative strategies for safer sample handling. There are various initiatives around Sweden in which MSCG is actively partnering to provide single cell genomics services. These include:</p> <ul style="list-style-type: none"> • The national BSL3 network • The KAW funded Pandemic-Preparedness Network. • The KAW funded study on host responses to COVID-19 in a network with researchers at UU and MIMS (UmU). • The Zoonosis Science Center (UU) • The Uppsala Antibiotic Center (AMR) <p>R&D at MSCG has been focused at enabling protocols specifically for non-standardized experimental models and organisms. For example:</p> <ul style="list-style-type: none"> • Ongoing technology development projects with Danish-based company Samplix, including droplet-based MDA followed by long read sequencing to improve single-cell genome sequence coverage. • A collaboration with the California- based biotech company, QuantumCyte, linked to targeted multi-omics approaches on tissue samples. • A collaboration with NGI Uppsala to develop cheap and scalable sequencing library preparation methods for microbial and metagenomics samples (part of Technology Development Project: upSPLAT) <p>Examples of scientific achievements during 2021-2022 to which MSCG genomics have contributed;</p>	

- A study that applied sorting and scRNA-seq to characterize the immune cells of the malaria transmitting mosquito vector, *Anopheles gambiae*. The study provides important information for malaria eradication efforts, a disease that kills nearly half a million persons and infects approximately a quarter of a billion people per year. *eLife*, DOI:10.7554/eLife.66192
- A study that applied single cell genomics to reveal that plastid-lacking Picozoa are close relatives of red algae. The results of this study change our understanding of plastid evolution as they either represent the first complete plastid loss in a free-living taxon, or indicate that red algae and rhodophids obtained their plastids independently of other archaeplastids, *Nature Communications*. DOI: 10.1038/s41467-021-26918-0
- A study that used a human 3D lung cell model based on primary cells and scRNA-seq to identify host factors that regulate SARS-CoV-2 infection, DOI: 10.1128/mbio.00892-22

A new single cell genomics unit in Uppsala -a merger between MSCG and NGI Uppsala

The interest for single-cell services is ever growing and in response to the increased demand a process to merge the single-cell genomics activities at MSCG and NGI Uppsala has been initiated. The new single-cell unit under the umbrella of NGI Uppsala SNP&Seq is planned to launch in early 2023. This unit will have the capability to offer single-cell service to a broad user base in biology and medicine, whilst maintaining the unique competence and ability to provide researchers in the microbial and infection biology niches with services adapted for their specific needs. We anticipate many advantages and synergies to emerge from the merger:

- A critical mass: technical skills and knowledge will be focused, instead of scattered at several smaller units.
- More efficient usage of equipment and staff resources.
- MSCG's experience with custom-tailored solutions will be combined with NGI Uppsala's efficient routines for streamlined project handling, LIMS and experience of large-scale single-cell services.
- A new head of unit, with clearly defined leadership.

Single cell projects are often complex, and this especially holds true for projects with microbial samples. One of the challenging tasks within the newly formed unit will be to find the right balance between customized solutions and standardized SOPs to be offered as service. In this context we are currently working on implementing cost models that are better adapted for challenging projects with a high degree of customization.

Plans 2023-2024

General: During 2023-2024 we will continue to consolidate the new single cell genomics unit and take part in various outreach events. Moreover, we will work towards alignment and increased interaction with the new single cell genomics unit at NGI Stockholm. Since 2016 MSCG has organized annual workshops on the topic of microbial single cell genomics. In April 2023 we plan to organize this workshop again, comprising a practical lab-course and a seminar day with invited speakers representing the field.

Developments: We plan to test and implement a number of novel single-cell RNA-seq methods related to the microbial and infection biology areas within the new unit. For instance, we aim to:

- Continue to expand on the capability to handle clinical samples, also including infectious samples, by implementing fixation-based methods (Honeycomb, Parse, 10X Genomics).
- Implement new cost-effective plate based scRNA-Seq methods (SmartSeq3xpress or FLASH-seq).
- Test new single-cell RNA-seq techniques for prokaryotes in collaboration with MIMS at Umeå University.

Specific questions or comments for the reviewers: In order to ensure the success of the merged single cell genomics unit we need to recruit a Head of Unit and a bioinformatician dedicated to single-cell genomics projects. We therefore request 50% funding for a Head position. Funding to cover the rest of this salary has been applied for in the VR "Access to Infrastructure" recently submitted. We are looking into funding opportunities to cover salary for a bioinformatician.

Microbial Single Cell Genomics

Budget 2022

Costs	1 728 216
Personnel cost	326 592
Other personnel costs	171 386
Depreciation	402 192
Service and license costs	346 500
Other operating costs	504 590
Premises costs	0
Other costs	2 974 886
Sum costs (kSEK):	2 974 886

Revenues	2022
Funding from SciLifeLab	2 000 000
Funding from SFO UU	468 000
Funding from financier Y	500 000
Funding from financier Z	0
User fees	0
Sum revenues (kSEK):	2 968 000

Ancient DNA

Genomics Platform (Web links for Unit: [Webpage](#), [Publications](#))

Basic Information

Head(s) of Unit: Magnus Lundgren
PSD(s): Mattias Jakobsson, Anders Götherström
SciLifeLab Unit since: 2017
Host university: UU, SU
FTEs: 2.56
FTEs financed by SciLifeLab: 1.76

Funding in 2021 (kSEK)

SciLifeLab: 2000
UU: 800
Total: 2800

Resource Allocation 2021

Academia (national): 34%
Academia (international): 4%
Internal tech. dev.: 31%
Industry: 9%
Healthcare: -
Other gov. agencies: 22%

User Fees 2021

Total (kSEK): 522
Reagents: 19%
Instrument: 2%
Salaries: 45%
Rent: 16%
Other: 18%

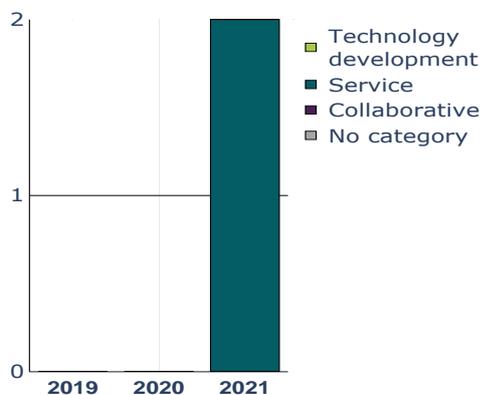
User Fees by Sector 2021

Academia (national): 45%
Academia (international): 6%
Industry: 12%
Healthcare: -
Other gov. agencies: 37%

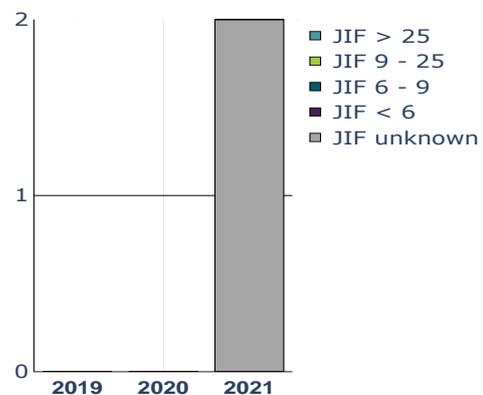
Services

- Extraction and processing of ancient DNA from different types of samples
- Processing of ancient DNA data incl. mapping to reference genome
- Analysis of ancient human DNA for sex, haplogroup, kinship and other features
- Analysis of ancient microbial DNA, including from pathogenic microorganisms

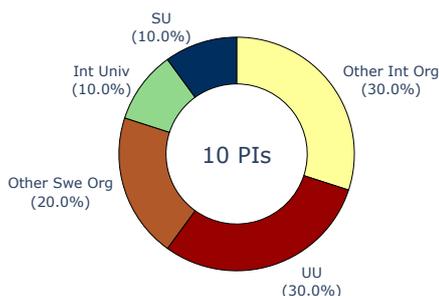
Publication by Category



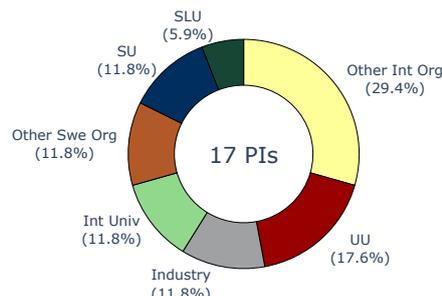
Publication by Journal Impact Factor



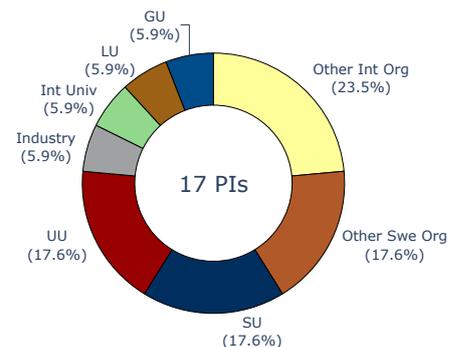
Users 2019



Users 2020



Users 2021





Unit:	Ancient DNA
Platform:	Genomics

Development, Achievements and Plans

i. Developments and major achievements in 2021 and 2022

The Ancient DNA unit provide processing and analysis of highly degraded DNA from historical and ancient materials. Our services provide users with access to the temporal dimension of DNA analysis, a type of analysis that have rewritten many aspects of our understanding of the past. We support investigation of *e.g.* evolution, ecology, migration, demography, traits, agriculture, prehistoric societies, pathogens and heritable disease.

Scientific highlights include analysis of the oldest human remains in Sweden, ecological changes on Gotland, extinct cattle breeds in Scandinavia, development of prehistoric sheep husbandry in southern Europe, stone-age hunter-gatherer settlements in Sweden, iron age population history of the Caucasus region, the crew of the 17th c. Kronan warship, violence in Scandinavian bronze age, Viking-age dental health, extinct wild animals in Scandinavia, and investigation of kinship and ancestry among Roman-age Britain, Early Christians in Sweden, Vikings with filed teeth, and Kazakh medieval royalty, to name a few.

Our unit have dedicated clean-room laboratories for sampling ancient material and processing DNA, as well as pre-PCR and post-PCR laboratories to enable analysis of a range of projects. We have a research engineer and Head of Unit/coordinator at Uppsala University, and a bioinformatician and a part-time research engineer at Stockholm University, but we operate in a fully integrated manner.

During 2021-2022 we have implemented methods to provide services relating to DNA from sediments and performed our first sediment-based user projects, and we are collaborating with the Bioinformatics platform for in-depth analysis of the data. We have also analyzed soil samples, rocks and meteorite material using similar approach.

In 2022 we have initiated a project to developing methods for analysis of ancient DNA (aDNA) in plant and herbarium specimens, supported by a SciLifeLab Technology Development Project grant. The project includes national and international experts and sample providers. Special procedures are required to process morphologically and biochemical heterogenous material that frequently contain enzyme inhibitors. Pilot projects include analysis of biodiversity and the development of food crops.

Human and animal bone material is our most frequently analyzed material and we are improving laboratory procedures for DNA extraction and library preparation. In addition, we are continuously gathering experience on selecting bone material for DNA analysis for a range of species, and where and how to sample the specimens, which often is crucial to successful analysis.

Bioinformatic data analysis is also a large part of our service, and we provide services relating to both data processing and specific analyses. We analyze both data we generate ourselves and published data. We investigate DNA preservation, and validate ancient DNA data though analysis of fragmentation and chemical modifications. Further, we also investigate presence of mixed genotypes to detect DNA contamination. We have developed and implemented methods for analysis of paternal ancestry (Y-chromosome haplogroup), close kinship (first and second degree), metagenomics analysis (incl. analysis of pathogens), and of genetic traits incl. polygenic analysis. We also have performed population genetic analysis to investigate ancestry, migration and

demography. We also interact with the SciLifeLab Bioinformatics platform that can provides users with additional in-depth analysis of DNA data we produce.

Our user base is growing among biologists, archaeologists and other user groups as the understanding of benefits of aDNA analysis increase. As many users are not trained in DNA analysis, we engage in extensive project discussions and outreach efforts. We arrange symposia and seminars, participate in meetings and conferences, and visit research departments, museums, contract archaeology companies, county administrative boards, and other organizations. Our users are distributed widely across Sweden and we also have a large international interest in our services, and many users are recurring. As a recently established unit, most user projects are yet to be published. Many of our users also make their findings public through books, museum exhibitions and excavation reports, in addition to research articles.

The Ancient DNA unit is thoroughly embedded in analysis of cultural heritage as part of the Heritage Science Sweden network, the EU-funded Iperion Heritage Science research infrastructure, and the VR-funded Swedish National Infrastructure for Digital Archaeology (SweDigArch).

Apart from the close interaction with the Bioinformatics platform discussed above, we are also interacting with the Clinical Proteomics and Immunology platform to perform ancient protein analysis and have initiated pilot projects in the area. We are of course interacting very closely with the SciLifeLab National Genomics Infrastructure (NGI) that sequence the DNA libraries we prepare, and we also have ongoing discussion about methods development together with NGI. We also interact with the Uppsala University Tandem Laboratory, for whom we can collect samples for radiocarbon dating, in parallel with our DNA analysis.

ii. Development plans for 2023-2024 and beyond

Ancient DNA analysis is a rapidly developing approach with diverse scientific applications. Our unit have plans for a range of developments in the coming years, including the following:

- As part of SweDigArch, we will develop a data repository and cross-disciplinary analysis tools for archaeological information, incl. results of aDNA analysis. Through the project we will also provide support with deposition of aDNA raw data and metadata in international repositories according to FAIR principles.
- Development of services for analysis of highly degraded DNA in ancient and herbarium plant material. Includes partners at SU, UU and NRM, as well as in Israel and UK. Project funded as SciLifeLab technology development project 2022-2023.
- Development of tools for analysis of kinship using ancient DNA data. Kinship analysis is very valuable to archaeologists but aDNA-specific tools are required due to the highly fragmented nature of the DNA. The goal of the project is to enable analysis with less data and to implement methods for determine relationship of third degree and beyond. Project planned together with researchers at Uppsala University.
- Analysis of DNA in sediments and soil. Sediments are heterogenous in composition and chemistry. To increase success of analysis, we are planning to implement additional methods for DNA extraction tailored to different types of sediments.
- DNA enrichment. In specimens and materials where DNA preservation is very low analysis can be improved using in-solution capture to enrich target DNA.

iii. Specific comments for Midterm Checkup.

With a rapidly growing user base and project volume, and increasing breadth of service requests, our unit require a research engineer staff on open-ended contract at the Center for Palaeogenetics (CPG) in Stockholm. This allows continuing access to CPG's lab for less than 300-year-old samples, and CPG expertise in analyzing *e.g.* extremely old, plant and sediment DNA analysis. Our unit has acquired external support for a research engineer on a short-time contract but an increase in our core budget would greatly support retaining our skilled and experienced staff members at CPG.

Ancient DNA

Budget 2022

Costs	2022
Personnel cost	3 154 296
Other personnel costs	0
Depreciation	0
Service and license costs	0
Other operating costs	369 000
Premises costs	230 000
Other costs	0
Sum costs (kSEK):	3 753 296

Revenues	2022
Funding from SciLifeLab	2 000 000
Funding from Swedish research Council	490 000
Uppsala University SFO	1 200 000
Funding from financier Z	0
User fees	770 000
Sum revenues (kSEK):	4 460 000

Spatial and Single Cell Biology Platform

Platform Director: Mats Nilsson, SU

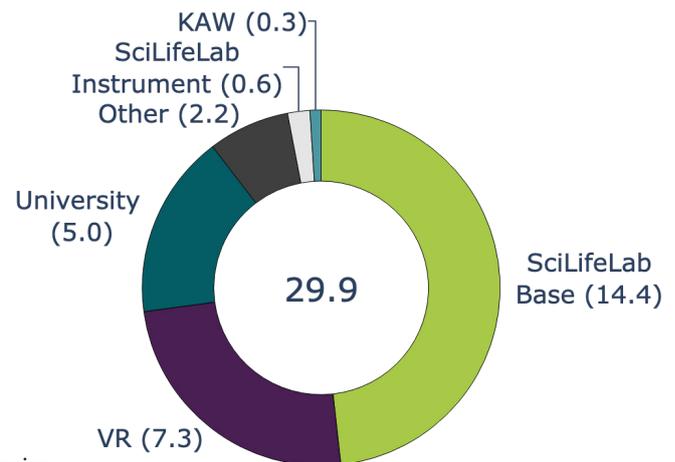
Platform Coordination Officer: Charlotte Stadler, KTH

Platform and Units SciLifeLab Funding 2021:

Unit*	(MSEK)
Eukaryotic Single Cell Genomics	5.0
Spatial Proteomics	3.5
In Situ Sequencing	2.4
Advanced FISH Technologies	1.3
Spatial Mass Spectrometry	1.5
PD, PCO, Platform Strategic Budget	0.8
Sum:	14.4

* The Spatial Transcriptomics Unit, formally part of NGI/Genomics platform, are included in the checkup of the SSCB Platform. The Unit has submitted a Midterm Report, but we do not currently have user statistics and budget for the Unit.

Total Funding 2021:



Platform Specific Terms and Conditions for Funding - Spatial and Single Cell Biology

This document concerns the terms and conditions for SciLifeLab funding of the Spatial and Single Cell Biology (SSCB) Platform and Units from 2021 and onwards and outlines the strategic direction MG wants the platform to take. The mid-term checkup in the middle of the 4-year funding period will focus on how well the Platform and Units have taken into account the items in this document.

- SciLifeLab funding to the Spatial and Single Cell Biology Platform and Units is meant for providing advanced and nationally unique services for single cell and *in situ* spatial biology. Over time the platform should strive to offer service combining single cell and spatial omics methods, as well as integrating different spatial omics methods and keep Sweden in the forefront of technologies in these areas.
- Ensure that SciLifeLab funds are used in the platform in a manner that aligns with the priorities and goals of the entire SciLifeLab organization
- Together with the SciLifeLab management suggest a clear platform governance and steering structure according to the suggested general policy for governance and steering of SciLifeLab infrastructure.
- Integrate and support the establishment of the Advanced FISH Technologies as a new Pilot Unit to be evaluated in 2022. For midterm, the AFT unit should primarily be evaluated on service related to probe design and low plex projects that can be performed with the current instrumentation and staff funded by SciLifeLab.
- We suggest the ECSG Unit together with the

associated research groups should focus on
i) continued technology leadership, adaptation, and dissemination,

ii) setup of a national network and iii) integrating its functions and services with the spatial biology capabilities as part of the platform. The unit should also continue its own single cell services in collaboration with the Genomics and Clinical Genomics platforms, which will also be active in national single cell services. Good coordination is essential here.

- Contribute to cross-platform capabilities such as the spatial biology itself as well as the Precision Medicine and Planetary Biology capabilities
- Contribute to the national SciLifeLab nodes formed on the backbone of Bioinformatics, Genomics and Clinical Genomics. Incorporate single cell / spatial biology capability.
- Together with single cell units of the Genomics and Clinical Genomics platforms, ESCG should take a lead in developing national training in sequenced based single cell methods. The SSCB platform should take the lead in national training of *in situ* spatial biology methods and promote transfer of technologies to local facilities and networks.
- Enhance collaboration with Bioinformatics platform and Data Centre to provide each user a bioinformatics services on one side, and a data sharing responsibility and links to the DDLS initiative on the other

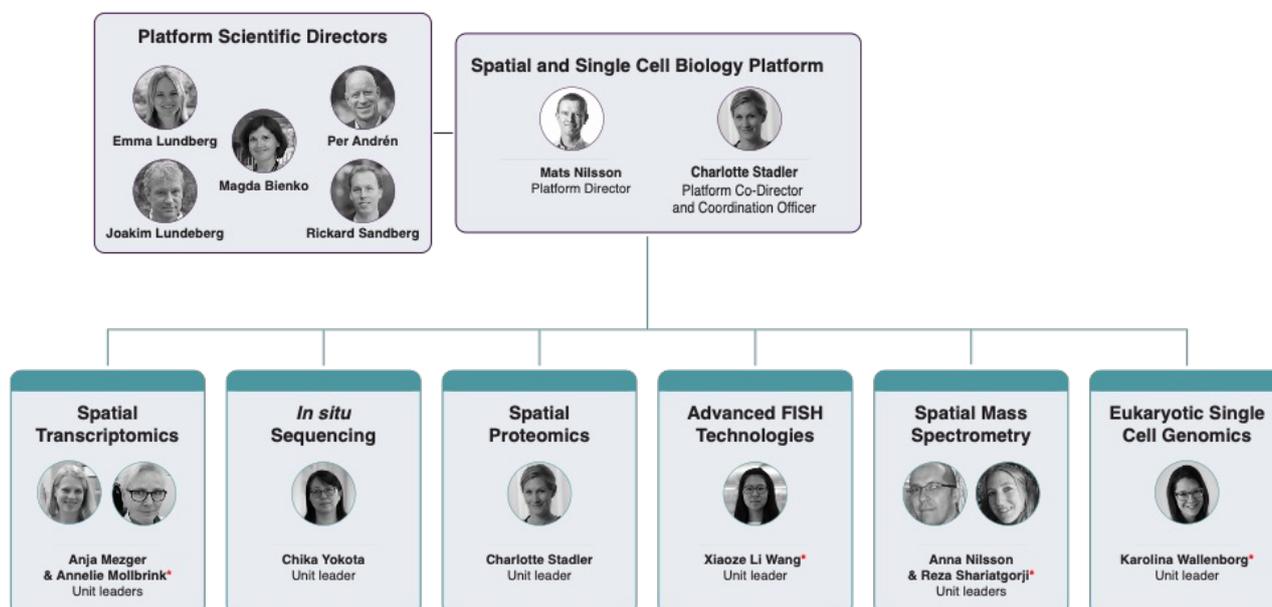
Organization and Management

Platform organization

The SSCB platform was formed after the evaluation in late 2020 with support from the IAB and brings together cutting-edge technologies for single cell and spatial omics, including spatial transcriptomics and *in situ* sequencing that both have been developed by researchers at SciLifeLab and KTH/SU respectively. The expertise is divided across 6 units with its own Head of Unit (HU) and covers all layers of omics in cells and tissue sections: genes, transcripts, proteins and small molecules (lipids, neuropeptides, metabolites). The Eukaryotic single cell Genomics unit (ESCG) was also organized under the SSCB platform to promote synergies. The platform has been organized according to SciLifeLab steering documents and is led by platform director (PD) Mats Nilsson and co-PD Charlotte Stadler. The platform

has five scientific directors (PSD) and together with the HU's, PD and co-PD they form the Platform Management Group (PMG), equivalent to the platform steering group. Members of the PMG is also acting as steering group in the VR instrument grant received by the SSCB platform in 2021.

The Platform has also put together an extended platform management group (extended PMG) with representatives from the Bioinformatics platform, the Genomics Platform and Data Center to promote discussions regarding data analysis and single cell activities. No advisory board is formally in place, but we have suggested to SciLifeLab MG to make use of the SciLifeLab IAB to specifically advice the platform. An overview of the platform organization is shown below.



SSCB Platform organization as of today and with appointed Head Of units when the platform was formed. * Represents HUs who has left the platform for industry. The AFT unit has a new HU, Quentin Verron and the ESCG unit is currently lead by Anja Mezger.

Platform management

The platform meets on a monthly basis in two separate meetings. The PMG meetings are organized with a scientific focus to promote new collaborations, grant initiatives, share relevant updates and handle strategic matters related to steering and governance. The HU meetings focus on operational matters and platform activities and are lead and called upon by the co-PD. Further each HU has their own team meetings within the respective unit and joint meetings across the units occur for several user projects. The PC and co-PD also meet with the Infrastructure Director on a monthly basis. The platform also has close contact with the Precision Medicine Capability, mainly through the co-PD Charlotte Stadler. A first SSCB platform retreat was held in

May, 2022.

Apart from the formal platform meetings, numerous connections across SSCB units and the associated research groups (of the PSDs) has been formed and each unit further engage in inter-platform collaborations and collaborations with industry. More details on this is presented in the respective unit reports and a few connections/collaboration partners are highlighted below:

- **SP** interacts closely with the precision medicine capability and is a co-applicant in VR grants together with the Integrative Microscopy Unit and Spatial Mass Spectrometry respectively. A research collaboration

with Lunaphore and Navinchi Diagnostics is initiated and a 3 year contract with Pfizer will start in 2023 where the unit will be involved to some extent.

- **SMS** have ongoing projects and collaborations with Spatial Transcriptomics and In situ sequencing, and have initiated a collaboration with Spatial Proteomics. SMS also have collaboration with the DDD platform. The unit will advertise their metabolomics capabilities at SciLifeLab together with the Swedish NMR center in Gothenburg and Swedish Metabolomics Centre in Umeå.
- **ST** is part of NGI (genomic platform) and we have a 2-year grant together with NBIS for pipeline development for spatial data.
- **ISS** has close collaborations with SMS, SP and AFT for integration of the multi-omic technologies and

data analysis. The unit also has worked closely with BIIF to further support users' data analysis, and has collaborated with the KGE unit.

- **ESCG** is co-applicant in a VR infrastructure application with the aim of setting up and coordinate a national single cell network. Other co-applicant are NGI, Clinical Genomics, Genomics Medicine Sweden and Skåne University Hospital.
- **AFT** is engaged in collaborations with in Situ Sequencing and Spatial Proteomics for multi-omics technology development.

The platform has also established connections with VIB and the co-director visited VIB in Ghent and Leuven in May to discuss organisation of spatial and single cell omics set-up and to gain some knowledge on their use of new technologies with the Tech Watch Team.

Development, Achievements and Plans

Platform development until today (i)

The SSCB was founded as a platform after the 2020 evaluation where it was recognized as a flagship capability with huge potential, given the expertise in spatial omics at Scilifelab. In 2021, the SSCB platform received 30 MSEK funding from VR Infrastructure to invest in instruments dedicated to the platform and to promote the infrastructure. Some of these instruments have now been installed and unique service using these instruments has been initiated. ISS and SP has expanded their respective teams thanks to other funding sources that has allowed for additional staff to be recruited at temporary positions. Together this has increased the throughput in number of projects (report increase of number of projects) and due to efforts in outreach activities the overall fraction of non-local users is now above 60 %. The platform steering and governance has come into place and has been described above. Our actions related to the other specific terms and conditions are summarized below.

Platform Specific Terms and Conditions

Technology developments and integrated omics

In 2020 three of the SSCB platform PSD's received a VR-Research Environment Interdisciplinary grant (30 MSEK) for developing integrated spatial omics methods to study dementia. Since then and in line with the Terms and Conditions from SciLifeLab, several projects across units have been initiated to promote integrated omics method development. This includes combining in situ sequencing with multiplexed IF, in situ sequencing with spatial mass spectrometry, multiplexed IF and DNA/RNA FISH and spatial transcriptomics with spatial mass spectrometry. A few manuscripts are in preparation and expected to be implemented within the coming two years. A VR-Infrastructure application has been submitted by SMS and

SP to develop a method for combined spatial proteomics and metabolomics. Several joint user meetings have been held and we see an increased number of user projects with multiple omics methods being requested.

Integrate AFT into the SSCB platform

The pilot unit AFT has been working closely with the SP unit and work towards implementing multiplexed DNA FISH as a new service of the platform. AFT and SP holds a TDP for this purpose

and a manuscript is in progress to demonstrate an integrated protocol for multiplexed DNA FISH and immunofluorescence using the Akoya platform.

Training, technology transfer and outreach activities

The ISS and the ST unit successfully hosted an EMBO practical course in May 2022 (Spatial analysis of gene expression in tissues) with huge success. The ST, SMS and SP units have hosted students, postdocs, and users to transfer know how of the respective technologies. ST has also assisted a research group in Lund to implement Visium in their lab. The PCO has held several educational/outreach webinars across Sweden and the platform (all HUs) has planned two webinars during the fall (<https://www.scilifelab.se/event/spatial-and-single-cell-biology-webinar/>) to educate the research community about the methods and services available. Given the uniqueness of the service and the use of expensive instruments and reagents, practical courses for many students are not yet feasible. Instead, dedicated training and involvement of the user in their accepted project is favorable and something we will increasingly offer.

Contribute to cross platform and Scilifelab Precision Medicine Capability

This has mainly been described in the previous section about cross platform collaborations. Contacts with the Precision Medicine Scientific leads have been strengthened and the platform is part of a VR application to promote the Precision medicine capability. The SP and SMS units currently work on proof-of-concept projects with help from TDP funding. SP is setting up a panel for lung cancer diagnosis using multiplexed IF in collaboration with Region Skåne. The SMS unit is developing single neuron imaging in combination with highly multiplexed immunohistochemical MALDI-MS imaging of proteins.

Enhance collaboration with Bioinformatics platform and Data Centre

We have appointed Johan Rung from Data Center and Åsa Björklund and Carolina Wählby from the Bioinformatics platform as members of the extended PMG of the platform. We have had several meetings with BIIF to discuss and overall

workflows of analysis support and involved them in several user meetings at an early stage. We have dedicated a person in the SP unit to be responsible in the communication with Data center.

ESCG, single cell networks and coordination with the Genomics Platform

We have started working on this by identifying relevant collaborators/infrastructures and submitted a VR infrastructure application (see above in collaboration part) with the aim to create such a network and set up a nationwide single cell capability. Jessica Nordlund from NGI has joined our extended PMG but the circumstances that ESCG lost their HU has put these efforts on hold. We see positive on the interim appointment of Anja Mezger at NGI to lead the ESCG unit and to continue the single cell networking activities.

Platform development plans for 2023 and beyond

Organization

We see several possibilities for creating a more stable and effective organization that promote synergies and leverage on the expertise. This involves merging of small units into larger entities and we suggest to go from 6 to 3 units within the coming year by making the following changes:

1. Fuse the pilot AFT unit into SP unit. This is supported by both units. See more under funding.
2. Merge ISS and ST units into one unit. This is supported by both HUs; Chika Yokota and Anja Mezger.

Further, we discuss with NGI and the Genomics platform on how to organize the spatial and single cell activities between the platforms as this continues to create confusion at the organizational level but also undermines our respective opportunities to gain additional resources. We (SSCB) see two main options here:

1. NGI transfer all their *spatial* omics activities to the SSCB platform and SSCB takes responsibility for seeking external funding for these activities. ST then becomes a formal unit of the SSCB platform (merged with ISS as suggested above) and SSCB can seek other funding for a *spatial omics infrastructure* without competition from NGI and vice versa. NGI continue to lead the single cell activities, including the ESCG unit, as part of the Genomics platform.
2. The entire spatial capability becomes part of NGI. Here

we suggest the spatial units of SSCB (AFT+SP, ISS+ST and SMS) to form a *spatial division*. This division within NGI would be the same as the current SSCB platform, and reporting to SciLifeLab can be kept the same. As a suggestion to NGI, a single cell division can be run side by side within NGI (including ESCG). The spatial division of NGI should preferentially be represented in the NGI steering group. We believe this solution could benefit both NGI and the SSCB platform as we bring together the strengths of both – the project management resources of NGI and the expertise in spatial omics from SSCB.

These are ongoing discussions and a meeting with the PD and co-PD of the Genomics platform has been planned later in September. We hope to make progress in the discussions until the meeting with MG in beginning of October.

Technology developments, increased service and education

We will continue our work with developing and implementing multi omics service that span across several units. We still see it as crucial to expand on our own ability to give analysis support to our users and will put resources into improving this. The spatial omics field is developing rapidly and we need to seamlessly integrate analysis with data generation until standardized analysis packages exist. We will continue to collaborate with the Bioinformatics platform but we cannot be dependent on them to analyze the data we generate.

Request for additional funding 2023–2024

The platform requests a budget increase of 6,2 MSEK from 2023 and an additional increase of 2,8 MSEK from 2024. In general, the increase is needed to employ more staff scientists to meet the growing number of user requests, and to implement and offer the new multi omics services

and technologies being developed within the platform. The platform also has an expensive instrument park and even with increased user fees we cannot cover the service contract costs as it would become too expensive for the users. Since the platform was formed, we lost 4 HUs to the

industry and we have a hard time to compete with industry in new recruitments due to salary levels and non-permanent positions. As a result, the small units spend lots of time to train new members instead of providing service to our users while lacking a stable core. The SSCB platform with its associated researchers has a huge potential to make impact and continue to be a world leading example of the SciLifeLab model, but the slim budget greatly limits our opportunities to leverage from our capability. We participated in VR's "behovsinventering" and received very high scores (A2) but were nevertheless not included in the next infrastructure call. Increased core funding from SciLifeLab will be absolutely essential for running and developing this national platform. The budget justification of each unit is summarized below.

Advanced FISH Technologies

We suggest to keep the pilot unit and its funding as it contributes to the platform uniqueness, mainly in the area of spatial genomics and DNA FISH. To better implement and integrate the service we suggest to merge the AFT unit into the SP unit, and redistribute 1 MSEK of the funding to KTH. The remaining budget of 0.5 MSEK to KI is needed to generate the FISH probes and image single molecule FISH projects in the Bienko Lab.

Spatial Proteomics

We apply for increased base funding of 0.7 MSEK in 2023 to contribute to instrument service contracts that will cost the unit 500-600 kSEK/year. This is a new cost as we previously did not have our own instruments. Due to already expensive reagents in our projects, we estimate our user fees to cover for 50 % of the service contracts. In addition, we see the need for offering a licensed analysis software to speed up and improve direct analysis support as this is a huge bottleneck. Relevant software and modules for this is in the range of 300 kSEK/year. While our service has greatly developed and expanded, the costs for the unit has increased. For 2024 we request additional 1 MSEK to fund 1 more FTE to retain the staff needed to run the service. It is worth noting that the unit has less funding from SciLifeLab today (3 MSEK) compared to when it started in 2013 (3.7 MSEK). In order to become less vulnerable and more effective as an infrastructure we suggest to merge the AFT pilot unit into the SP unit. The SP unit has already gained knowledge of some of the AFT service, mainly due to the

joint TDP project CODEX-DRP where a combined protocol for FISH and multiplexed IF is being developed.

In situ sequencing

The unit requests an additional 2 MSEK funding in 2023 and additional 1 MSEK in 2024 from Scilifelab that allows for increasing the number of FTEs, which is essential to 1) strengthen analytical support for users, 2) enhance technical development activities, and 3) expand the user base. The throughput (number of projects) has successfully doubled from 2019 to 2022. The unit is currently operating at maximum capacity, however, the number of FTEs needs to be increased as the increase in the number of requests, the operation of the new ISS system and the need for additional analytical support.

Spatial Mass Spectrometry

A bottle-neck is the limited number of FTE's that currently is employed with the funds we receive from SciLifeLab. Especially data analysis (using vendor/instrument specific software, regions-of-interest determination, statistical analysis) is very time-consuming. Further, considering our very expensive instruments (three MS imaging instruments, 9-13 MSEK each) it is difficult to fully charge the depreciation and service contract costs to our users, because the users fee would be too expensive. An increased budget would enable us to provide our services to a significantly larger number of projects and users.

Eukaryotic Single cell Genomics

In order to meet the high demand for single cell projects, we request 1M SEK/year in additional funding which would add another FTE to the unit and would allow us to accept more projects. As of now, approximately 20-30% of requested projects cannot be accepted due to too few FTE's.

Spatial Transcriptomics (ST)

We request 1 M SEK/year as a base funding which would allow us to dedicate 1 FTE to work on ST. As of now, ST does not receive any platform specific funding through SSCB. Furthermore, if the unit were to receive additional funding, we would have the resources to focus on platform integration using the new CytAssist instrument which can transfer the RNA from one tissue section to another glass slide. This has the potential to enable ST, ISS and SP or even new modalities from one tissue section.

Request for expanded funding 2023–202

Specify all costs in kSEK

Unit	SciLifeLab funding 2022 (kSEK)	Requested ScilifeLab funding 2023 (kSEK)	Requested SciLifeLab funding 2024 (kSEK)
Spatial Proteomics	3000	3700	4700
Spatial Mass spectrometry	2000	3500	4500
In situ sequencing	1900	3900	4700
Advanced FISH pilot	1500	1500	1500
ESCG	5000	6000	6000
ST	0 (from SSCB)	1000	1000

Spatial Proteomics

Spatial and Single Cell Biology Platform (Web links for Unit: [Webpage](#), [Publications](#))

Basic Information

Head(s) of Unit: Charlotte Stadler
PSD(s): Emma Lundberg
SciLifeLab Unit since: 2013
Host university: KTH
FTEs: 4.0
FTEs financed by SciLifeLab: 2.5

Funding in 2021 (kSEK)

SciLifeLab: 3500
SciLifeLab Instrument: 600
VR: 2800
Vinnova: 150
Other: 900
Total: 7950

Resource Allocation 2021

Academia (national): 50%
Academia (international): 20%
Internal tech. dev.: 20%
Industry: 10%
Healthcare: -
Other gov. agencies: -

User Fees 2021

Total (kSEK): 175
Reagents: 90%
Instrument: 10%
Salaries: -
Rent: -
Other: -

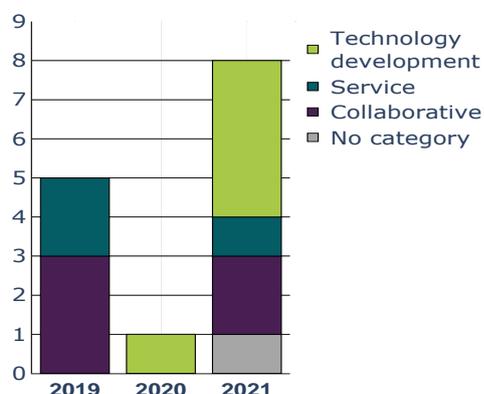
User Fees by Sector 2021

Academia (national): 42%
Academia (international): 58%
Industry: -
Healthcare: -
Other gov. agencies: -

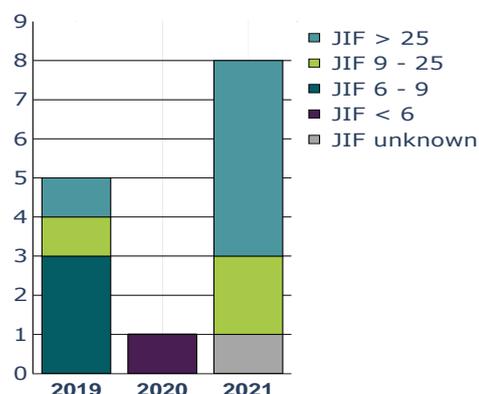
Services

- Highly multiplexed immunofluorescence of cells and tissues using CODEX
- Custom antibody conjugation for CODEX
- High throughput immunofluorescence of cells using Human Protein Atlas antibodies
- Initial image analysis support of generated data

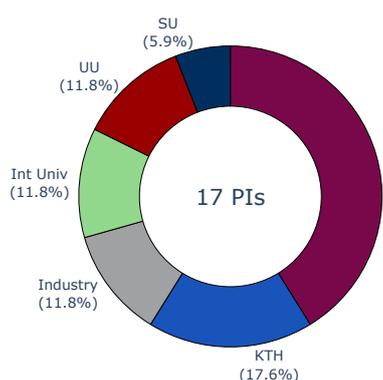
Publication by Category



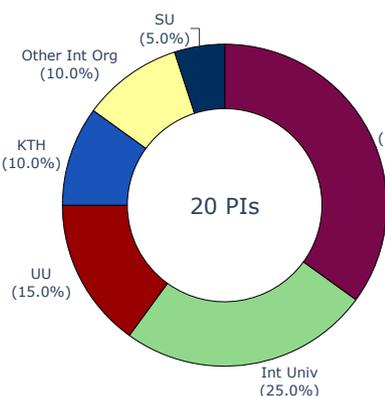
Publication by Journal Impact Factor



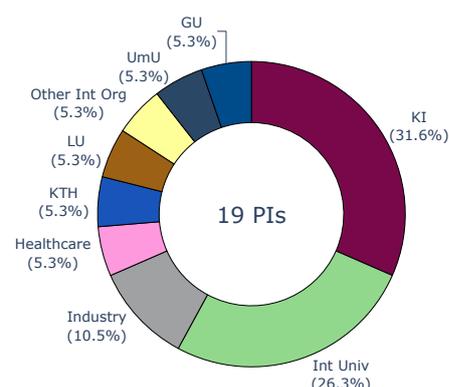
Users 2019



Users 2020



Users 2021





Unit:	Spatial Proteomics
Platform:	Spatial and Single Cell Biology

Development, Achievements and Plans

Developments and achievements (i)

The SP unit has refocused its service since last mid-term in 2018. From being an HPA centric facility doing high throughput IF in cell lines we performed our first highly multiplexed tissue projects in the fall of 2020 and are now among the world leading facilities offering highly multiplexed spatial proteomics. The first user publication was recently published (**PMID: 35688160**) and 4 others are in preparation. The unit has been selected as beta tester for two cutting-edge instruments (CODEX in 2018 and COMET in 2021 respectively) and is now one of a few labs in Europe offering service with these technologies from Akoya Biosciences and Lunaphore respectively. The unit has gained global reputation and been invited to international conferences and workshops to present the activities of the unit, including European Association of Cancer Research and Advances in Proteomics and Metabolomics, the latter as a keynote presenter. The platform scientific director Prof Lundberg has published several high impact factor research articles on the topic of spatial proteomics (**PMID: 35859028, PMID: 35590073, PMID: 34819669, PMID: 34811556**). The HU was also a scientific organizer of an international conference organized by VIB in the spring of 2022 – Next generation Protein Analysis and Detection including spatial proteomics and co-author of a Nature publication for subcellular proteomics (**PMID: 34549195**).

Since last evaluation we have worked hard to increase national spread of users. Webinars have been organized in Gothenburg, Linköping, Umeå and Örebro, as well as within the STORM network and other national workshops. The unit has also co-hosted outreach events with Lunaphore and Akoya Biosciences. The fraction of users outside of Stockholm has increased from <40 % in 2020 to 70 % in 2022. The unit has also hosted a PhD student from Sahlgrenska academy during his project and from October the unit will host a visiting post doc during his project to educate and transfer knowledge.

The collaborations in which the unit is involved has also increased since last evaluation with ongoing industry collaborations with Swedish and international partners including Atlas Antibodies, Navinci Diagnostics and Lunaphore. We also perform service projects with larger pharma companies like Roche and thanks to our platform scientific director Prof Emma Lundberg we will be involved in a 3-year project with Pfizer. Within academia the unit has initiated projects with most of the other units of the platform (all but ESCG). Together with the ISS and AFT we received a grant from VR (2020-06182) in 2020 for developing integrated spatial omics methods and 2021 another VR grant (2021-00189) of nearly 30 MSEK was granted to SP, ISS, SMS and ST for new instrumentation. The unit also worked together with CBCS during the COVID pandemic where the subcellular landscape of SARS-CoV-2 infected cells was explored in combination with drug repurposing (doi: <https://doi.org/10.1101/2022.03.29.482838>). We have also reached out to BIIF and directed more of our users this way for analysis support early on in the projects. However, we still find it crucial to offer image/spatial analysis support ourselves, as we've noticed that this is where most of our users struggle and fail.

The unit currently holds two TDP projects, one in collaboration with the AFT unit to develop an integrated automated FISH/IF protocol and implement it into a new service, and one focusing on proof of concept projects (PoC) for multiplexed IF applications within the precision medicine

capability. Using the COMET platform we have developed a 7 plex panel for diagnosis of primary lung cancers in collaboration with Region Skåne and this project is now continuing to expand the panel to cover markers of lung metastases.

Last, since 2021 the team has grown from 3 to 6 people, mainly due to other external grants but also from contribution of the extra start-up funding from SciLifeLab of 0.5 MSEK. This has been a crucial step to create a more stable operation with establishment of SOPs, standardized workflows and analysis pipelines, and it has enabled internal development of the service, while creating a more balanced workload on the team members.

Plans for 2023 and beyond (ii)

These 2 years of hard work has put us in a position where we are now ready to truly create impact and leverage on our resources. With several new instruments in place, a (temporarily) larger team and well-established contacts with industry and research groups across Sweden and Europe, we can accept more projects while still offer better project support. The new instruments also enables more diverse projects and thus expansion of the service portfolio to range from moderate to hyperplex imaging. For project support the most important parameter involves analysis, which cannot be fully dependent on external units. Therefore we will focus on improving this part and we are currently exploring licensed software that could potentially speed up analysis workflows. We have already invested in a good analysis workstation and a powerful GPU funded at the platform level to meet the demands on data analysis software. Further, control of the analysis of the data is important for internal development projects and will be crucial in our contribution to the precision medicine capability.

For technology developments we will work together with Prof Emma Lundberg and her team to further develop and implement *Deep Visual Proteomics* (PMID: **35590073**) as a new service. Our multiplexed spatial proteomics will be combined with deep mass spectrometry in the Proteogenomics unit and create a cross-platform capability that combines the benefits of spatial information from imaging with the depth of mass spectrometry.

We will also increase our efforts into the precision medicine capability by conducting PoC projects in collaboration with pathologists and clinicians, mainly on lung and bladder cancer. This is a strategic move in our long-term mission of implementing spatial proteomics as a core pillar within future precision medicine.

In addition, we await decision on two VR grants both focusing on technology development and implementation. If granted, we will contribute to the development of 3D tissue spatial proteomics together with the Integrated Microscopy Technologies/Advanced Light Microscopy unit which is the requested next step of spatial omics. The second application is together with the Spatial Mass Spectrometry unit and the platform scientific director Prof Per Andrén, where we will develop a new method for simultaneous protein and small molecule detection (metabolites, neuropeptides etc). This is in line with the SSCB platform mission to further integrate spatial omics methods and fills a current gap within the spatial omics field that has mainly been focused on combining transcriptomics and proteomics in space. While these plans are ambitious, we see that many of these activities are needed to continue the successful journey and continue to gain attraction in the rapidly moving field.

Our concern is the stability of the team, as this is the core in a successful operation. Despite the expansion from 3 to 6 members since last evaluation, only 2,25 FTE are covered by SciLifeLab funds and 3 out of 6 holds temporary positions from external grants. This undermines long term stability of the team and makes the operation vulnerable as new staff have to be recruited and trained on a yearly basis. Increased base funding from SciLifeLab would allow to permanently employ a larger part of the team that would serve as a highly skilled foundation of the operation. We see external grants as opportunities for increased activities and improvements of the service and will continue our efforts in gaining additional funding. However, the unit needs a critical mass and stable core and 2,25 FTE cannot fill that role.

Spatial Proteomics

Budget 2022

Costs	2022
Personnel cost	3 935 805
Other personnel costs	0
Depreciation	1 693 333
Service and license costs	345 000
Other operating costs	550 000
Premises costs	820 500
Other costs	75 000
Sum costs (kSEK):	7 419 638

Revenues	2022
Funding from SciLifeLab	3 000 000
VR-NMI	600 000
EPIC-XS	900 000
VR- TDP (fr 2018)	1 200 000
Vinnova	270 000
Scilife TDP 2021	150 000
Scilifelab base budget (from 2021)	500 000
SciLife Instrument call /year	600 000
VR instrument funding/year	1 000 000
User fees	350 000
Sum of Revenues	8 570 000

In Situ Sequencing

Spatial and Single Cell Biology Platform (Web links for Unit: [Webpage](#), [Publications](#))

Basic Information

Head(s) of Unit: Chika Yokota
PSD(s): Mats Nilsson
SciLifeLab Unit since: 2019
Host university: SU
FTEs: 2.1
FTEs financed by SciLifeLab: 1.3

Funding in 2021 (kSEK)

SciLifeLab: 2400
EU: 860
Total: 3260

Resource Allocation 2021

Academia (national): 50%
Academia (international): 35%
Internal tech. dev.: 15%
Industry: -
Healthcare: -
Other gov. agencies: -

User Fees 2021

Total (kSEK): 822
Reagents: 95%
Instrument: 5%
Salaries: -
Rent: -
Other: -

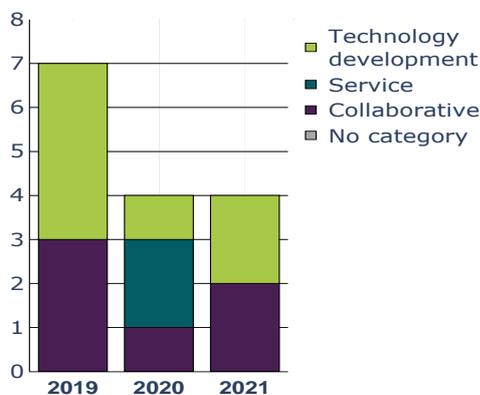
User Fees by Sector 2021

Academia (national): 73%
Academia (international): 27%
Industry: -
Healthcare: -
Other gov. agencies: -

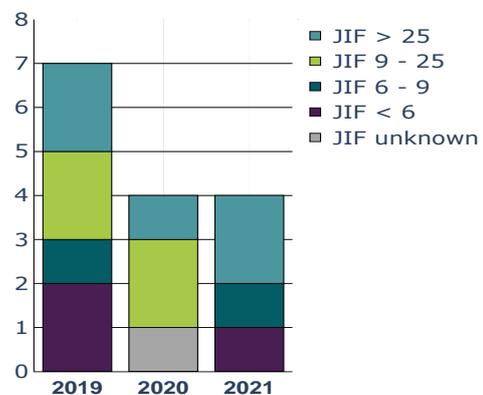
Services

- Multiplex mRNA profiling in situ
- In situ sequencing probe and assay design
- In situ sequencing library preparation and training
- In situ sequencing barcode decoding
- Primary image analysis (transcript and cell coordinates in tissues)

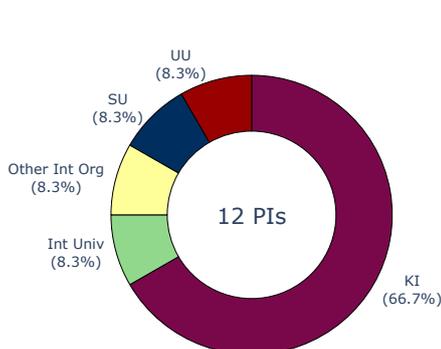
Publication by Category



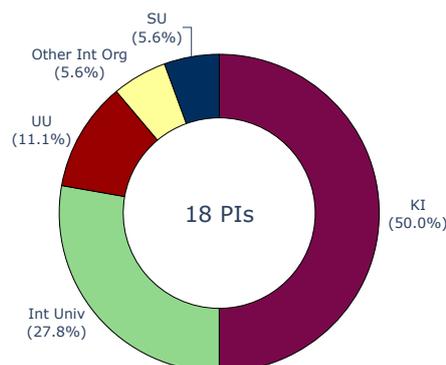
Publication by Journal Impact Factor



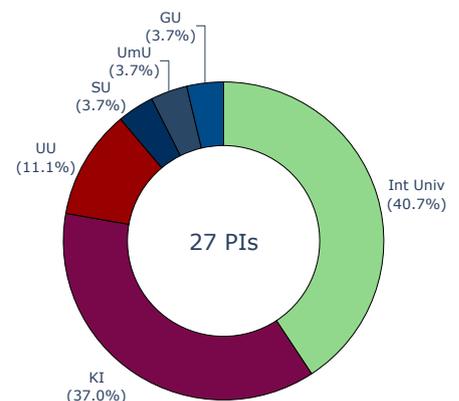
Users 2019



Users 2020



Users 2021





Unit:	In Situ Sequencing
Platform:	Spatial and Single Cell Biology

Development, Achievements and Plans

i) Development and Achievements

Technology development

A major technological breakthrough at our unit in the past two years has been the dramatic increase in the quantity and quality of data obtained from the same sample due to improvements in ISS reagents. When the unit started operations in 2019, a conventional method, the SBL method was used and highly evaluated by users. Then the SBH method (<https://doi.org/10.1093/nar/gkaa792>) was introduced to our service in 2020, successfully increasing resolution by 2-3times compared to the SBL, followed by the implementation of the 10X Genomics' products, direct RNA reagents, into our services in 2021, and have succeeded in detecting signals with 5X higher sensitivity than the cDNA-based SBH method (<https://doi.org/10.1038/s41598-022-11534-9>). Thus the unit was able to provide services with a tenfold increase in sensitivity over a three-year period. The implementation of the new reagents required a fundamental change of the analytical pipelines, and optimization conditions to accommodate a variety of samples, which we think is a great achievement considering the limited staff of our unit (2 FTEs until January 2022). The unit have a program partnership with 10X Genomics for the direct RNA reagents, which is available only to selected partners. The fact that we are the only partner in Sweden and one of the few in Europe to have such a program contract attests to our high reputation. Together with the ST unit, we are procuring two fully automated ISS systems (Xenium, 10x Genomics). The installation will be completed by the end of this year.

Scientific Achievements, New user groups and Outreach efforts

Since the establishment of the unit in 2019, we have made efforts to expand the number of users. By participated in several webinars, including STORM network (December 2020) and DiGifZ in Germany (September 2021), where HU gave invited talks about the ISS technology, the unit received great interest for its services and offerings. The unit have also succeeded in further expanding the user base through outreach events arranged by EASI-Genomics, an EU project in which the unit participates. As a result of these efforts, the number of users outside of Stockholm has increased from 31% (4 projects out of 13) in 2019 to 57% (15 projects out of 27) by 2021. The ISS unit also contribute to high-quality research proven in publications of users in high-impact journals such as Nature (collaboration work in 2021:<https://doi.org/10.1038/s41586-021-03775-x>, service in 2022: <https://doi.org/10.1101/2021.04.16.439912> in bioRxiv, and just accepted by Nature). In addition, participation in three EU projects, including EASI-Genomics (HUGODECA and DiscovAIR), demonstrated that the unit is widely recognized as a provider of state-of-the-art technology.

Training and education

The ISS and the ST unit successfully hosted an EMBO practical course in May 2022 (Spatial analysis of gene expression in tissues) at SciLifeLab. This was the first practical course, bringing in experts from a broader community of spatially resolved transcriptomics technologies. As such, the

course attracted a high level of interest with more than 100 applications received in less than four weeks, and inquiries continued to come in even after the application period. The course was attended by 24 participants selected from Sweden and other countries around the world and was very well received by the participants. A separate bioinformatic course organized by NBIS and BIIF provides course participants with the skills necessary to interpret data obtained by different spatial transcriptomics methods, and arrangements have been made to give priority to the EMBO course participants.

Cross-unit and cross-platform initiatives

The ISS, SP and AFT received a grant from VR in 2020 (2020-06182) for the development of integrated spatial omics methods. In addition, a 30 MSEK VR infrastructure grant (2021-00189) for expensive equipments was awarded in 2021 to install new instruments in the SP, ISS, SMS, and ST units. As part of our efforts to eliminate bottlenecks in our services, the unit works together with BIIF from the early stages of many projects and holding joint meetings to provide better analytical support to our users. We also have a collaboration with the KGE unit. This collaboration aims to combine CRISPR/Cas technology with the ISS method to establish a novel approach for in situ CRISPR-guided RNA detection.

ii) Development plans for 2023–2024

Since launching the facility in 2019, the unit has been constantly improving our technology and enhancing our services, and has expanded the staff from 2 to 3 FTEs. Significant progress has been made over the past two years toward improving service quality and throughput.

To further impact research in this area, we will incorporate fully automated ISS systems into our services next year. The Xenium system from 10X Genomics, is planned to be installed during 2022. Only five units of this system are currently scheduled for installation in Europe, and the ISS unit was chosen as one of the nodes. The new system will be put into operation in early next year, with the aim to provide service in the middle of next year. Implementation of the system will simplify operations, thereby increase throughput. In addition, the new system-compatible reagents developed by 10X are expected to have higher sensitivity than previous reagent (based on early data we have received, about a factor of 10 increase), permitting a wider variety of samples and scientific questions. This is particularly important for samples that are less well preserved, including clinical samples. We will continue offering service using "home brew" ISS reagents to support projects that will not be available on the Xenium platform, such as in situ mutation detection, multi-omics experiments, and other species than mouse and human.

Sweden (including our unit) has pioneered the field of spatial biology, and we will continue to provide beyond state-of-the-art technology that benefits national users. In an effort to keep our position as one of the leaders in this field, and to continue to contribute to research by providing scientists with the latest technology, the followings need to be addressed.

- 1) Enhance analytical support: Our analytical support currently depends on outside units, however, providing this support within the unit would be ideal. Hence, we are currently looking into implementing a system to speed up the analysis workflow. To meet our requirements for data analysis, a good analysis workstation that has a powerful GPU must be invested.
- 2) Multi-omic technology, and data integration: This is one of the platform's missions, and being able to take on this challenge is the strength of the platform.
- 3) Expanding the number of users, especially in the clinical and industrial fields, is essential to contribute to the field of precision medicine.

Increasing the number of FTEs is essential to achieve the above goals. First, dedicated personnel are needed to operate the new automated systems. Another major challenge is to improve analytical support, which also requires dedicated personnel. Therefore, at least 2 FTEs should be added to the current 3 FTEs, for a total of 5 FTEs. Currently less than 2 FTEs are covered by SciLifeLab funds, and external funding is essential to sustain staffing. Efforts to obtain external grants will continue, but the funds should be directed primarily to expanding and improving the research side of our activities, and the personnel that can be hired with external grants are extremely limited and have short tenures. For this reason, we will need a minimum of 4 SciLifeLab funded FTEs to run the expanded operations, and then we will aim to have 1 FTE funded by external grants and user fees.

Budget 2022

In Situ Sequencing

Costs	2022
Personnel cost	2 886 206
Other personnel costs	10 000
Depreciation	251 458
Service and license costs	0
Other operating costs	1 500 000
Premises costs	275 000
Other costs	205 500
Sum costs (kSEK):	5 128 164

Revenues	2022
Funding from SciLifeLab	1 900 000
Funding from financier X	251 458
Funding from financier Y	603 630
Funding from financier Z	632 700
User fees	1 750 000
Sum revenues (kSEK):	5 137 788

Advanced FISH Technologies

Spatial and Single Cell Biology Platform (**Web links for Unit:** [Webpage](#), [Publications](#))

Basic Information

Head(s) of Unit: Quentin Verron

PSD(s): Magda Bienko

SciLifeLab Unit since: 2021

Host university: KI

FTEs: 1.0

FTEs financed by SciLifeLab: 1.0

Funding in 2021 (kSEK)

SciLifeLab: 1250

SciLifeLab Instrument: 850

Total: 2100

Resource Allocation 2021

Academia (national): 25%

Academia (international): 75%

Internal tech. dev.: -

Industry: -

Healthcare: -

Other gov. agencies: -

User Fees 2021

Total (kSEK): 14

Reagents: 60%

Instrument: 10%

Salaries: 10%

Rent: 10%

Other: 10%

User Fees by Sector 2021

Academia (national): -

Academia (international): 100%

Industry: -

Healthcare: -

Other gov. agencies: -

Services

- DNA/RNA FISH probe and assay design
- DNA/RNA FISH probe production and training
- DNA/RNA FISH hybridization on cells/frozen tissues or FFPE tissue section and training
- DNA/RNA FISH imaging

Publication by Category

No publication data available

Publication by Journal Impact Factor

No publication data available

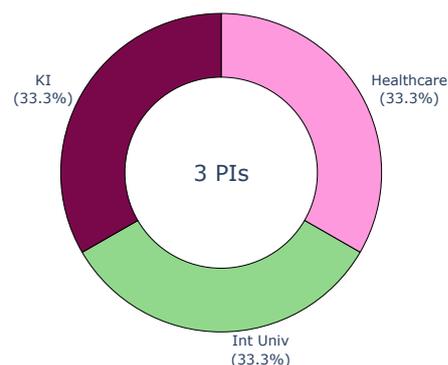
Users 2019

No user information

Users 2020

No user information

Users 2021





Unit:	Advanced FISH Technologies (AFT)
Platform:	Spatial and Single Cell Biology
Development, Achievements and Plans	
<p>i) Developments and major achievements</p> <p>Services</p> <p>The Advanced FISH Technologies (AFT) unit started its operations as a pilot facility in July 2021, offering a variety of fluorescence in situ hybridization (FISH) services to academic and corporate customers. Currently, the services offered include:</p> <ul style="list-style-type: none"> • Custom design and production of oligonucleotide (oligo)-based FISH probes • Full DNA/RNA oligo-based FISH services (from sample preparation to image acquisition) on cell and tissue samples (fresh frozen) • Custom assay development on challenging samples (FFPE) <p>We received so far 13 service requests through the iLAB facility management platform of Karolinska Institutet (KI). Of these, we successfully completed 4 projects (1 internal at KI, 1 external academic in EU, 1 external academic outside of EU, 1 corporate in Sweden) and are in the process of completing 3 additional projects (1 KI internal, 1 external academic in EU, 1 external academic out of EU).</p> <p>In spring 2022, our Head of unit, dr. Xiaoze Wang, who was in charge of all AFT operations, moved to a corporate position and therefore the capacity of the facility was abruptly interrupted. We have now recruited a new Head of unit (dr. Quentin Verron) and will soon expand the technical personnel of one unit. However, this personnel turnover has unavoidably slowed down our capacity of offering full services and therefore the only type of service that we have been able to offer in the second quarter of 2022 is FISH probe design and production. We expect that full-scale operations will resume at the beginning of 2023, when the training of our newly recruited technical assistant will be completed.</p> <p>R&D activities</p> <p>Being a pilot facility, a considerable amount of our efforts in AFT has been dedicated to expanding the knowledge base and toolkit with the goal of being able to offer to customers in Sweden and internationally a diverse spectrum of services.</p> <p>In particular, we have successfully pursued four major technology developments efforts, aiming at expanding the toolkit offered to our users in 2023-2024 and keeping SciLifeLab at the cutting edge of FISH method development:</p> <ol style="list-style-type: none"> 1. <i>Integration of DNA/RNA FISH with CODEX.</i> In a cross-unit collaboration with the Spatial Proteomics unit within our platform, we are working towards combining multiplex DNA/RNA FISH with multiplex protein detection on the CODEX instrument available at the Spatial Proteomics unit. This effort is supported by a SciLifeLab TDP grant (1 MSEK) and driven by dr. Verron in the AFT, who has tremendous expertise in microscopy and microfluidics. This 	

development has showed fruitful results on a pilot customer project and we are working towards a publication in 2023-2024.

2. *Integration of DNA FISH with ISS.* In a second cross-unit collaboration with the In Situ Sequencing (ISS) unit within our platform, we have performed a proof-of-principle experiment demonstrating the possibility of performing RNA detection by ISS followed by DNA detection with FISH on the same tissue section. This project is currently ongoing and we feel confident that we will be able to offer combined ISS and DNA FISH to the users of our platform from the second half of 2023.
3. *Development of FFPE-iFISH.* In collaboration with Prof. Anders Zetterberg at KI, we have built on our iFISH method (Gelali et al, Nat Comm 2019) and extensively scouted experimental conditions enabling ultra-sensitive DNA FISH in formalin-fixed paraffin-embedded (FFPE) tissue sections (patent application submitted). Our optimized protocol yields more than 5-fold higher signal-to-noise values compared to existing DNA FISH protocols, achieving essentially 100% detection efficiency of single loci in cancer tissue sections using iFISH probes composed of 2,000–4,000 oligos—a result that has not been achieved with any standard DNA FISH approach. We are now working towards implementing serial cycles of hybridization-imaging-stripping, with the goal of simultaneously imaging 40–50 genetic loci in each FFPE section. Previous work from Prof. Zetterberg has led to the identification of ~40 loci exhibiting copy number alterations in early-stage localized breast cancer, with a strong predicting value for deadly metastasis. We plan to submit a manuscript describing these results in 2023 and start offering multiplex FFPE-iFISH as service to our facility users from 2024 onwards.
4. *Development of Deconvolf.* Finally, we have developed an open-source image deconvolution software, Deconvolf (DW), which dramatically surpasses the performance of existing tools such as Huygens and DeconvolutionLab2, and considerably improves the sensitivity of single-molecule FISH (smFISH) and multiplex methods such as ISS and Oligo-FISSEQ. We have described DW in a manuscript that we are currently revising for *Nat Biotechnol* (<https://www.researchsquare.com/article/rs-1303463/v1>) and are now offering DW-based image processing as a service to the users of our facility.

Outreach and education

In order to popularize our activities, in November 2021 we organized a FISH workshop as part of the EU Horizon 2020 MSCA ITN network ‘Cell2Cell’, which dr. Magda Bienko is part of. The workshop, which took place at the AFT facility premises and was run by dr. Bienko and the AFT HU, dr. Wang, was attended by 19 young researchers from 10 academic institutions and companies around the EU. The participants actively learnt about FISH probe design and production, sample preparation, imaging and analysis, and ran their own FISH experiment under the supervision of drs. Bienko and Wang.

ii) Development plans for 2023–2024

With the departure of our Head of unit in spring 2022, we realized the fragility of having only one full-time employee in the AFT facility. Therefore, we have now recruited a research assistant who will work alongside the new Head of unit, dr. Verron and hopefully contribute to expand the AFT users base. However, since we cannot recruit more personnel due to limited funding, we propose that a more sustainable solution is to merge the AFT unit with the Spatial Proteomics unit, within our platform. This would allow a more efficient and coordinated use of resources, as well as faster technology integration between the units, while still allowing us to continue our R&D activities.

Advanced FISH Technologies

Budget 2022

Costs	2022
Personnel cost	1 882 973
Other personnel costs	0
Depreciation	190 009
Service and license costs	3 690
Other operating costs	73 800
Premises costs	150 000
Other costs	0
Sum costs (kSEK):	2 300 472

Revenues	2022
Funding from SciLifeLab	1 400 000
Funding from financier X	800 000
Funding from financier Y	0
Funding from financier Z	0
User fees	150 000
Sum revenues (kSEK):	2 350 000



Unit:	Spatial Transcriptomics
Platform:	Spatial and Single Cell Biology

Development, Achievements and Plans

Developments and major achievements:

Technology development:

The first method that was available to users through the Spatial Transcriptomic (ST) platform worked only on fresh frozen tissue. Biobanks have huge collections of FFPE tissue samples as these can be easily stored and their morphology is well preserved. However, until recently, it was not possible to apply spatial transcriptomics to FFPE samples and this vast resource could not be utilized. We have now implemented a protocol for FFPE samples and successfully completed our first pilot study. Since 10X Genomics released the FFPE kit, we have seen a steady increase in demand for spatial projects using FFPE tissue.

The 10X Visium protocol for fresh frozen tissue is completely manual and thus, prone to technical variability and throughput is limited. In collaboration with Stefania Giacomello's group at KTH, we worked on an automated workflow to increase reproducibility and throughput. The results are now published and robot scripts are available to the scientific community and the automated service is available for users at our facility.

We now have access to a new instrument, the Cytassist, which enables the spatial analysis of FFPE samples collected on a regular glass slide by transferring the RNA to Visium array. Pathologist can directly evaluate tissue sections by microscopy and if the area-of-interest is present, the glass slide can be sent to NGI for further transferring of the RNA and processing with a Visium FFPE kit. This will simplify our tissue sectioning workflow and will have a positive impact on both quality and throughput.

Scientific achievements:

In total during this period we have had 16 projects whereof 13 are national and of them 8 are regional. Twelve projects are on fresh frozen samples and 4 are FFPE samples.

Cross-unit initiatives:

In May, we co-organized the EMBO course "Spatial analysis of gene expression in tissues" together with the In Situ Sequencing unit with 24 participants (23 international and 1 national). The course was both practical and theoretical and aimed at deepen the participants' understanding of the different spatially resolved transcriptome mapping techniques.

Outreach

In early spring 2022, we held a talk during a webinar at Scilifelab with around 100 participants. Before the summer we have strengthened up our team with a new colleague to be able to meet the demands of projects.

Developmental plan 2023-2024:

We have initiated an industry collaboration to set up a workflow to combine immunofluorescence staining and spatial transcriptomics on the same tissue section. This will give a more complete understanding of the spatial relationship between the proteome and transcriptome.

In case of increased funding to the spatial transcriptomic unit, we will work on a full platform integration using the CytAssist with the aim to enable ST, ISS and codex or even new modalities on the same tissue section.

Comments to the reviewers:

As the unit does not receive any platform specific funding but is funded through NCI, there is no dedicated FTE who can focus on ST user projects and technology development. Thus, additional funding would enable us to take on more user projects and focus more on technology development.

Spatial Mass Spectrometry

Spatial and Single Cell Biology Platform (Web links for Unit: [Webpage](#), [Publications](#))

Basic Information

Head(s) of Unit: Anna Nilsson, Reza Shariatgorji
PSD(s): Per Andrén
SciLifeLab Unit since: 2021
Host university: UU
FTEs: 4.2
FTEs financed by SciLifeLab: 2.0

Funding in 2021 (kSEK)

SciLifeLab: 1500
UU: 3500
SSF: 2000
Total: 7000

Resource Allocation 2021

Academia (national): 60%
Academia (international): 5%
Internal tech. dev.: 20%
Industry: 10%
Healthcare: 5%
Other gov. agencies: -

User Fees 2021

Total (kSEK): 410
Reagents: 14%
Instrument: 22%
Salaries: 45%
Rent: 5%
Other: 14%

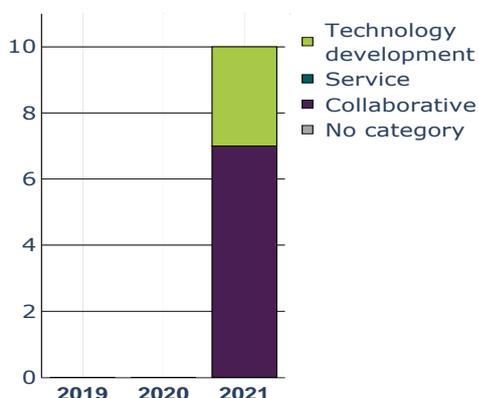
User Fees by Sector 2021

Academia (national): 25%
Academia (international): -
Industry: 75%
Healthcare: -
Other gov. agencies: -

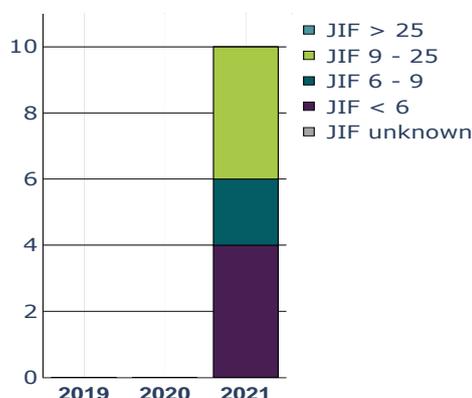
Services

- Project planning, pilot study design
- Mass spectrometry imaging of neurotransmitters, metabolites, peptides, lipids, and drugs
- Method optimization for detection of target compounds
- Mass spectrometry imaging data analysis and analysis support

Publication by Category



Publication by Journal Impact Factor



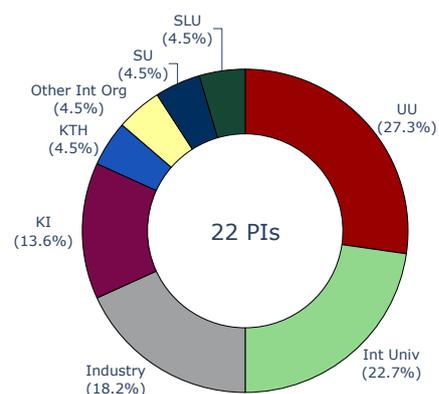
Users 2019

No user information

Users 2020

No user information

Users 2021





Unit:	Spatial Mass Spectrometry
Platform:	Spatial and Single Cell Biology
Development, Achievements and Plans	
<p>i) Developments and major achievements</p> <p>Technology developments We have developed protocols for a) embedding small fragile specimens (e.g., zebra fish brains) using cryo-microtome cutting, b) integration of MALDI mass spectrometry imaging (MSI) with spatial transcriptomics using the same tissue section (manuscript in progress), c) new on-tissue derivatization (reactive MALDI matrices – chemical tools) enabling sensitive detection of carbonyl, carboxylic acid, and aldehyde metabolites (manuscript in progress), and d) MALDI MSI profiling of nanoliter volumes of biofluids (cerebrospinal fluid) for disease characterization (manuscript in progress).</p> <p>Scientific achievements We have published in total 17 papers (2021–July 2022). Key publications, i.e., method developments papers, are the following: a) Spatial visualization of comprehensive brain neurotransmitter systems and neuroactive substances by selective in situ chemical derivatization mass spectrometry imaging. <i>Nature Protocols</i>, 2021 (7):3298-3321, b) Mass spectrometry imaging identifies abnormally elevated brain L-dopa levels and extrastriatal monoaminergic dysregulation in L-dopa-induced dyskinesia. <i>Scientific Advances</i>, 7(2):eabe5948, and c) Neuropharmacokinetic visualization of regional and subregional unbound antipsychotic drug transport across the blood-brain barrier. <i>Mol Psychiatry</i>, 26(12):7732-7745. We were recently funded by a VR Research Environment grant, Interdisciplinary Research (2021-03293, 30 MSEK, 2022–2027), where Scientific Directors from two other units of the SSCB platform were co-applicants (Prof. Mats Nilsson, Prof. Emma Lundberg; Prof. Per Andrén, PI). The aim is to study Parkinson’s disease dementia and Lewy Body dementia using a multiomics approach.</p> <p>New user groups The following new groups have used our Unit: a) Dr. Henri Leinonen, School of Pharmacy, University of Eastern Finland, Kuopio, FI (neurotransmitter imaging of the eye), b) Prof. Per Gerde, KI and Inhalation Sciences Sweden AB (drug distribution in lung), c) Doloradix AB, Uppsala and Prof. Ken Welsh, UU, a Vinnova funded collaboration (targeted and untargeted imaging of muscle pain source in humans), d) Prof. Ed Levin, Duke University, Durham, NC, USA (neurotransmitter imaging of zebra fish brains), e) Prof. Svante Winberg, Dept. of Medical Cell Biology, UU (neurotransmitter imaging of zebra fish brains), f) Dr. Liam McDonnel, Fondazione Pisana per la Scienza Onlus, Pisa, IT (neurotransmitter characterization of organoids), g) Prof. Vladimir Havlicek, Acad Sci Czech Republic, Prague, CZ (neurotransmitter imaging of stroke model), h) Dr. Egle Cekanaviciute, Space Biosciences Research Branch, NASA Ames Research Center, San Francisco, US and Stefania Giacomello, SciLifeLab and KTH (neurotransmitter imaging of mice from the International Space Station).</p> <p>Outreach efforts A number of seminar, presentation and workshop activities has been held to increase the visibility of our Spatial Mass Spectrometry unit, such as: 210120 – Web meeting/presentation, H. Lundbeck A/S, Denmark and Waters Corp., UK; 210204 – Web meeting/presentation, SciLifeLab Drug Discovery platform; 210412 – Web presentation, Bruker Daltonics Nordic Mass Spectrometry Imaging meeting; 210603 – Web meeting/presentation, Orion Corp., Espoo, FI; 210608 – Web</p>	

presentation, Waters Corp., UK, International Mass Spectrometry Imaging meeting; **210829** – Web presentation, RDPA (Recent Developments in Pharmaceutical Analysis) conference, Modena, IT; **211004** – Seminar, Space Biosciences Research Branch, NASA Ames Research Center, San Francisco, US and Stefania Giacomello, SciLifeLab; **211109** – Seminar, Dept. of Pharmaceutical Biosciences, UU; **211126** – Seminar, Dept. of Clinical Neurology, KI; **211211** – Presentation, Role of Mass Spectrometry in Neurodegenerative Disease Research, Amer. Soc. Mass Spectrom. (ASMS), Asilomar, CA, US; **220512** – Seminar at the University of the Witwatersrand, Johannesburg, SA; **220607** – Presentation at ASMS Annual Conference, Minneapolis, MN, US; **220621** – Presentation at 2nd Annual Meeting of Swedish Chemistry Society (SWECEM2022); **220702** – Workshop, ULLA Summer School 2022 in Uppsala (July 2-9). Summer School for 200 PhD students from 10 universities across Europe.

Training and education

The following PhD students and postdocs have received on-site training in MALDI Mass Spectrometry Imaging: **a)** Emanuela Salviati, PhD student, Department of Pharmacy (DIFARMA), University of Salerno, Fisciano, IT (4 month); **b)** Dr. Bram Heijs, PhD, Leiden University Medical Center, Leiden, NL (3 weeks); **c)** Hands-on training of participants from the ULLA summer school (2-day workshop).

Contribution to cross-unit and cross-platform initiatives

Within the SSCB platform we have ongoing method development projects and collaborations with Spatial Transcriptomics and In situ sequencing, and have recently initiated collaboration with Spatial Proteomics. We also collaborate with the DDD platform (drug imaging). To increase our visibility even further we will advertise our metabolomics capabilities together with the Swedish NMR Centre, Gothenburg and the Swedish Metabolomics Centre, Umeå.

ii) Development plans for 2023–24 and beyond

a) The laboratory is in the process of acquiring an additional MALDI-MSI instrument (13.2 MSEK) which will be installed in end of 2022, funded in part through a VR-Infrastructure grant (no. 2021-00189) awarded to the SSCB platform. The new instrument can perform integrated high-speed and high-spatial resolution MALDI imaging with ion mobility mass spectrometry. A novel, two-laser MALDI source increases the sensitivity by up to three orders of magnitude, depending on the analyte. Its trapped ion mobility separation feature facilitates isobaric or isomeric identification of molecules in complex biological tissue samples and improves molecule characterization. **b)** We will also develop and make available a new technology based on novel photocleavable mass-tags that enables highly multiplexed immunohistochemistry analysis of proteins in tissue sections. It enables simultaneous mapping of hundreds of targeted proteins based on MALDI-MS imaging. **c)** We aim to improve the MALDI-MS imaging spatial resolution to <1 µm by using morphology-guided deep learning, thereby enabling imaging of untargeted and targeted molecules in single cells directly in tissue sections. The approach will allow measurement of both small molecules (such as metabolites, neurotransmitters, lipids, glycans, neuropeptides) and targeted macromolecules (such as proteins) in the same tissue section by MALDI-MSI. **d)** We will develop on-tissue novel chemical derivatization tools to vastly improve the number of potential biomarkers visualized using our imaging platforms. Although we have made significant advances in the analysis of catecholamines and indolamines, reliable and sensitive imaging tools are still lacking for many important compound classes, e.g., neurosteroids **e)** With the new instrument (described above), which is a considerable faster imaging instrument than the ones we currently use, we expect to increase the number of projects and project throughput.

However, a bottle-neck is the limited number of FTE's that currently is employed with the funds we receive from SciLifeLab. Especially data analysis (using vendor/instrument specific software, regions-of-interest determination, statistical analysis) is very time-consuming. Further, considering our very expensive instruments (3 instruments, 9-13 MSEK each) it is difficult to fully charge the depreciation and service contract costs to our users, because the users fee would be too expensive. An increased budget would enable us to provide our services to a significantly larger number of projects and users.

Spatial Mass Spectrometry

Budget 2022

Costs	2022
Personnel cost	4 223 269
Other personnel costs	0
Depreciation	2 280 210
Service and license costs	1 324 129
Other operating costs	520 000
Premises costs	629 016
Other costs	0
Sum costs (kSEK):	8 976 625

Revenues	2022
Funding from SciLifeLab	1 500 000
Funding from UU (Kommittén för forskningsinfrastruktur)	2 500 000
Funding from UU-SciLifeLab (SFO funding from 2021)	1 000 000
Funding from VR Research Infrastructure grant (2021-00189, SciLifeLab Spatial Omics)	2 071 000
User fees	600 000
Sum revenues (kSEK):	7 671 000

Eukaryotic Single Cell Genomics

Genomics Platform (Web links for Unit: [Webpage](#), [Publications](#))

Basic Information

Head(s) of Unit: Anja Mezger
PSD(s): Rickard Sandberg
SciLifeLab Unit since: 2015
Host university: KI
FTEs: 5.0
FTEs financed by SciLifeLab: 5.0

Funding in 2021 (kSEK)

SciLifeLab: 5000
SciLifeLab Instrument: 496
KI: 2750
Total: 8246

Resource Allocation 2021

Academia (national): 90%
Academia (international): 5%
Internal tech. dev.: 5%
Industry: -
Healthcare: -
Other gov. agencies: -

User Fees 2021

Total (kSEK): 10300
Reagents: 80%
Instrument: 10%
Salaries: 10%
Rent: -
Other: -

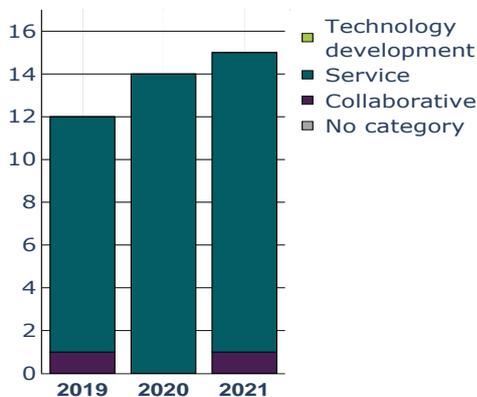
User Fees by Sector 2021

Academia (national): 95%
Academia (international): 5%
Industry: -
Healthcare: -
Other gov. agencies: -

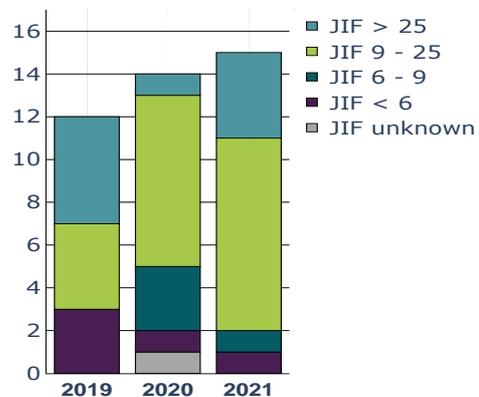
Services

- SC Genomics Analysis: Gene expression, Immune profiling, Chromatin accessibility, Epigenetics, Protein detection, Multiomics, Multiplexing, Sequencing, Biosafety level 1/2/3, Fresh/frozen/fixed samples
- Platform: Smart-seq3, 10x Genomics, Takara/iCELL8
- Project planning, Bioinformatics

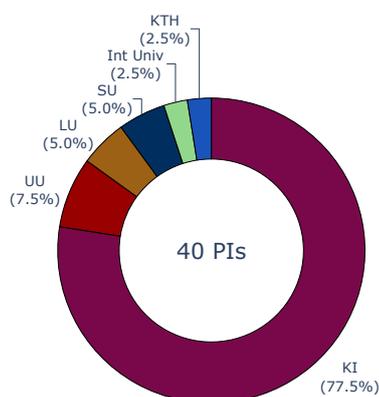
Publication by Category



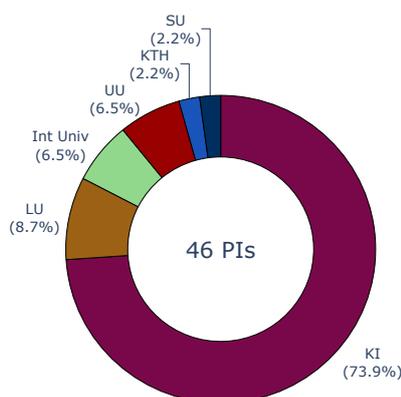
Publication by Journal Impact Factor



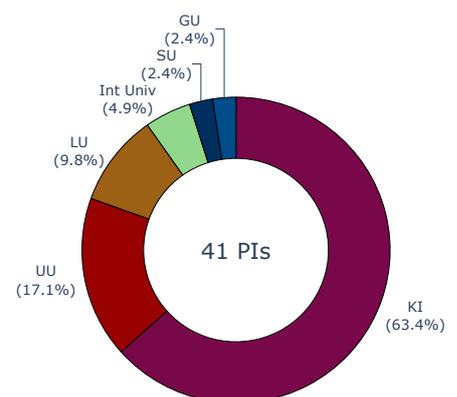
Users 2019



Users 2020



Users 2021





Unit:	Eukaryotic Single Cell Genomics
Platform:	Spatial and Single Cell Biology

Development, Achievements and Plans

Developments and major achievements:

Technology development

We have recently purchased a 10X ChromiumX Controller. This instrument allows increased sample throughput, doubling our sample processing capacity and higher cell numbers (20,000 cells without multiplexing and 60,000 cells with multiplexing per reaction). The Chromium X is the only instrument from 10X Genomics that is compatible with the new assays for fixed RNA profiling. This new controller will allow for accepting more and larger user projects as well as diversifying the types of assays runs. We will now be able to accept samples nation-wide as users can simply fix their cells and ship them to us, omitting the need for fresh, live cells. In connection with this, more staff has received training on how to run the instrument to allow for a more agile workflow with knowledge redundancy.

We are constantly updating our methods and technologies to be able to offer users state-of-the art methods and helping them to stay at the forefront of research. Currently, we are in the process to upgrade from Smart-seq3 to [Smart-seq3 Xpress](#) which was developed in the Sandberg lab. Smart-seq3 Xpress offers the benefit of using much smaller reaction volumes, decreasing consumables, and being substantially less time-consuming than smart-seq3 while retaining comparable quality. Therefore, having this method set up, will allow us to take in more projects, increasing turn-around time, while drastically reducing the cost for users (0.25 €/cell). We expect it to be available in Q3 2023.

Cross-unit/-platform initiatives

The entire unit participated in a platform retreat during spring in which the different facilities presented their technologies in an effort to further understanding and open up for cross-unit collaboration. The entire unit also participated in discussions on how to further increase exchange, benefit users and training in the future.

In an effort to make ESCG an attractive workplace and retain highly skilled employees, we have started together with NGI (part of genomic platform) to offer cross-training to interested staff. Furthermore, this will enable us to quickly adapt to changes in demand for specific technologies.

We have a close collaboration with the BSL3 facility on Solna Campus enabling users to run 10X Genomics' single cell assays on infectious samples.

In an effort to set up a national single cell network, we have submitted a VR grant application aiming to coordinate the development of a national infrastructure and capabilities in single cell genomics with a focus on clinical projects. The application is a joint effort between ESCG, NGI, Clinical Genomics, Genomic Medicine Sweden and the Skåne University Hospital.

Scientific achievements: 34 SmartSeq projects (50% non-Stockholm projects), 54 10X projects (11% non-Stockholm projects due to the limitation of requiring fresh samples)

ESCG contributes to high quality research, evidenced by 15 user publications (JIF > 25: 5 publications, JIF 9–25: 7) in 2021.

Plans for 2023–2024:

We are currently working on having the smart-seq3 Xpress method fully implemented and offered as a service to users. This will streamline sample processing, decrease turn-around time and price and will significantly increase our capacity.

We are planning to implement new assay types on our Chromium, such as ECCITE-seq (CRISPR+surface proteins+RNA), evaluate novel single cell methods (ParseBio etc.) and automate the library prep for our most common single cell protocols in order to standardize and decrease technical variance.

At the moment, users are limited to using our services during standard working hours, thus often limiting clinical researchers to process samples directly after surgery as these may occur outside our hours of operation. Therefore, we will evaluate if we can train users to run the 10X Chromium controller themselves, increasing their flexibility in accessing our infrastructure.

As a result of Karolina Wallenborg, HU, leaving, ESCG's operation was transferred to be under the leadership of Anja Mezger, HU at NGI. To ensure continuity, for both the staff and for the users, ESCG will merge permanently with NGI. This transition has already started and will be completed in 2023. ESCG will benefit from NGI's competence in quality assurance (e.g. usage of a LIMS system will be introduced), project coordination and experience in data handling and analysis.

Comments to the reviewers:

Karolina Wallenborg was an integral part of ESCG and with her leaving, a lot of knowledge was lost due to the very short transfer period (only 2 week overlap). This, and a shortage of staff, led to decreased capacity and longer turn-around times of user projects. With new staff starting and the planned recruitment of a new team leader, we anticipate that ESCG will be able to handle more projects and have a faster turn-around time.

However, the demand from our users exceeds by far our capacity and we will only be able to meet their needs with additional funding to hire new staff and by purchasing liquid handling robots to minimize hands-on time.

Eukaryotic Single Cell Genomics

Budget 2022

Costs	2022
Personnel cost	5 704 446
Other personnel costs	166 260
Depreciation	1 173 985
Service and license costs	623 842
Other operating costs	6 913 238
Premises costs	1 041 000
Other costs	0
Sum costs (kSEK):	15 622 770

Revenues	2022
Funding from SciLifeLab	5 500 000
KI Core funding	2 750 000
User fees	6 500 000
Sum revenues (kSEK):	14 750 000

► Metabolomics Platform

Platform Director: Thomas Moritz, SLU (acting)

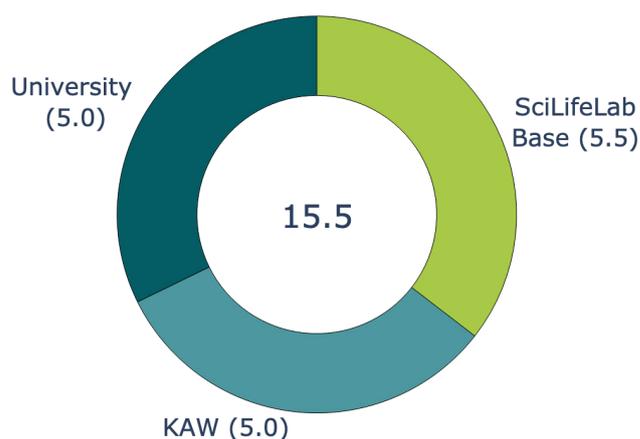
Co-Platform Director: Thomas Moritz, SLU

Platform Coordination Officer: Annika Johansson, UmU

Platform and Units SciLifeLab Funding 2021:

Unit	(MSEK)
Swedish Metabolomics Centre	3.0
Exposomics	1.9
PD, PCO, Platform Strategic Budget	0.6
Sum:	5.5

Total Funding 2021:



Platform Specific Terms and Conditions for Funding - Metabolomics

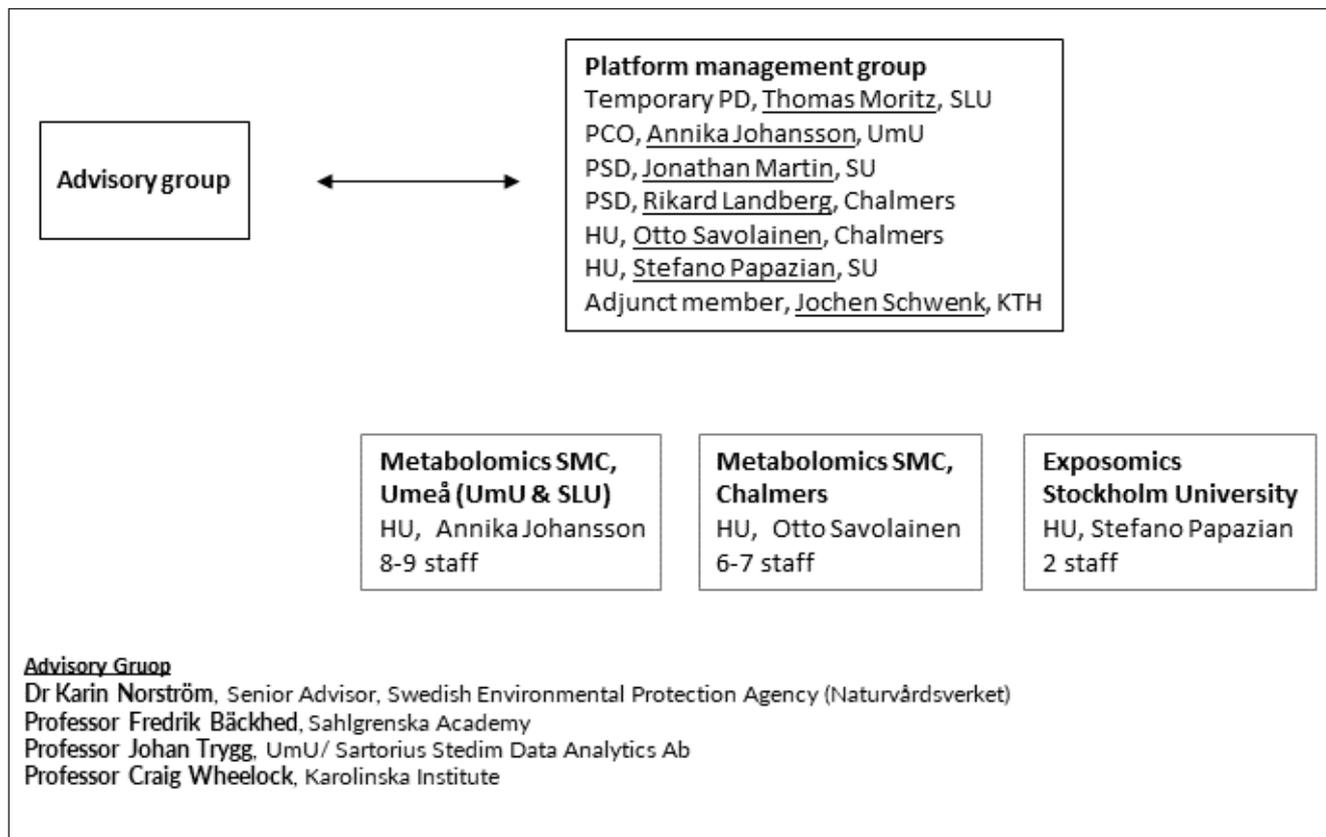
This document concerns the terms and conditions for SciLifeLab funding of the Metabolomics Platform and Units from 2021 and onwards and outlines the strategic direction MG wants the platform to take. The mid-term checkup in the middle of the 4-year funding period will focus on how well the Platform and Units have taken into account the items in this document.

- SciLifeLab funding to the Metabolomics Platform and Units is meant for providing nationally unique technologies and services within metabolomics and exposomics
- Ensure that SciLifeLab funds are used in the platform in a manner that aligns with the priorities and goals of the entire SciLifeLab organization
- Together with the SciLifeLab management suggest a clear platform governance and steering structure according to the suggested general policy for governance and steering of SciLifeLab infrastructure
- Integrate and support the establishment of Exposomics as a Pilot Unit to be evaluated again in 2022
- Enhance collaboration and coordination between the Metabolomics nodes at Umeå and Chalmers to optimize guidance and service offerings to users
- Contribute to cross-Platform and -Unit use with e.g. the Clinical Proteomics and Immunology platform and the Swedish NMR Centre at GU and UmU
- Contribute to the Precision Medicine and Planetary Biology capabilities
- Enhance collaboration with the Bioinformatics platform and Data Centre to establish FAIR data sharing and links to the DDLS initiative, as well as integration of healthcare data

Organization and Management

The Scilifelab Metabolomics Platform operates as a national service provider and knowledge resource for small molecule analysis in metabolomics and exposomics. The Platform and

its activities are led through a Platform Management Group with representation from the individual units in Stockholm, Gothenburg and Umeå.



The Advisory Board should be kept informed by the Platform Management Group on the range of current technologies and services available. The role of the Advisory Board is to advise on emerging opportunities or challenges, scientific development, and long-term strategy. The first SAB meeting is planned for December 2022 in connection to a platform

retreat organized in Stockholm by the Exposomics unit.

The Platform Management Group has meetings 3–4 times per semester, more often if needed. During the spring the platform organised its first Head of Unit meeting.

Development, Achievements and Plans

Development

From the Platform strategic budget for 2021 a large proportion of the money was allocated to allow for an open call for “Exposome-Metabolome Interaction Pilot Study” to highlight and advertise the new Exposomics unit. The call was launched in February 2022 and 5 relevant applications were received. Following an internal Platform review, 2 projects were selected and will be performed as Platform cross-unit activities throughout 2023 (1 with full support, 1 with support in method development).

In a joint TDP project, (Hans Stenlund (UmU), Carl Brunius (CTH), Jonathan Martin (SU)) the Platform has started develop routines, modules and pipelines with a specific focus on enabling and accelerating LC-MS and rapid-

Fire-MS data preprocessing to support SciLifeLab's DDLS initiative. The overall goal is to overcome problems and challenges associated with combining big data from different studies and instruments in order to reuse and aggregate large amounts of previously acquired raw data, while operating in accordance with FAIR principles.

The first Metabolomics Platform retreat was arranged in Umeå in December 2022. This was the first time for the platform and the platform personnel at the different sites to meet and interact in real life. The meeting was arranged as a lunch-to-lunch meeting with overview presentations and discussions. Hanna Kultima from the Data Centre and Björn Nystedt from NBIS were also invited to introduce their work

and discuss the platforms needs. Exposomics will host the next Platform meeting in December 2022 at Campus Solna.

In March 2022, the platform organized (with NBIS) a (1-day), held onsite at SciLifeLab Uppsala with the goal was to introduce NBIS personnel on aspects of mass spectrometry small-molecule applications. The Platform highlighted current needs for bioinformatic support, and as an outcome NBIS appointed a contact person for metabolomics and exposomics.

In Aug 2022 the Platform submitted the joint VR application: "User-friendly Comprehensive Metabolomics and Exposomics for Precision Health" with Otto Savolainen as the main applicant and co-applicants from all other partners. The Swedish NMR centre is also included as a co-applicant with the goal to further integrate LC-HRMS and NMR techniques.

Future plans

In the upcoming year the Metabolomics platform will expand our collaborations with other platforms units. We will explore collaboration opportunities with the Swedish NMR centre (discussions already initiated by the joint VR application) and the Spatial Mass Spectrometry unit to explore the possibility of screening for metabolite/pollutant distribution within biological tissues. We will start these cross-platform/unit interactions by inviting representatives from the different units/platforms to present their technology at our PMG meetings.

With the newly appointed NBIS contact person we aim to improve the collaboration and communication with the Bioinformatics platform. Both for specific user projects but also for future method development. In the future, NBIS and SciLifeLab Data Centre will be central in developing high-performance computing pipelines and safe cloud-based long-term data storage system to support sustainable FAIR practices across the Exposomics and Metabolomics users.

The major goal for the Exposomics unit through 2023–2024 will be to consolidate the growing user-base and expand its network across academic research, health agencies and private companies. In 2023, projects which demonstrate Exposomics applications on national cohorts, e.g. the *Swedish CardioPulmonary bioImage Study (ScapIS/S3WP)* and the *Västerbotten Intervention Programme (VIP)* will be completed while other major projects will focus on breast cancer and exposure during pregnancy, effects of air pollution exposure on chronic obstructive pulmonary disease and indoor air pollution in European households. From a technological development, the input from the Exposomics unit to the whole Platform will allow to expand nontarget workflows for comprehensive analysis of human exposure towards environmental pollutants and integrate this data with metabolomics and other omics platform. In this context, collaborations within DDLS fellows will be instrumental to successfully integrate exposomics with

Moreover, the application fits into the SciLifeLab Precision Medicine capability, with the aim to investigate how to optimize the implementation of small sample volumes microfluidistic capillary devices (e.g. "Capitainer") in large cohort metabolomics analysis.

The Platform was also presented at the Planetary Biology Workshop in Heidelberg in May 2022 with Annika Johansson (UmU) as an invited panel member. The panel discussed possibilities and highlighted the importance of analysis of small molecules in the Planetary Biology Capability. SMC in Umeå has over 20 years of experience in the field of small molecule analysis in plants, and with its tight connection with the Umeå Plant Science Centre the unit is continuously developing within this field, a well fitted area in the planetary biology capability.

systems biology, and to link the effects of human chemical exposures to internal biological responses. As mentioned in the last IAB report, personell in the pilot unit will need to increase to withstand increase user demands and project volumes. To this end, Exposomics will invest user-fees from projects performed in 2022–23 to expand the unit staff, and new laboratory equipment (high-throughput robotics systems for extraction, evaporation, etc.) will be procured to scale-up/automate workflows.

SMC, will continue their focus on improved libraries and annotation rates to allow for biological interpretation of metabolomics data. Together with the CBMR Metabolomics Platform at Copenhagen University SMC will methodology development and particular on computational data analysis (including multi-omics strategies, chemoinformatic tools for metabolite annotation, and metabolite flux analysis) also in collaboration with the chemometrics group of Umeå University led by professor Johan Trygg.

Chalmers has a central role in the 2nd round of the national infrastructure SIMPLER (2023–2028). Chalmers will provide targeted and untargeted metabolomics data on samples from the clinical subcohort comprising >12 000 people. Methods for dietary biomarker panels will be applied and untargeted metabolomics methods will be tested on urine samples. We will also investigate if untargeted metabolomics can be conducted on small volume self-samples taken at home.

The long-term goal for the metabolomics platform is to establish it as an outstanding platform in its field, enabling world leading science within the field of small molecule analysis to be conducted in Sweden. This requires both a strong, sustainable and adaptable service organization, as well as as engagement and tight collaboration with national and international scientists to secure scientific development. Enabling metabolomics and exposomics data and support as an integral part of to large national initiatives, such as DDLS,

Precision Medicine and Biobanks/cohort infrastructures, and securing the data as an integral part of them will be a key success factor for these initiatives. This will require active collaboration with e.g. data centers and NBIS, together

with resource allocation from each stakeholder. The Metabolomics platform is committed to provide suitable tools, scientific development, data and support for achieving this.

Request for additional funding 2023–2024

Currently 70% of Exposomics base funding goes to salary and benefits of HoU (SP), and 30% to depreciation costs on the new Orbitrap instrument. In 2023, an increase in base budget of 750.000 SEK is required to support the recruitment of a lab manager. In longer term we project a laboratory technician to be hired in 2024/2025 to support increased project volumes.

SMC is currently funded 3 MSEK/y out of which 0.6 MSEK is funding for Chalmers. The size of internal and external analyses at Chalmers mass spectrometry facility in 2021 was in brief 26,143 analysed samples, 375 requests, 45 PI's served, highlighting an mismatch between the low funding and the provided service and scientific output. Chalmers

requires increased base funding in order to allow sustainable development of the platform for external users, especially for integrating the activities with data-driven precision health initiatives. We request an additional 1.5 MSEK base funding that will be directed to Chalmers. The funding will be used to recruit a staff scientist with expert competence in computational metabolomics data-analytics and will serve the development of the whole platform and will link to data driven precision health activities. The requested funding is also in alignment with the point raised by iab regarding Metabolomics funding.

Requests for expanded funding 2023–2024

Specify all costs in kSEK

Unit	SciLifeLab funding 2022 (kSEK)	Requested ScilifeLab funding 2023 (kSEK)	Requested SciLifeLab funding 2024 (kSEK)
Exposomics	1800	2550	2550
SMC (Chalmers)	600	1350	2100

Swedish Metabolomics Centre

Metabolomics Platform (Web links for Unit: [Webpage](#), [Publications](#))

Basic Information

Head(s) of Unit: Annika Johansson, Otto Savolainen
PSD(s): Thomas Moritz, Anders Nordström, Rikard Landberg
SciLifeLab Unit since: 2017
Host university: SLU, UmU, Chalmers
FTEs: 11.8
FTEs financed by SciLifeLab: 2.0

Funding in 2021 (kSEK)

SciLifeLab: 3000
SciLifeLab Instrument: 300
SLU: 2500
UmU: 2500
Chalmers: 1115
KAW: 5000
VR: 1389
Total: 15804

Resource Allocation 2021

Academia (national): 73%
Academia (international): 2%
Internal tech. dev.: 24%
Industry: 1%
Healthcare: -
Other gov. agencies: -

User Fees 2021

Total (kSEK): 7100
Reagents: 15%
Instrument: 30%
Salaries: 45%
Rent: 10%
Other: -

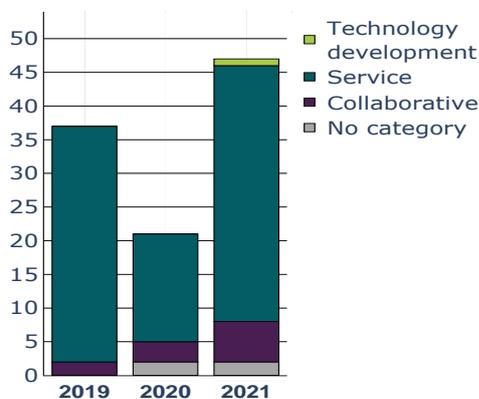
User Fees by Sector 2021

Academia (national): 85%
Academia (international): 10%
Industry: 5%
Healthcare: -
Other gov. agencies: -

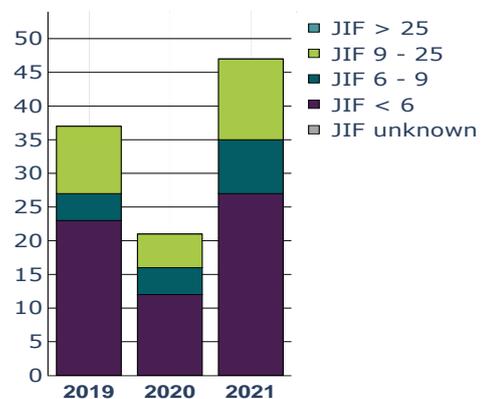
Services

- Untargeted and targeted metabolite profiling
- Targeted lipid profiling
- Study design and method development
- Basic statistics
- Open lab access services

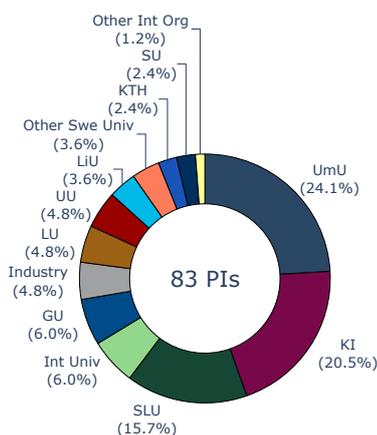
Publication by Category



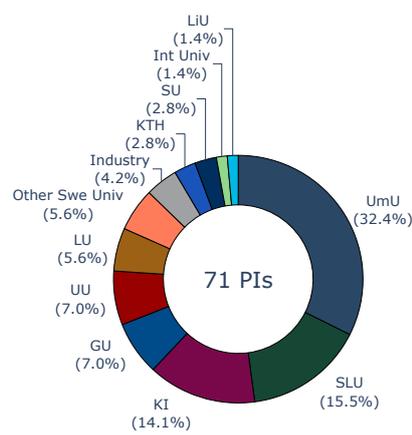
Publication by Journal Impact Factor



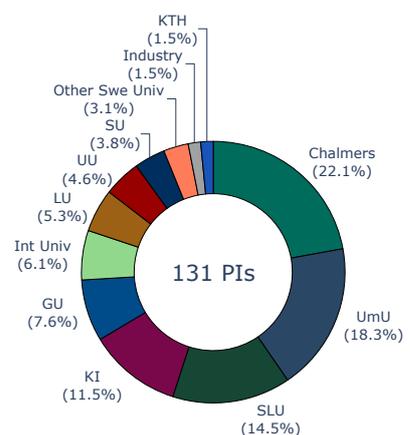
Users 2019



Users 2020



Users 2021





Unit:	Swedish Metabolomics Centre
Platform:	Metabolomics Platform
Development, Achievements and Plans	
<p>i) Developments 2021–2022 <i>Technology development and scientific achievements</i></p> <p>During 2021–2022 Several methods for targeted analysis developed at SMC upon request from users: Among these: glycoalkaloids (manuscript in preparation), mycotoxins (manuscript in preparation), and the bacteria signalling compound cyclic di-GMP. Within the Met 2.0 program targeted analysis (Hodek, Argemi-Muntadas, Khan, & Moritz, 2022, doi:10.1039/D1AY02143E) and profiling methods of polar metabolites by HILIC chromatography (manuscript in preparation) have been developed and will during the autumn be launched as a new service. The amino acid quantification platform has been transferred to 96 well plate format and sample preparation on our BRAVO robot to allow for larger sample cohorts in an automated manner. In 2021-2022, Chalmers developed and validated a method for quantitative extraction and LC-MS/MS measurement of vitamin D metabolites in small sample volumes collected in a at home setting (Capitainer). Further, a simultaneous vitamin D and metabolomics extraction method for blood samples were developed and compared against accredited laboratories with agreeing results, allowing reduced workload and cost for analyses requiring both vitamin D and metabolomics measurements in the same samples. The method is currently applied to samples from a large national research infrastructure, SIMPLER. Chalmers is also involved in several development projects aiming at establishing comprehensive targeted and semiquantitative/quantitative metabolite panels reflecting specific food intake and lifestyle patterns to be applied to prospective cohort studies and lifestyle intervention under the precision health paradigm.</p> <p>While metabolomics can provide instantaneous information on the metabolites in a biological sample, however metabolism is a dynamic process. To determine metabolic rates (fluxomics) metabolic precursors labelled with stable isotopes $^{13}\text{C}/^{15}\text{N}$ are being introduced to the biological system and the level of incorporation of $^{13}\text{C}/^{15}\text{N}$ into various metabolites can be measured by mass spectrometry. SMC has developed software to pre-process raw data and calculate the incorporation of stable isotopes in biological samples, including statistics (Liebsch et al., 2022, doi:10.1093/plphys/kiac244). In a collaboration with Dr Thomas McWilliams at Helsinki University, a detailed temporal analysis of the metabolome and lipidome was performed. The project revealed lipid biosynthesis and lipid droplets and DGAT1 to be a major regulators in the process of mitophagy (Long et al., 2022, doi:https://doi.org/10.15252/embj.2021109390).</p> <p>In a joint TDP project, SMC (Hans Stenlund, UmU) and CMSI (Carl Brunius, Chalmers) have developed routines, modules and pipelines with a specific focus on enabling and accelerating LC-MS data pre-processing to support SciLifeLab's DDLS initiative. The overall goal is to overcome problems and challenges that come with combining big data from different studies and instruments to reuse and combine large amounts of already existing raw data, in accordance with the FAIR principles.</p> <p>A large focus of Chalmers's work is also on the development of algorithms for computational metabolomics and mass spectrometry to enhance data quality, automation, and sample throughput. Recent developments include improved routines for data-preprocessing including improved peak</p>	

picking quality in the XCMS workflow (Pirtillä et al., 2022, 10.3390/metabo12020137), continuous monitoring of sample and data quality (submitted), and a complete workover of practices and algorithms for metabolite identification (ongoing).

Outreach efforts, Training and Education

On March 2022, the platform organized (with NBIS) a (1-day), held on-site at SciLifeLab Uppsala with the goal to train NBIS personnel on aspects of mass spectrometry small-molecule applications. In October 2021, SMC was invited to the CBCS group meeting to present the RapidFire technology and discuss future collaborations on drug candidate screening. One pilot project has now started, to confirm existing biochemical assay with mass spectrometry. SMCs ambitions are to continue this development, which would serve a completely new user group within and outside SciLifeLab.

Annika Johansson acting as Head of Unit and platform coordination officer has represented SMC and the platform at different events, among these the NMMP meeting in Ystad in May 2022, the Planetary Biology Workshop in Heidelberg in May 2022, she also attended the SciLifeLab Group Leader Retreat in Aronsborg in June. Chalmers is hosting the Nordic Metabolomics Society organization and currently, Otto Savolainen/Chalmers is serving as a member of the board. The whole SMC will be visible at the upcoming Nordic Metabolomics meeting in Copenhagen in September 2022. Three representatives of SMC attended the Metabolomics2022 meeting in Valencia in June, Chalmers was also represented at the ASMS2022 (Minneapolis, US) in June. Platform personnel at SMC have been teachers at courses at several different universities: “Genomfunktion” at Uppsala University, the “Functional genomics” course at Umeå University, the “Introduction to Plant Biology for Sustainable Production” course at SLU, “Proteomics and Metabolomics” and “Bioanalytical Chemistry” at Chalmers. Since September 2021, 15 new Open Access users have received training on-site at the instrument and for data pre-processing at SMCs Open Access Lab. In addition, individual training and guidance of PhD students, master students and postdocs entering the field of metabolomics via SMC have been performed (about 10).

ii) Development plans 2023–2024

One of the major bottlenecks in metabolomics today is the low proportion of annotated peaks. Annotation/ Identification in metabolomics relies on libraries of synthetic standards, when synthetic standards are not commercially available the annotation relies on mass spectral interpretation a manual and very tedious task. To meet the needs of the planetary biology capability where a high the number of species-specific secondary metabolites will be enormous, we will need to expand our knowledge and libraries for a broader panel of species. SMC received support from KAW in the Ukrainian Scientist Support Call to employ Oleksandr Ilchenko for one year. Oleksandr’s main task will be to create bacteria-specific databases and libraries. Also related to the planetary biology capability we will develop a plant hormone analysis service – currently only offered in Olomouc (Czech Republic). A panel that is expected to increase the proportion of international users of the Centre. SMC foresee that the requests for fluxomics analyses will increase, SMC will continue to develop the Fluxomics portfolio to follow metabolic turnover, and the ambition is to slowly move from collaboration studies into full service. SMC will also deepen the collaboration with the CBMR Metabolomics Platform at Copenhagen University. The collaboration focuses on methodology development and particular on computational data analysis (including multi-omics strategies, chemoinformatic tools for metabolite annotation, and metabolite flux analysis) also in collaboration with the chemometrics group of Umeå University led by professor Johan Trygg.

Chalmers will implement new instruments into service in 2023, requiring further testing and development both on data acquisition and in data-analytical workflows. In 2023, the development is expected to be finalized and put in service methods aiming at providing quantitative information on food intake and plant food phytochemicals. Further, Chalmers has a central role in the 2nd round of the national infrastructure SIMPLER (2023–2028). Chalmers will provide targeted and untargeted metabolomics data on samples from the clinical subcohort comprising >12 000 people. Furthermore, the metabolomics platform will investigate if metabolomics exposomics can be conducted on small volume self-samples taken at home.

Swedish Metabolomics Centre

Budget 2022

Costs	2022
Personnel cost	12 418 185
Other personnel costs	43 830
Depreciation	3 871 807
Service and license costs	2 521 397
Other operating costs	2 951 041
Premises costs	1 680 931
Other costs	0
Sum costs (kSEK):	23 487 191

Revenues	2022
Funding from SciLifeLab	3 000 000
Funding from KAW	5 000 000
Funding from UmU	2 500 000
Funding from SLU	2 500 000
User fees (Umeå)	3 100 000
Funding from VR Bio MS - operations	300 000
Funding from VR Bio MS - investments	743 571
Funding from VR infrastrucure - investments	345 740
Funding from financier Chalmers (base funding)	1 115 000
User fees (Chalmers)	4 579 471
Sum revenues (kSEK):	23 183 782

Exposomics

Metabolomics Platform (Web links for Unit: [Webpage](#), [Publications](#))

Basic Information

Head(s) of Unit: Stefano Papazian
PSD(s): Jonathan Martin
SciLifeLab Unit since: 2021
Host university: SU
FTEs: 1.2
FTEs financed by SciLifeLab: 1.0

Funding in 2021 (kSEK)

SciLifeLab: 1900
Total: 1900

Resource Allocation 2021

Academia (national): 5%
Academia (international): 5%
Internal tech. dev.: 90%
Industry: -
Healthcare: -
Other gov. agencies: -

User Fees 2021

Total (kSEK): 0
Reagents: -
Instrument: -
Salaries: -
Rent: -
Other: -

User Fees by Sector 2021

Academia (national): -
Academia (international): -
Industry: -
Healthcare: -
Other gov. agencies: -

Services

- Trace analysis by LC/GC with HR-MS detection using Orbitrap technology
- Combined target & non-target acquisition by DDA & DIA MS/MS, with electrospray/atmospheric pressure chemical ionisation
- Sample preparation in ultratrace clean laboratory for a range of samples
- In-line solid phase extraction for water/biofluids
- Structural elucidation of small molecules at trace concentrations in complex samples

Publication by Category

No publication data available

Publication by Journal Impact Factor

No publication data available

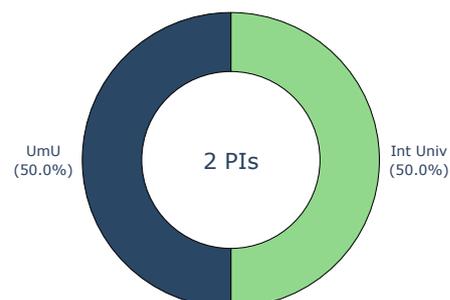
Users 2019

No user information

Users 2020

No user information

Users 2021



Unit:	Exposomics
Platform:	Metabolomics
Development, Achievements and Plans	
<p><i>i) <u>Developments 2021–2022</u></i></p> <ul style="list-style-type: none"> <i>• Technology development and scientific achievements</i> In 2021-22, activities in synergy with the Exposomics research group (JM) led to mature nontargeted methods for biofluids, tissue and water that are now provided as services for user researchers of the Exposomics unit. Main developments included: 1) validated procedures for extractions, sample clean-up, and mass spectrometry analyses of chemical pollutants (pesticides, PFAS, cosmetics, drugs, etc.) in complex sample matrices; and 2) the integration of FAIR and open science workflows for nontarget high-resolution mass spectrometry (e.g. see DOI: 10.1038/s43247-022-00365-1). These techniques are already applied in ongoing projects at the Exposomics unit, including for human plasma, seawater, and marine wildlife tissues. We also designed a novel passive air sampling media that we intend to apply for measuring personal airborne exposomes and global air pollution (<i>in review, minor revisions</i>); this media already supports air quality research in European households (Horizon Europe project <i>INQUIRE</i>) and is being adopted by Environment Canada's Global Atmospheric Passive Sampling Network. <i>• New user groups</i> In 2021-22 Exposomics engaged new users by participating in research funding applications spanning from technological development to environmental monitoring, including indoor air quality (<i>INQUIRE</i>; Bohlin-Nizzetto P., Norwegian Institute for Air Research - Horizon Europe/<i>funded</i>), adductomics for environmental health assessment (<i>AddECO</i>; Motwani H., ACES/SU – VR), coastal marine biodiversity and climate (<i>COAST-VOCM</i>; Roth F., ACES/SU - BNP Paribas), deep learning prediction for endocrine disruptive potency in complex chemical mixtures (<i>MS2Tox</i>; Krueve A., MMK/ACES - VR/3R), and methods for community-based high-throughput untargeted metabolite identification (<i>CoMetID</i>; Brunius C., CMSI/Chalmers -VR). Costs of analyses are budgeted for Exposomics (~100-400 samples/project), and methods developed in these programs will later be integrated into new services to attract new users in the area of monitoring, planetary biology and public health. <u>Over the last 9 months (Nov-21), we have secured ca. 3MSEK income in future user-fees based on current projects.</u> <p>In Feb-22, the call <u><i>Exposome-Metabolome Interaction Pilot Study grants</i></u> (sponsored by the Platform strategic budget) was launched to further engage users and advertise our unit. Following internal Platform review, out of 5 relevant applications received, 2 projects will be performed as Platform cross-unit activities throughout 2023 (1 with full support, 1 with support in method development); notably, a third project will likely proceed from external user fees, despite that it was not selected.</p> <ul style="list-style-type: none"> <i>• Cross-unit/cross-platform initiatives and outreach, training and education:</i> In Dec-21, the first Metabolomics Platform meeting allowed us to interact with the nodes in Umeå (SMC) and Gothenburg (Chalmers/CMSI). Exposomics will host the next Platform meeting in Dec-22 at Campus Solna. In Jan-22, Exposomics services were officially added to the <u><i>SciLifeLab Infrastructure</i></u> website, while the launch of Exposomics unit was widely advertised in newsletters at <u><i>ACES (SU)</i></u> and <u><i>SciLifeLab (Infrastructure Update)</i></u>. In Feb-22, a cover article detailing SU/SciLifeLab <u><i>Exposomics research</i></u> was published to further highlight services of our unit. 	

In Mar-22, Exposomics and Metabolomics co-organized a (1-day) [NBIS-workshop](#), held onsite at SciLifeLab Uppsala with the goal to train NBIS personnel on aspects of mass spectrometry small-molecule applications. The Platform highlighted current needs for bioinformatic support, and appointed a NBIS contact person. In Aug-22, Exposomics Metabolomics co-applied to the VR Infrastructure grant to develop high-throughput microsampling for metabolomics and exposomics in precision health research (main applicant Savolainen O., CMSI).

During 2022, SciLifeLab and Exposomics services were highly advertised in meetings, lectures, and conferences. In Jan-22, SP held a workshop dedicated to open science and FAIR tools with focus on Exposomics applications. The (online) workshop was attended by international colleagues from high-profile research institutes (Yale, Columbia University, Mount Sinai, etc). In Jun-22, SP held an (online) lecture on nontarget mass-spectrometry workflow in the context of the “*International Workshop on Air Pollution Monitoring & Effects*” organized by JM. In Mar-22, SP was invited by Chalmers/CMSI (Savolainen O.) as lecturer on Exposomics in a Bioanalytical chemistry MSc course. In May-22, SP attended and presented scientific results at international conferences of the *Society of Environmental Toxicology and Chemistry (SETAC)*, held in Copenhagen (DK) and in Durham (USA). In Jun-22, SP participated and networked in the SciLifeLab Group Leader retreat, actively discussing research overlaps with other HoUs and young DDLS fellows, especially in the context of Exposomics contribution to proteomics, precision health, and planetary biology. In Aug-22, SP participated in the Open House KI Science Park and presented the Exposomics facility to visiting stakeholders.

ii) Development plans 2023–2024

Exposomics infrastructures are receiving support elsewhere in Europe, in part through the Research Infrastructure for Environmental Exposure Assessment in Europe (***EIRENE***; ESFRI Roadmap 2021). SU participates in *EIRENE* and will host a workshop October 12th (JM, SP) with 8 other Swedish Universities to develop the associated application “*Swedish Infrastructure for Research on Environmental and Human Health Exposomics*” (***SIRENE***, 2023) to be submitted to VR in 2023 (Research Infrastructure of National Importance). This ongoing development should expand the national support for exposomics infrastructures in Sweden. In 2023, projects will be completed which demonstrate exposomics application on national cohorts, e.g. the *Swedish CardioPulmonary bioImage Study (Scapis/S3WP)* and the *Västerbotten Intervention Programme (VIP)*. Other projects will focus on breast cancer and exposure during pregnancy (Harlid S., Umeå University) and effects of air pollution exposure on chronic obstructive pulmonary disease (Wheelock C., KI). Another major project will address indoor air pollution for the Horizon Europe program *INQUIRE*.

In Dec-21, a new LC-Orbitrap instrument was procured to support our core services. The instrument installation was finalized in Aug-22 due to major delays by the vendor and some misconfiguration of gas-lines in the new Exposomics MS-lab (Alpha-1). Through 2023, Orbitrap services will be optimized to offer state-of-the-art acquisition on a dual column setup for parallel measurement of polar and semi-polar contaminants and endogenous metabolites. The goal for 2024 and beyond is to expand the current Exposomics workflows towards a unique variety of user applications in different sample types for extensive characterization of chemical pollutants and transformation byproducts from human biofluids, tissues, and environmental media. Notably, Exposomics research group (JM) and infrastructure unit (SP) agreed to move to Alpha-1, pending renovations in 2023. This will consolidate laboratory operations and create new synergy with Proteomics, including DDLS fellow (Edfors F.) with whom we collaborate and will apply for a “*Red equipment grant*”. Collaborations within DDLS national activities will be instrumental to successfully integrate exposomics with systems biology, and to link the effects of human chemical exposures to internal biological responses (i.e. metabolome, proteome, epigenome). NBIS and SciLifeLab Data Centre will also be pivotal in developing high-performance computing pipelines and safe cloud-based long-term data storage systems to support sustainable FAIR practices across the Exposomics and Metabolomics users, which will be trained to render their data open and accessible.

Throughout and beyond 2024, Exposomics will invest user-fees from projects performed in 2022–23 in new laboratory equipment to scale-up/automate workflows, and to expand the unit staff. High-throughput robotics systems for extraction, evaporation, and fast chromatography screenings will be procured. In Apr-22, the research engineer Athanassiadis I. (ACES/SU) formally joined the Exposomics facility (25%) as technician in laboratory preparations and GC-HRMS analysis.

Exposomics

Budget 2022

Costs	2022
Personnel cost	2 252 390
Other personnel costs	28 000
Depreciation	1 519 682
Service and license costs	1 756 842
Other operating costs	794 882
Premises costs	444 303
Other costs	0
Sum costs (kSEK):	6 796 099

Revenues	2022
Funding from SciLifeLab - 2021 (remaining after 2 months HU salary, Nov-Dec 2021)	1 655 392
Funding from SciLifeLab - 2022	1 800 000
SciLifeLab / Strategic-fund INFRA 2021-engångsutb nov, 400/1940015	200 000
Funding from ACES/SU Faculty (20% salary Scientific director +OH)	510 000
Funding from SFO/SU Science Faculty	1 000 000
Funding from ACES/SU - Jon Martin research grant (480 Exploris Orbitrap - 50% to the Unit)	880 000
Research engineer (funding from ACES/SU)	275 558
User fees	870 000
Sun of revenue	7 190 950

► Clinical Proteomics and Immunology Platform

Platform Director: Masood Kamali-Moghaddam, UU

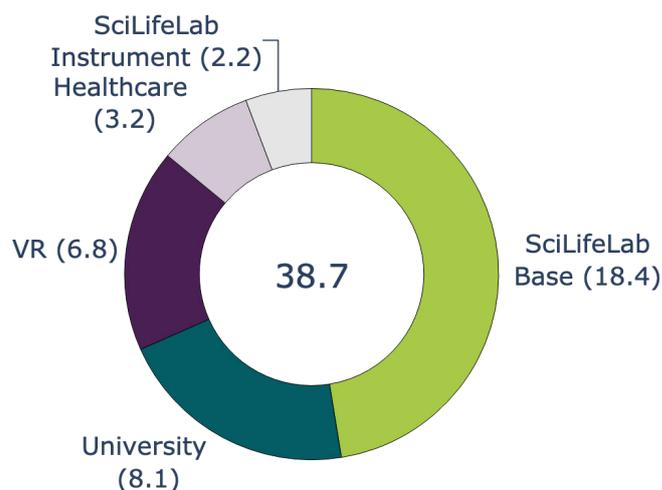
Co-Platform Director: Claudia Fredolini, KTH

Platform Coordination Officer: Claudia Fredolini, KTH

Platform and Units SciLifeLab Funding 2021:

Unit	(MSEK)
Autoimmunity and Serology Profiling	2.4
Affinity Proteomics	5.1
Cellular Immunomonitoring	5.6
Global Proteomics and Proteogenomics	3.0
Glycoproteomics	1.5
PD, PCO, Platform Strategic Budget	0.8
Sum:	18.4

Total Funding 2021:



Platform Specific Terms and Conditions for Funding - Clinical Proteomics and Immunology

This document concerns the terms and conditions for SciLifeLab funding of the Clinical Proteomics and Immunology Platform and Units from 2021 and onwards and outlines the strategic direction MG wants the platform to take. The mid-term checkup in the middle of the 4-year funding period will focus on how well the Platform and Units have taken into account the items in this document.

- SciLifeLab funding to the Clinical Proteomics and Immunology Platform and Units is meant for providing nationally unique clinical proteomics services with a focus on immuno-monitoring of people and patients
- Ensure that SciLifeLab funds are used in the platform in a manner that aligns with the priorities and goals of the entire SciLifeLab organization
- Define how to integrate the services under the new platform and the added value to the users.
- Together with the SciLifeLab management suggest a clear platform governance and steering structure according to the general *SciLifeLab Infrastructure Terms and Conditions for Funding* document
- Provide resources to engage in the SciLifeLab capabilities, integrating data and know-how from several different platforms
- Require supported projects to commit to FAIR data sharing
- Integrate functions and coordination between the Affinity Proteomics units in Stockholm and Uppsala.
- Contribute to the Precision Medicine and Biomarker Discovery capability, working together with the Clinical Genomics platform, GMS, biobanks, Metabolomics platform and the Bioinformatics platform.
- The platform is expected to play an important role in the development of the *Pandemic Laboratory Preparedness* capability.
- Enhance collaboration with Bioinformatics and Data Centre on promoting integration of technology and data-driven services, as well as integration of healthcare data.
- Contribute in data production for the DDLS program (precision medicine and diagnostics (precision medicine and diagnostics) with focus on data sharing.

Organization and Management

The CPI platform is composed by five units belonging to four Swedish Universities: Autoimmunity and Serology Profiling (ASP, KTH); Affinity Proteomics, nodes at Stockholm (APS, KTH) and Uppsala (APU, UU); Cellular Immunomonitoring (CIMMR, KI); Glycoproteomics (GP, GU) and Global Proteomics and Proteogenomics (GPP, KI).

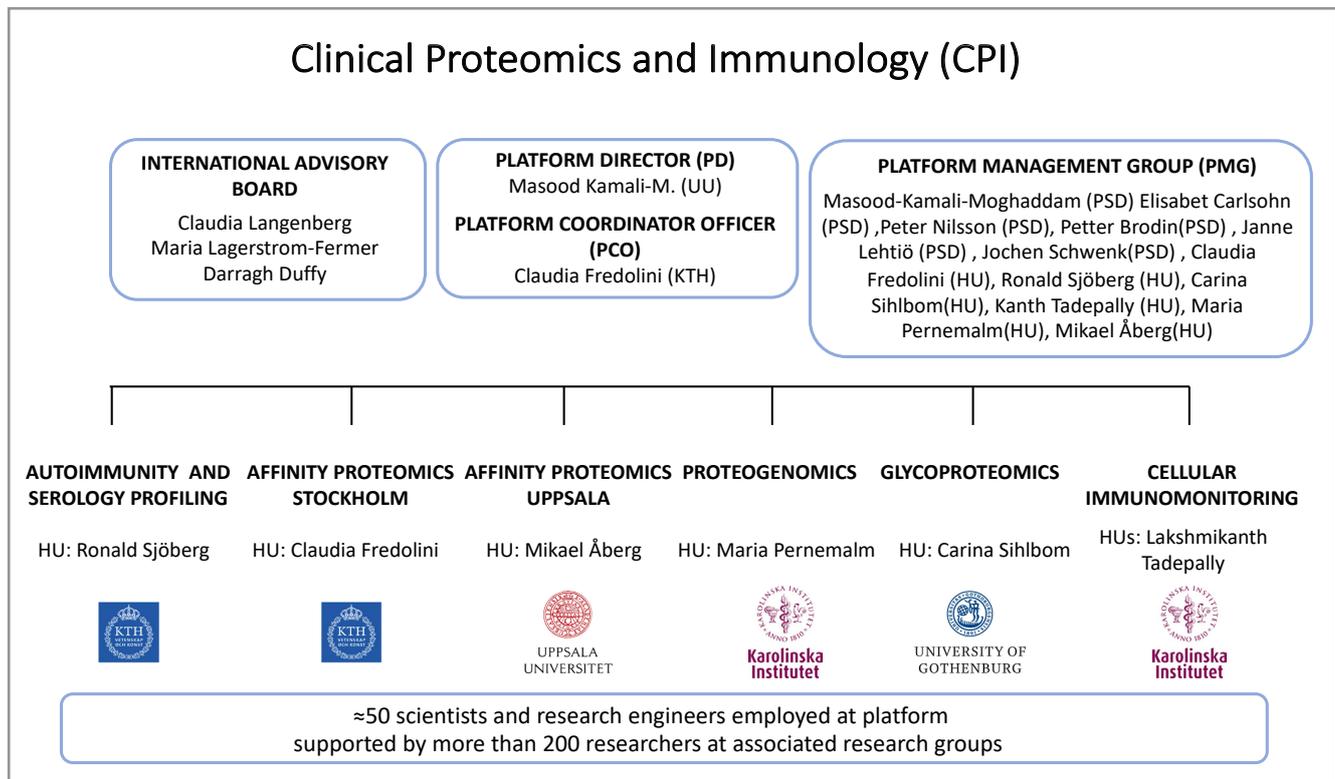
Each Unit is managed by a Head of Unit (HU). In 2022, following Scilifelab's recommendations and the regulations of the hosting universities, HUs at CPI become formally responsible for personnel, budget and operative activities. HUs are also responsible for the scientific and the strategic development of the Units together with the Platform Scientific Directors (PSD). In general, PSDs are the principle investigators and group leaders of research groups to which the Units are associated with. Units and research groups work synergistically to develop and implement new technologies.

The Platform Director (PD) Masood Kamali-M is responsible for the activities in the Platform Management Group (PMG) which includes all the PSDs and HUs, for the platform budget and deliverables. The Platform Coordination Officer (PCO) coordinates operations and communication in the platform, assists the PD in drafting documents, organizes

the PMG and HU meetings, represent the platform in outreach events and PCO forums.

HUs meets every second week to discuss the operations within the platform such as outreach events, organization of courses at platform level, share routines and prepare documents. HUs have occasionally organized meetings with staff from other platforms such as NBIS to discuss and plan collaborations.

The PMG meets four times per year to evaluate platform achievement and discuss strategies and direction for future development. The PMG is joined by the advisory board, which currently comprise representatives and experts from Academia and Industry. Dr. Claudia Langenberg, is an expert in computational medicine and program leader at Charité - Universitätsmedizin Berlin; Dr. Darragh Duffy is the group leader of the Translational Immunology lab at the Institut Pasteur, Paris, his research interest lies in the mechanisms behind inter-individual differences in immune responses. Dr. Maria Lagerstrom-Fermer is the Head of Clinical Innovation and Business Planning at AstraZeneca. The members of the advisory board provide their complementary perspective and suggestions for platform scientific development.



Development, Achievements and Plans

Platform development 2021-now

The Clinical Proteomics and Immunology (CPI) was formed in 2021 after the re-organization of the former Proteomics

and Metabolomics platform. CPI today provides exclusively proteomics technologies, services, and expertise within

the field of state-of-the-art mass spectrometry (MS), affinity proteomics and single cell analyzing tools for advanced protein analyses in body fluids, cells and tissues. CPI's clinical proteomics services include assays to profile immune-responses through quantification of autoantibodies and circulating blood proteins, as well as single-cell functional and immunophenotypic analysis using mass cytometry. Furthermore, the CPI units develop new advanced technologies and assays for tailored applications, such as ultra-sensitive immunoassays for novel candidate biomarkers, unique proximity assays, antibody validation workflows, custom designed protein, peptide arrays and MS-assays, genome annotation, independent proteogenomics analysis, characterization of glycans and glycopeptides, and innovative sample preparation methods that can enable studies with longitudinal sampling in large clinical trials at health care units for mass cytometry analysis.

Platform re-organization: action taken

To address Scilifelab's suggestions indicated in the Infrastructure Terms and Conditions for Funding document, the following actions were taken:

(i) In order to promote interaction and collaboration between CPI's Units, a routine of biweekly HU meeting and initially monthly PMG meetings were established. HU meetings have facilitated the mutual understanding of the technologies offered, and of daily routines to identify common grounds for collaborations, technology integration and to harmonize, when applicable, routines and operations. HUs discussed practical aspects of platform re-organization (eg. update/create new webpages), outreach events, opportunity for training at the platform level. Furthermore, HUs engaged in meeting with NBIS staff to facilitate the creation of a comprehensive clinical proteomics service which includes support to data analysis, as well as the challenges and advantages of service to industry. Two NBIS referent members were nominated to support the cooperation with CPI. During 2022, HUs have compiled the first comprehensive draft of services offered at platform level. Collaborations between Units were established and consolidated by granted funding.

(ii) The Affinity Proteomics node in Stockholm and Uppsala have worked closely to coordinate and integrate their services. Regular meetings have been established between the respective HUs to establish common costs and routines and to discuss and share project requests. Full Unit meeting and Slack channel have been used to allow the personal to meet and interact easily to facilitate an exchange in daily activities. These two units are now engaged in inter-Unit collaborations and serve when necessary common users proposing complementary services.

Creation of a nationally unique clinical proteomics services with a focus on immuno-monitoring.

During 2021 and 2022 the platform has consolidated its focus on individuals' immuno-monitoring and precision medicine and on integration of different technologies into workflows and pipelines that can valuably contribute to Scilifelab Precision Medicine (PM) and Pandemic Laboratory Preparedness (PLP) capabilities. This has been possible only through a close collaboration and interaction across the Units.

Four CPI units became engaged in PLP projects funded by SciLifeLab (with a sum of 17 MSEK). Briefly the projects concern:

- Creation of a pandemic sample center to facilitate handling of clinical specimens between university hospitals and Scilifelab units (Lehtio Lab and GPP).
- Large-scale serology profiling to investigate the humoral response against pathogens protein variants using protein beads arrays (Nilsson Lab and APS)
- Systems-level immuno-monitoring by humoral and cellular analysis to unravel immune response to novel pathogens (Brodin Lab and CIMMR in collaboration with Schwenk Lab and APS)
- Advanced molecular analysis of self-sampled micro-specimen to survey population health and monitoring pandemic effects (APS and Schwenk Lab in collaboration with APU and ASP)

During the first wave of the COVID-19 pandemic, a highly performing, high-throughput and multiplex SARS-CoV-2 serology assay was developed by a multidisciplinary team from KTH (Nilsson Lab). The assay is now offered by the ASP Unit and it has been used to analyze more than 200,000 plasma and serum samples. APS and APU have also contributed substantially to the large serological effort introducing microsampling for population studies and sensitive assays to quantify neutralizing COVID-19 antibodies against different variant of interest in serum, saliva and nasal mucosa.

New technologies and instrumentation to promote precision medicine:

In 2021, the Affinity Proteomics-Uppsala in collaboration with the national research infrastructure for genome sequencing (NGI) created the SciLifeLab Explore Lab, a collaborative infrastructure offering Explore, an Olink PEA technology where quantitative PCR readout was substituted with next generation sequencing, allowing to increase the multiplex level from 92 to 3072 proteins. Since the implementation, more than 10,000 plasma samples have been analyzed.

The GPP Unit was in 2022 granted TDP fundings to develop a unique plasma biomarker discovery pipeline integrating HiRIEF LC MS/MS with Olink Explore 3072 offered by APU with targeted quantitative affinity assay offered at APS

(for canonical proteins) and MS-based PRM assays (for non-canonical protein variants) available at GPP.

The MS units also part of BioMS (GPP and GP) were granted VR infrastructure funding for a total of 33 MSEK. New MS instrumentation was introduced by CIMMR and GP units such as CyTOF XT, Thermo Exploris 480 and a Orbitrap

Eclipse Tribrid to allow, through more automated systems, a higher sample throughput required in the analysis of clinical samples. Furthermore, a Waters cyclic ion mobility MS was introduced to enhances structural analysis of glycans and glycopeptides

Platform development plan 2023–2024.

Plans for 2023–2024 will include:

1. Strengthen the collaboration across CPI units to offer world-unique clinical proteomic services with impactful contribution to the SciLifeLab's PM capability. Several ideas and proposals for development have been concretized in two VR accessibility to Infrastructure applications focused on (i) the creation of an Affinity Proteomics Hub for Precision and Population Medicine (AFPM), which will provide the combination of technologies currently offered by APS, APU and ASP. The long term project impact is expected to lead to: a greater access to cutting-edge affinity proteomics technologies to users such as the Swedish public health agency (Folkhälsomyndigheten; FoHM), biotech and pharma industries with the ultimate goal to facilitate the translation of proteomics technology into clinical applications; (ii) The development, validation and certification of robust quantitative immunoassays instrumental for diagnosing immune system dysregulation to enable PM in patients with inflammatory disorders using instruments and expertise available at CIMMR and APS. This is in line with CPI platform's strategies as the services provided will be translating advanced diagnostics from the research space into healthcare and precision medicine capabilities.
2. Acquire quality certification and accreditation from SWEDAC. With the future goal to implement proteomics technologies in clinical setting in support of a clinical approach based on PM, we aim to guarantee high quality standards in data generation. To become eligible to offer services capable to industry and FoHM, we will apply for appropriate certifications such as ISO 17025 to, among others, serve clinical trials and cohort analysis.
3. Harmonization of services and activities across units with common project pipelines.
4. Developing data flows and clinical data reporting tools together with Data Centre and DDLs program.
5. Continuing development of combined project support with the NBIS for seamless integration of analysis and bioinformatics support.
6. Outreach and contribution to academic education to prepare the next generation scientists, and to increase public awareness and education about proteomics technologies.

Request for additional funding 2023–2024

According to the current situation, the Mass Spectrometry technologies at CPI provided via GPP, CIMMR and GP Units are substantially financed by SciLifeLab, VR and/or University fundings. We believe that the affinity proteomics services, running on a lower budget, risk to be penalized in terms of quality and efficiency. According to the annual number of projects and publications reported by each CPI units, affinity proteomics technologies are currently underfunded to maintain their excellence while increasing the number of technologies, projects and requests. Our suggestion is therefore for 2023–2024 to invest more fundings for the Units that dispose of lower budget, creating eventually for those the conditions for further development that may result, in the future, in an increased external funding. Units receiving the lowest economic support from Scilifelab currently are:

Autoimmunity and Serology Profiling (ASP): one research engineer or researcher (1 FTE) is required to fulfil the increasing amount of requests for service projects and to develop, and maintain, new processes and systems for

quality assurance, analytical capabilities, and data handling.

Affinity Proteomics Stockholm (APS): one research engineer or researcher (1 FTE) is required to efficient process for larger and highly diversified projects, including customize assay development which requires larger resources in term of personal

Affinity Proteomics Uppsala (APU): the increasing amount of project requests for the Explore Lab is creating the need for a research engineer fully dedicated to hands-on work Explore service.

Moreover, the Glycoproteomics (GP) despite being funded by VR via BioMS, serves as pilot unit and received limited support in 2020–2021 for the services it provides within CPI. The recent introduction of new methods for glycoprotein analysis, has created a need for data analysis tools specific for glycosylation and personnel dedicated to their development and application.

Request for expanded funding 2023–2024

Specify all costs in kSEK

Unit	SciLifeLab funding 2022 (kSEK)	Requested ScilifeLab funding 2023 (kSEK)	Requested SciLifeLab funding 2024 (kSEK)
Affinity Proteomics-Stockholm	2560	3000	3800
Affinity Proteomics-Uppsala	2500	3000	3800
Autoimmunity and Serology Profiling	2400	3000	3800
Cellular Immunomonitoring	4000	3800	3800
Global Proteomics and Proteogenomics	3000	3000	3800
Glycoproteomics	2000	2600	3800

Affinity Proteomics Stockholm

Clinical Proteomics and Immunology Platform (Web links for Unit: [Webpage](#), [Publications](#))

Basic Information

Head(s) of Unit: Claudia Fredolini
PSD(s): Jochen Schwenk
SciLifeLab Unit since: 2013
Host university: KTH
FTEs: 5.0
FTEs financed by SciLifeLab: 4.0

Funding in 2021 (kSEK)

SciLifeLab: 2560
KAW: 100
Industry: 400
Total: 3060

Resource Allocation 2021

Academia (national): 63%
Academia (international): -
Internal tech. dev.: 20%
Industry: 10%
Healthcare: 2%
Other gov. agencies: 5%

User Fees 2021

Total (kSEK): 4000
Reagents: 78%
Instrument: 8%
Salaries: 2%
Rent: 10%
Other: 2%

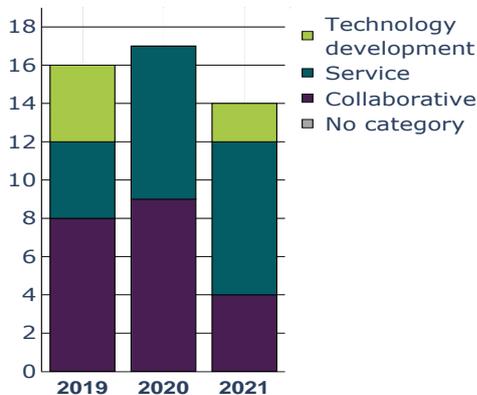
User Fees by Sector 2021

Academia (national): 89%
Academia (international): -
Industry: 5%
Healthcare: 2%
Other gov. agencies: 4%

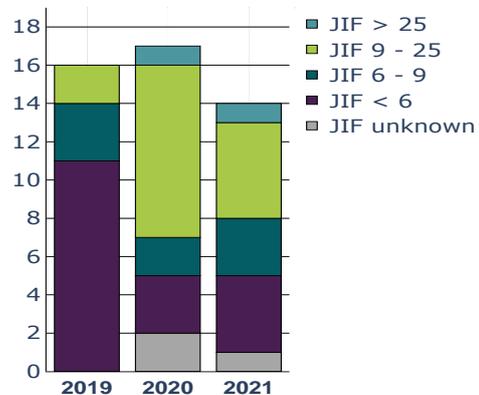
Services

- Discovery and validation of circulating biomarkers (all)
- High-throughput protein profiling (Olink, Luminex)
- Quantitative protein analyses (Quanterix, Luminex, ProteinSimple, Olink)
- Development of novel and customized immunoassays (all)
- Consultation about protein analysis by affinity proteomics (all)

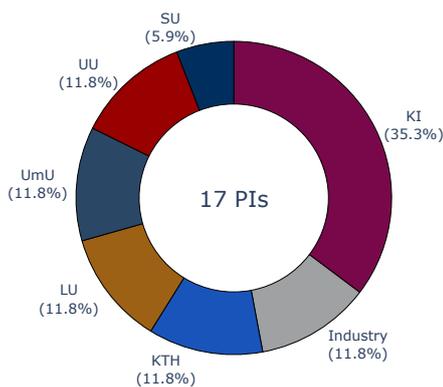
Publication by Category



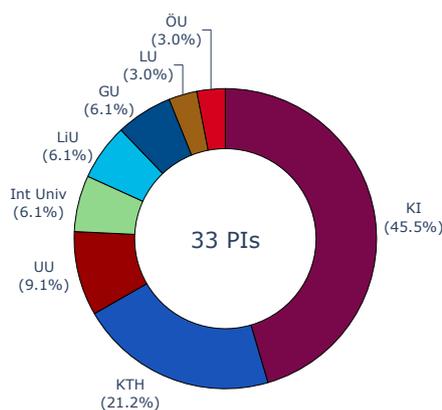
Publication by Journal Impact Factor



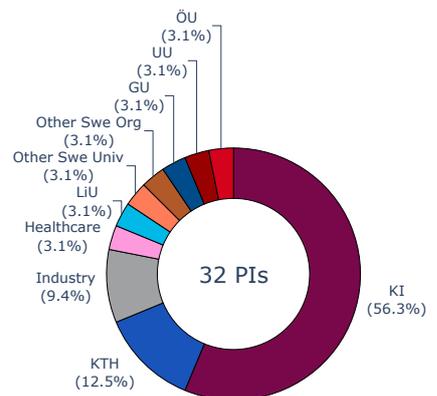
Users 2019



Users 2020



Users 2021





Unit:	Affinity Proteomics Stockholm(APS)
Platform:	Clinical Proteomics and Immunology
<p>Development, Achievements and Plans</p> <p><i>i) Briefly describe the development and major achievements (technology development, scientific achievements, new user groups, outreach efforts, training and education, contribution to cross-unit and cross-platform initiatives etc.) of the unit 2021–2022.</i></p> <p><i>ii) Briefly describe the development plans for the unit 2023–2024 and beyond</i></p> <p><i>iii) If you have specific questions or comments for the reviewers to consider during the Midterm Checkup, you may add these here.</i></p>	
<p><i>Development and major achievements.</i></p> <p>During 2021 and 2022, the Affinity Proteomics-Stockholm (APS) Unit continued developing and applying technologies that could support different aspects of COVID19 research and contribute to the <i>Pandemic Laboratory Preparedness</i> and <i>Molecular Medicine</i> SciLifeLab capabilities: Service (65%), collaborative (23%) and technological development (12%) resulted in 17 publications (IF: range 1,2-60, avg: 12; updated list Jan 2021-August 2022) and contributed to two patent applications.</p> <p><i>(i) <u>Provided access to our sensitive assays formats and expertise in assay development.</u></i></p> <p>In 2021 and 2022 we continued to contribute substantially to the fight against COVID19. National and international researchers using our unit were investigating cellular and the humoral immune response associated to moderate and severe COVID19 (Karolinska COVID19 Study Group PNAS, PMID: 33479167), as well as treatments efficacy (Clinical Trial Adv Sci, 2021, PMID: 34180141; Viruses,2021 PMID: 34960725). While giving priority to COVID19 projects when requested, we were also capable to deliver our service to non-COVID19 researchers. Among others we have been supporting a longitudinal study in preterm babies with retinopathy (Pediatr. Res.,2022, PMID:33895781); plasma profiling of patients with or without malaria after being exposed to Plasmodium falciparum (Cell Rep 2022. PMID: 35443186) and kept serving large cohort studies such as the KARMA (Transl Oncol. 2022 PMID: 35033985); and SNAC-K The Swedish National study on Aging (L.Fratiglioni and D.Vetrano, KI Aging Research Center (ARC). Since 2021, APS is also part of the EATRIS CanSERV project financed by the European Commission.</p> <p><i>(ii) <u>Develop microsampling strategies to facilitate population studies of DBS.</u></i></p> <p>Patient-centric sampling strategies based on less invasive, self-sampling microdevices such as volumetric Dried Blood Spot (qDBS) from Capitainer AB have demonstrated to be extremely valuable in any in large epidemiological studies or day by day patients monitoring. This is powerful in pandemic emergencies (Nature Communications 2021; PMID: 34140485). The method developed in 2020 by Schwenk Lab and Roxhed Lab with the support of the APS Unit. Since 2021, it is integrated in services offerings of the facility and tested by Folkhälsomyndigheten (Fohm) and the company Xerum for analysis of SARS-CoV-2 seroprevalence in the Västerbotten region. The project was conducted together with the Autoimmunity and Serology Profiling (ASP) and Affinity Proteomics Uppsala (APU) Units. At the moment, APS supports a longitudinal DBS study of the BAMSE cohort (Prof. Erik Melén, KI).</p> <p><i>(iii) <u>Develop assays for alternative microsampling strategies.</u></i></p> <p>We extended our collaboration with Roxhed Lab and Prof. O. Beck, into the development and evaluation of alternative microsampling devices such microneedle based collection of few μL of blood or skin interstitial fluid (ISF) (publications submitted) and a capillary-driven microfluidic multiplexed bead-based immunoassay to speed up the analysis of labile biomarkers in non-hospitalized individuals (patent: PRV 2130266-6).</p> <p><i>(ii) <u>Support to Industry</u></i></p>	

During 2021 and 2022, we increased our support to industry. consolidating our collaboration with Capitainer AB performing with them analysis of qDBS stability and analytical reproducibility and to develop new home sampling devices. Supported by a VINNOVA grant and in collaboration with the Schwenk and Roxhed Labs we have also implemented a qDBS Olink PEA assay. [Fredolini et al. medRxiv 2021.11.15.21266315] (revision resubmitted). We are currently collaborating with Olink , NGI-Uppsala and the APU Unit to develop an alternative technical pipeline for the Explore assay. Furthermore, we supported phase II clinical trials at Kancera (in collaboration with the Cellular Immunomonitoring (CIM-IM) Unit and at AlzeCurePharma (new Alzheimer's Disease treatment). We have also hosted the Beta-Testing of a new Luminex instrument (INTELLIFLEX).

(iii) Cross-Unit and cross platform activities

The Affinity Proteomics nodes in Stockholm and Uppsala, following SciLifeLab recommendation, have since 2021, worked closely to coordinate and integrate their services as well as exchanging users to reduce queue and waiting times (L.Jonasson LiU VIP project).. In 2021, they established a collaboration with the GPP Unit to combine mass spectrometry and high-multiplexed affinity proteomics methods such as HiRIEF LC MS/MS with Olink Explore 3072 available at APU), with targeted quantitative affinity assay offered at APS (for canonical proteins) and MS-based PRM assays (for non-canonical protein variants) available at GPP into a unique pipeline for plasma biomarker discovery and validation. The project was granted in 2021 SciLifeLab TDP funds.

Other cross-units and cross-platforms projects concerning APS exclusively include: developed a bead-based/MS assay to capture and deep profile proteins incorporated in SARS-CoV-2 particles (with Human Antibody Therapeutics Unit (DDD Platform) and the GPP Units at SciLifeLab and Prof. F. Chiodi (KI), and Dr. J Klingstöm (KI and Fohm).

Finally, the APS has recently welcomed the request of several Swedish researchers to use the Luminex platform for multiplex nucleic acid assays, an application that could open a ground for collaboration with the Genomics and Clinical Genomics Platforms.

(iv) Outreach events, training, education and other

In 2021-2022, the Affinity Proteomics Unit has been promoting education about proteomics technologies through courses at academic level contributing with lectures at courses at MS and PhD level at Stockholm and Uppsala University at KI and KTH). We have also organized and /or participated to webinar and seminars dedicated to a broader audience including biotech and pharma companies (eg. Affinity Proteomics Simoa mini-symposium, 2022; NGI and Affinity Proteomics seminar about next-generation affinity proteomics,2022, Olink webinar on multiomics approaches in precision medicine 2021). Students at different levels have been welcome to join the Unit team for a short period to be trained favoring technology transfer. Initiated already during early 2020, the APS laboratory is finally undergoing renovation during the second half of 2022 to fully meet all new biosafety level 2 laboratory (BSL2) requirements set forth by the Swedish work environment authority (AFS 2018:4).

Development plans for the unit 2023–2024 and beyond

(i) the Pandemic Laboratory Preparedness (PLP) received in 2022 will allow APS and collaborating researcher groups, Units (APU, ASP) and companies (Capitainer and Breath Explore) to further develop microsampling strategies and automated workflows for the proteome analysis of alternative self-sampled biofluids (eg. ISF, breath). The goal is to establish a workflow that can support researchers in health monitoring at a population scale.

(ii) we will strengthen the collaboration with the other CPI Units, as proposed the VR Infrastructure grant application, to create a unique Affinity Proteomics Hub for Precision and Population Medicine (AFPM). This will secure and facilitate access to cutting-edge affinity proteomics technologies to Folkhälsomyndigheten; (FoHM), biotech and pharma industries

(iii) Jointly with the other Units at the Clinical Proteomics and Immunology Platform (CPI) we will apply for quality certification from SWEDAC (ISO 17025). We aim to guarantee high quality standards in data generation to meet the strict requirements of industry and FoHM,

(iv) we will evaluate the introduction of new commercial platforms that may be of interest for the Swedish scientific community such as SomaScan. A multiplex immunoassay platform based on Slow Off-rate Modified Aptamer (SOMAmers),The exquisite specificity of reagents and assay format allows the simultaneous quantification of ~7000 proteins at the same time; Quanterix SPX or HD, to expand our portfolio of ultrasensitive quantitative assays.

Affinity Proteomics Stockholm

Budget 2022

Costs	2022
Personnel cost	3 369 189
Other personnel costs	50 000
Depreciation	76 038
Service and license costs	304 000
Other operating costs	3 200 000
Premises costs	437 995
Other costs	20 000
Sum costs (kSEK):	7 457 222

Revenues	2022
Funding from SciLifeLab	2 560 000
Consumables/Reagents	3 000 000
Scilifelab fundings for PCO	300 000
VR C Fredolini Co-Applicant	402 000
User fees	1 000 000
Sum revenues (kSEK):	7 262 000

Affinity Proteomics Uppsala

Clinical Proteomics and Immunology Platform (Web links for Unit: [Webpage](#), [Publications](#))

Basic Information

Head(s) of Unit: Mikael Åberg
PSD(s): Masood Kamali-Moghaddam
SciLifeLab Unit since: 2013
Host university: UU
FTEs: 4.75
FTEs financed by SciLifeLab: 3.0

Funding in 2021 (kSEK)

SciLifeLab: 2500
UU: 1800
Total: 4300

Resource Allocation 2021

Academia (national): 75%
Academia (international): 4%
Internal tech. dev.: 17%
Industry: 2%
Healthcare: -
Other gov. agencies: 2%

User Fees 2021

Total (kSEK): 18198
Reagents: 80%
Instrument: 10%
Salaries: 5%
Rent: 5%
Other: -

User Fees by Sector 2021

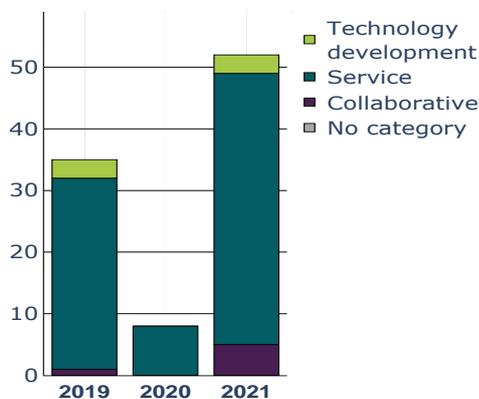
Academia (national): 96%
Academia (international): 1%
Industry: 1%
Healthcare: -
Other gov. agencies: 2%

Services

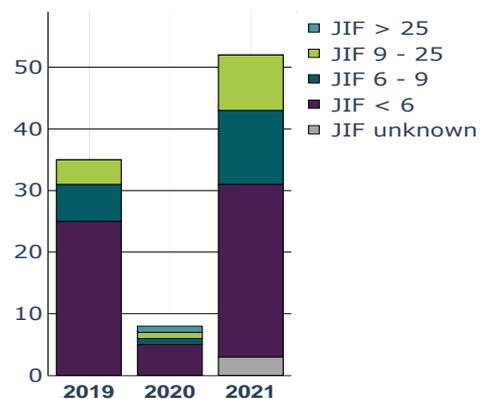
- Full-service protein detection in wet & dry samples (e.g. DBS)
- In situ PLA and SP-PLA for detecting proteins, their interactions & post-translational modifications in fixed cells/tissues
- Detection of antibodies against viruses, e.g. Sars-CoV-2 variants (MesoScale, PEA)
- Conjugation of oligonucleotides to antibodies for customised assays

Note: Pre-2021 publication data is from 'Clinical Biomarkers' and 'PLA and Single Cell Proteomics'.

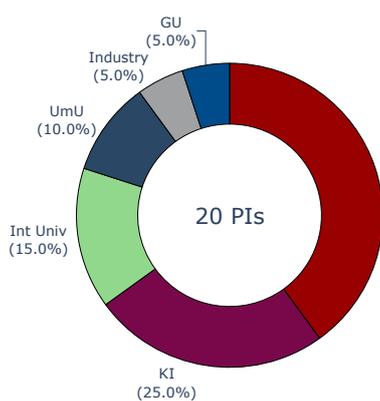
Publication by Category



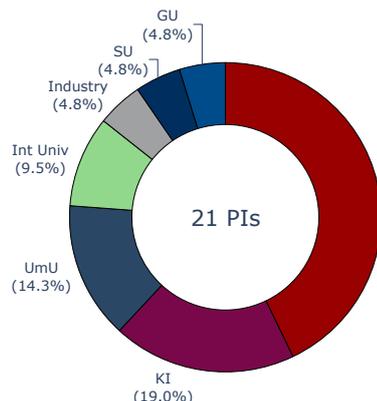
Publication by Journal Impact Factor



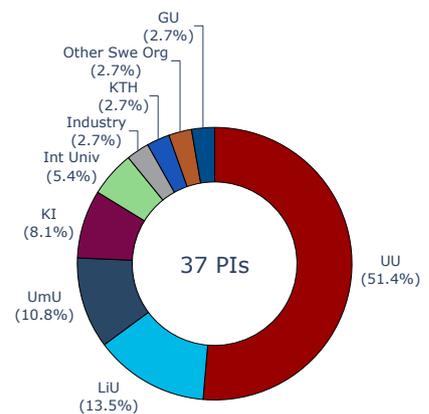
Users 2019



Users 2020



Users 2021



Unit:	Affinity Proteomics Uppsala
Platform:	Clinical Proteomics and Immunology

Development and achievements etc: The major topics during the last year and a half has been Olink Explore, covid-analyses and the increased interplay within the platform, particularly with AP Stockholm (please see the CPI platform report for details). Since 2021 CPI/APU offers the Olink Explore platform which permits the analysis of large protein panels (today <3000 proteins). The Explore analyzes are done in close collaboration with NGI Uppsala under the name SciLifeLab [Explore Lab](#). APU financed during 2022 the purchase of a second pipetting robot (1.2 Mkr, SPT Labs Mosquito) that doubled the theoretical throughput. Several projects are finished or ongoing (e.g. J Ernerudh LiU, Tomas Olsson KI, Lars Lind UU, A. Bjartell and J. Nilsson LU, B Melin and B. van Guelpen UmU, T Omland Oslo uni.) The majority of samples have, however, been analyzed within the Disease Atlas Projects, where in the first run ~100 samples from ~100 diseases are analyzed for 1500 proteins (PI M Uhlén, a first cancer focused manuscript submitted). A project for implementing Explore in a multi-omics readout is ongoing (PI U Gyllensten UU). For outreach, a proof-of-concept paper has been published (Enroth et al, Cancers 2022), an online Explore seminar organized (<https://www.scilifelab.se/event/ngi-and-affinity-proteomics-seminar/>) and the Explore lab presented at the EU-LIFE Tech Watchseries. Within the frame of a SciLifeLab TDP, the unit is collaborating with the Global Proteomics and Proteogenomics unit and AP Stockholm in combining Explore with mass spectrometry. We have recently installed the new Olink Signature qPCR and now have three lines for analyzing the smaller Olink Target 48 and 96 panels in Uppsala. Although the two older Biomark HD qPCR systems have better throughput than the Signature, they are dated products and the new all-in-one qPCR is for the future. After the incorporation of Explore, the unit is now a Platinum badge service provider for all Olink products, the only non-commercial lab in the nordics.

Variant	First documented	Date VOC by WHO	Dominant strain in Sweden	Date first analyzed at APU
Alpha	Sep 2020	2020-12-18	Feb. 2021	2021-04-16
Beta	May 2020	2020-12-18	-	2021-04-16
Gamma	Nov 2020	2021-01-11	-	2021-04-16
Delta	Oct 2020	2021-05-11	July 2021	2021-06-28
Omicron BA.1	Nov 2021	2021-11-26	January 2022	2022-01-24
Omicron BA.2	Nov 2021	2022-01-22	Mars 2022	2022-03-11
BA.4 and BA.5	Jan/Feb 2022	2022-05-12	June 2022 (BA.5)	2022-08-08
BA.2.75	May 2022	?	?	Sep 2022

APU is also a trained core lab for the MesoScale electrochemiluminescence platform, which is a versatile and sensitive tool for doing multiplex proteomics. Several studies have been analyzed during the last years of which a cardiology focused substudy in Scapis (PI F Nyström LiU) and an Uppsala based study in immunopsychiatry

(PI J Cunningham UU) stands out both regarding their size and complexity. The Stockholm and Uppsala nodes combined our resources in another Linköping study concerning IL-6 signaling (PI L Jonasson), where the same sample set was analyzed using complementary technologies. Since April 2021 APU has also analyzed >60 000 samples for the presence of binding and neutralizing Covid-19 antibodies in serum, saliva, nasal mucosa and dried blood spots (DBS) by utilizing dedicated panels that are rapidly updated as new variants emerge (Table 1). The curated results are calibrated against the WHO International Standard and reported back to authorities such as the Public Health Agency of Sweden for internal use (e.g. the GLORIA and SÄBO surveillance studies, ongoing) and to researchers to be presented in publications and at ECDC and WHO meetings (PIs C Thålin at KI, M Forsell at UmU, M Sällberg Chen at KI, H-G Ljunggren at KI, A Smed-Sörensen at KI, G Enblad at UU, J Burman at UU, S Mangsbo at UU and others). T-cell responses have been assessed by monitoring mainly IFN- γ release and vaccine spike antigen successfully measured at fg/ml concentrations in serum (PI K Loré at KI). During this summer all samples from the Covaxid study (<https://clinicaltrials.gov/ct2/show/NCT04780659>), consisting of 540 regularly sampled patients with immunocompromised disorders, were analyzed at the unit for spike, RBD and nucleocapsid antibody responses and neutralizing capacity in both plasma and saliva. One saliva manuscript is already submitted and others will follow. A number of papers originating from the omicron surge during the spring was recently accepted in prestigious journals after close collaboration with the COMMUNITY study and FoHM (Blom et al, Lancet Inf Dis, Havervall et al, NEJM (accepted), Marking et al, Nat

Comm (in revision)). In the NEJM paper, IgG and IgA antibodies extracted from nasal swab samples were analyzed and we could show that high mucosal IgA levels protect from omicron breakthrough infections. This is of interest when it comes to e.g. the development of nasal vaccines.

Apart from the high throughput assays, APU also offers customized assays for proteins and exosomes in blood and tissues using the MSD platform, Proximity Ligation Assays (In situ PLA), solid-phase PLA and Proximity Extension Assays (PEA). Several projects have been initiated and/or finished during the last year. As a reach out, a seminar about the latest PLA methods was arranged (<https://www.scilifelab.se/event/navinci-scilifelab-collaboration-seminar-navinci-open-house-and-vernissage/>). APU has also contributed with staff and knowledge to KAW funded development projects (PIs U Landegren and M Kamali-Moghaddam) for PEA based detection of antibodies (serum, saliva, DBS) and virus using these technologies. Two manuscripts are prepared for the antibody test and the virus method is now being commercialized.

Future plans:

- The Explore platform is continuously being updated and improved. The planned increase in the number of targets, the addition of new matrixes and the numbers of consultations concerning study design and quotes we have provided to research applications likely means that the user base will grow during the coming years. This also means that we need to be prepared and first and foremost have additional updated and trained staff in the lab which could require additional funding. The installment of a third analysis line must also be considered in order to keep the throughput for the coming, larger panels and would decrease the analysis time for a 1000 patient 3072 panel project from months to weeks.
- By doing in-house modifications to the commercial covid antibody panels we are using, we now have a high-throughput multiplex method for antibody avidity, which measures the binding quality of the antibodies and is a nice complement our neutralization assay. In a similar fashion we are now working on other modifications which will allow us to discriminate between antibodies produced in mucosa or blood, to look at different post-translational modifications, to determine different IgG classes etc. To have this type of depth on top of broad high-throughput variant screening is unique and will hopefully move the field forward.
- Although the operators at APU are fully trained and proficient in the MesoScale platform, they will receive a more formalized training that is typically only performed for a very few bioanalytical labs in regulated environments. The training will commence in October 2022 and will also be offered to future new operators. This is planned to be complemented with a new instrument with a better camera and 384-well capacity as well as an automated pipetting system. This would decrease the hands-on time for all MesoScale analyses.
- Since antigen expression is transient, antibody testing in serum and milk etc. is often the only way to do disease surveillance in animal herds. The PEA based covid serology test works on all species and is now being modified for other types of diseases. This has gained interest and discussions are ongoing with e.g. the National veterinary institute.
- We are also working to establish a multiplex isPLA for detection of proteins in signaling pathways of interest in oncology. The project has been awarded a SciLifeLab Uppsala TDP for 2022-2023 of 2 Mkr and a first publication is under preparation.
- APU's associated laboratory of Kamali-Moghaddam has developed a large number of tools for specific and sensitive detection and characterization of exosomes/extracellular vesicles in bulk and on single vesicle levels. For instance, the proximity barcoding assay (PBA) allows profiling of EV surface proteins, and detection of molecular profile of single EVs [PMID: 31451692]. The addition of such a method that has a sequencing readout could mean more cross-platform collaborations with NGL.
- We are finally investigating the possibility to obtain an oligonucleotide synthesis instrument that would open up for a more efficient and faster work flow in developing new PLA and PEA methods. We are discussing a potential collaboration with a company providing synthesis instruments, both for oligonucleotide synthesis with a very competitive price range per base-pair, and protein synthesis instrument. A fruitful collaboration could open up for a more customized multiplex PLA service for our clinical customers.

Affinity Proteomics Uppsala

Budget 2022

Costs	2022
Personnel cost	4 420 476
Other personnel costs	62 310
Depreciation	826 225
Service and license costs	583 550
Other operating costs	10 550 000
Premises costs	628 567
Other costs	0
Sum costs (kSEK):	17 071 128

Revenues	2022
Funding from SciLifeLab	2 920 000
Funding from financier X	1 500 000
User fees	13 000 000
Sum revenues (kSEK):	17 420 000

Autoimmunity and Serology Profiling

Proteomics and Metabolomics Platform (Web links for Unit: [Webpage](#), [Publications](#))

Basic Information

Head(s) of Unit: Ronald Sjöberg
PSD(s): Peter Nilsson
SciLifeLab Unit since: 2013
Host university: KTH
FTEs: 6.0
FTEs financed by SciLifeLab: 2.6

Funding in 2021 (kSEK)

SciLifeLab: 2400
SciLifeLab Instrument: 520
KTH: 180
Total: 3100

Resource Allocation 2021

Academia (national): 45%
Academia (international): 15%
Internal tech. dev.: 10%
Industry: 10%
Healthcare: 15%
Other gov. agencies: 5%

User Fees 2021

Total (kSEK): 1269
Reagents: 20%
Instrument: 50%
Salaries: 10%
Rent: 20%
Other: -

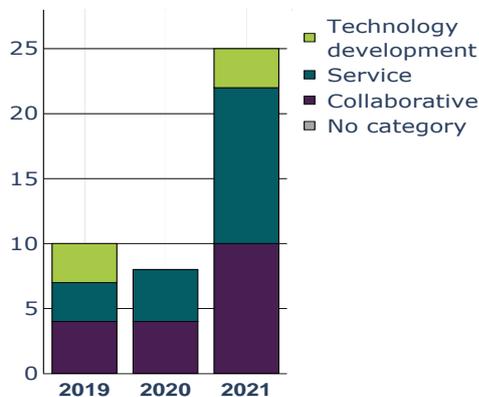
User Fees by Sector 2021

Academia (national): 55%
Academia (international): 40%
Industry: 5%
Healthcare: -
Other gov. agencies: -

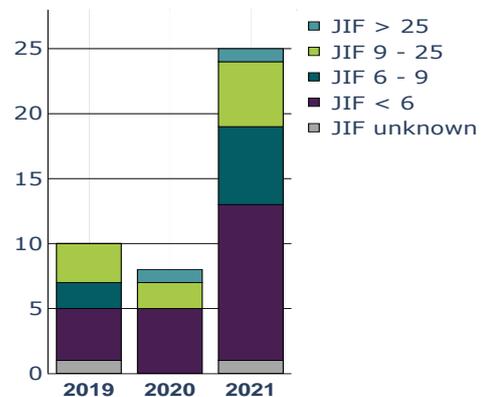
Services

- Autoantibody profiling
- Epitope mapping
- Antibody validation
- Infrastructure for commercial protein arrays
- SARS-CoV-2 Serology

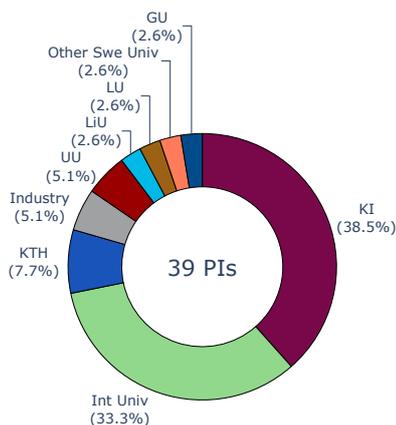
Publication by Category



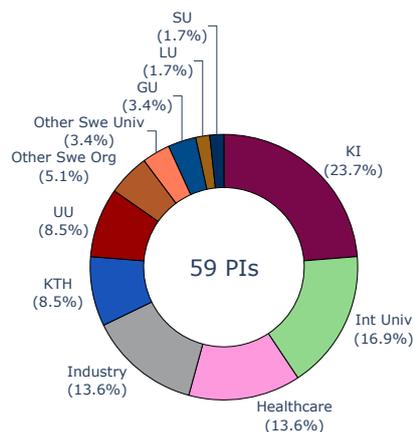
Publication by Journal Impact Factor



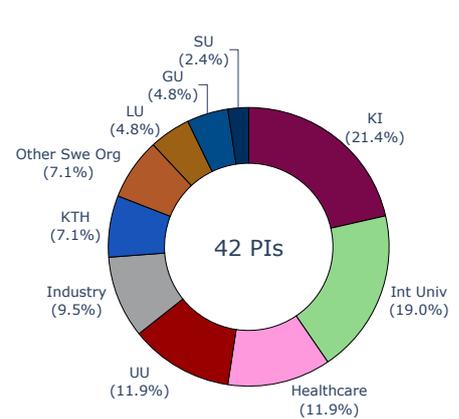
Users 2019



Users 2020



Users 2021





Unit:	Autoimmunity and Serology Profiling
Platform:	Clinical Proteomics and Immunology

Development, Achievements and Plans

The unit have continued to play an important role in monitoring and understanding the effects of the ongoing pandemic by continuing to take part in multiple large research projects tracking the prevalence of antibodies towards not only the original SARS-CoV-2 variant but also, by continuously updating the antigen panel, towards any new variant of interest. Currently several Omikron variants are being implemented in the workflow for the SARS-CoV-2 serology together with the previous variants. During 2021 an additional 100.000 samples were analysed and the projected number of samples for 2022 is 30.000. The total number of reactions during 2021 was 2.9 million, for a total of 105.000 samples and for 2022 the projected number of reactions is 1.6 million for 38.000 samples, as incoming user projects shifts over from SARS-CoV-2 status screenings to standard autoimmunity screenings.

Twenty-five publications were associated to the unit during 2021 and ten additional publications during the first two quarters of 2022. Of these in total 35 publications twenty-six were Covid-19 related. Of extra interest would be the article “Persisting Salivary IgG Against SARS-CoV-2 at 9 Months After Mild COVID-19: A Complementary Approach to Population Surveys.” (Journal of Infectious Diseases) which was made possible by the development of a new analysis protocol that enables us to detect IgG and IgA against SARS-CoV-2 in saliva. By expanding the types of biofluids which we can utilize for detection of SARS-CoV-2 infection to saliva we can make it easier for collaborators to sample individual who otherwise might not choose to be sampled due to the invasive nature of blood sampling.

To combat the emergence of new and more infectious SARSCoV-2 variants an assay for high throughput analysis of antibodies able to neutralize SARS-CoV-2 have been developed and validated. This robust high throughput method enables assessment of antibodies inhibiting binding between SARS-CoV-2 spike protein and (ACE2. The assay uses recombinantly produced spike-f and ACE2 and is performed in a bead array format and allows analysis of up to 384 samples in parallel per instrument.

Seventy-four percent of active projects ongoing at the unit during 2021 originated in Sweden, this includes both Swedish academia, Swedish industry, Swedish healthcare, and Swedish governmental organisations. Swedish academia alone accounted for a total of forty-two percent of the projects at the unit, while international academia accounted for sixteen percent of the projects during 2021. Remaining ten percent were technology development projects, this is less than the projected twenty percent due to prioritisation of service projects. For 2022 the projected split between national and international users is expected to remain largely similar. However, the total number of PIs and projects is expected to contract from the pandemic levels (73 projects in 2020 and 69 projects in 2021) towards the pre-pandemic levels (32 projects in 2018 and 59 projects in 2019), and correspondingly the types of projects are expected to shift back to the even more resource intensive autoimmunity screenings again.

A planar microarray-platform comprising approximately 1500 secreted full-length proteins, represented in almost 2000 variants have been developed in collaboration with Sophia Hober lab at KTH and the Human Protein Atlas. Based on Uniprot keywords for the 1500 proteins currently

included in the “secretome”-array over 30% of the proteins are related to either enzymatic functions or receptors. Consequently, this represents a collection of proteins of great interest for development within biomarkers, diagnostics, and drug development. This will be an important complement to the protein fragment arrays the unit currently offers. Full-length proteins are preferred for many prospective users and until now the unit have not been able to offer an inhouse alternative in this area. This also represent an initial step in the units’ efforts to expand its repertoire of offered platforms further into the field of full-length protein arrays.

The unit is also expanding into serology arrays comprising a large number of known pathogens to enable high throughput investigations of serostatus of ongoing or previous infection. It will enable us to track the spread of known pathogens over time and to relate this to possible outcomes such as autoimmune disease. This effort will be an integral part of the pandemic laboratory preparedness program

Production of the new “secretome-array” will be prioritized in order to enable it to be introduced to prospective unit users starting 2023, with the extended goal that users can utilise the results gained from the planar array format for large scale screening using bead arrays, similar to the current setup that the unit offers for investigations using protein fragments.

The unit will also continue its effort to create an automated quality control of data generated by these arrays to automatically and simultaneously analyse up to four detection channels. Additionally, work will continue on a setup for storing and recalling stored data when analysing data will, thus enabling comparison to previously generated data.

The unit aim to introduce a new array-based, label-free, instrument for high throughput analysis of affinity binders (Carterra LSA). This is an SPR-based instrument that can generate full antibody kinetics for over a thousand clones per day and which could be of great interest for both academic and industry users. This platform has been proven to be of great usefulness for high throughput screening of antibody clones and the unit expects this instrument to be of great interest for any affinity binder project within Swedish academia. As the instrument represent a substantial investment the financing will need to be divided into multiple sources. An initial source of the funding could be the Swedish Research Council as the unit has authored an application in collaboration with Affinity Proteomics Stockholm and Affinity Proteomics Uppsala, where funding for the Carterra LSA instrument represents part of the request for funding.

The unit additionally aim for increasing its capacity by expanding its personnel with an additional research engineer. This would relieve the current staff of some of their, today considerably heavy, workload, and additionally enable a larger focus on technology development which currently often are neglected in favour of less demanding service requests. Additionally, one of the current research engineers have, due to the ever increasing demands directly associated with all phases of all projects, developed into a data engineering role during the pandemic, and is expected to remain in that role for the foreseeable future. This means that there is a need for additional personnel to fill the resulting lack of wet lab capability. While the statistical analysis is performed by the user, or by NBIS on the request of the user, the unit still have strong need for a data engineer to build and maintain the systems and structures that are needed for quality assurance and data packaging prior to deliver to user. Although increased prioritisation of larger projects could ease the current personnel shortage somewhat by allowing the engineers to spend less time on user meeting and reporting, the increased complexity of larger projects would further drive the need for a dedicated data engineer.

The development of the new pathogen array will be continuous over the next few years as more antigens from various viruses will be introduced to the array and tested for their ability to be detected by antibodies in positive sera. The first user accessible version is planned for release in 2024, with continuous updates with new interesting antigens being added as they become accessible and implemented in the general protocol.

Autoimmunity and Serology Profiling

Budget 2022

Costs	2022
Personnel cost	2 330 000
Other personnel costs	100 000
Depreciation	1 060 000
Service and license costs	390 000
Other operating costs	220 000
Premises costs	200 000
Other costs	0
Sum costs (kSEK):	4 300 000

Revenues	2022
Funding from SciLifeLab	2 400 000
Funding from SciLifeLab, expensive instruments: 2 600 000 /5 year	520 000
Funding from KTH SFO, expensive instruments, 900 000/5 year	180 000
User fees	1 200 000
Sum revenues (kSEK):	4 300 000

Cellular Immunomonitoring

Clinical Proteomics and Immunology Platform (Web links for Unit: [Webpage](#), [Publications](#))

Basic Information

Head(s) of Unit: Lakshmikanth Tadeppally, Jörgen Adolfsson
PSD(s): Petter Brodin
SciLifeLab Unit since: 2015
Host university: KI, LiU
FTEs: 2.5
FTEs financed by SciLifeLab: 2.5

Funding in 2021 (kSEK)

SciLifeLab: 5600
Total: 5600

Resource Allocation 2021

Academia (national): 50%
Academia (international): 20%
Internal tech. dev.: 10%
Industry: 20%
Healthcare: -
Other gov. agencies: -

User Fees 2021

Total (kSEK): 1210
Reagents: 50%
Instrument: 50%
Salaries: -
Rent: -
Other: -

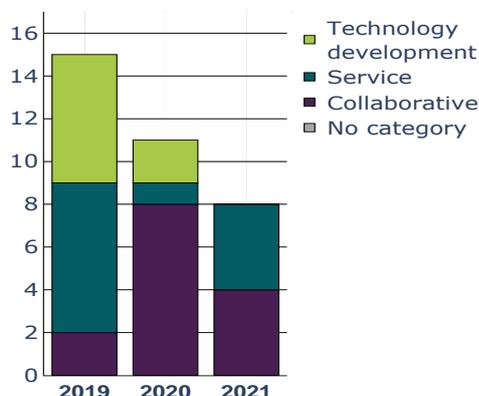
User Fees by Sector 2021

Academia (national): 60%
Academia (international): 20%
Industry: 20%
Healthcare: -
Other gov. agencies: -

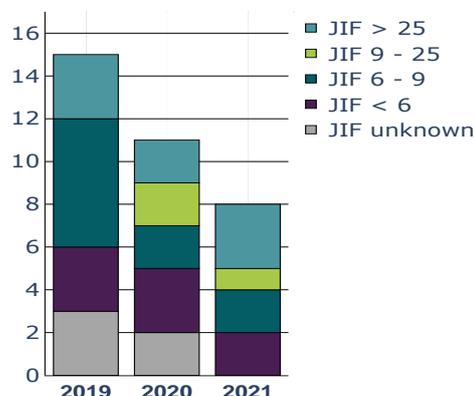
Services

- Single-cell functional analysis based on intracellular cytokine/chemokine production
- Single-cell phenotypic analysis by mass cytometry (CyTOF)
- Single-cell phospho-proteomic analysis of intracellular signalling pathways upon drug treatment or stimulation.

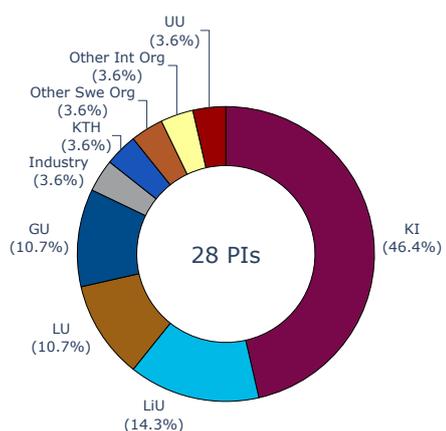
Publication by Category



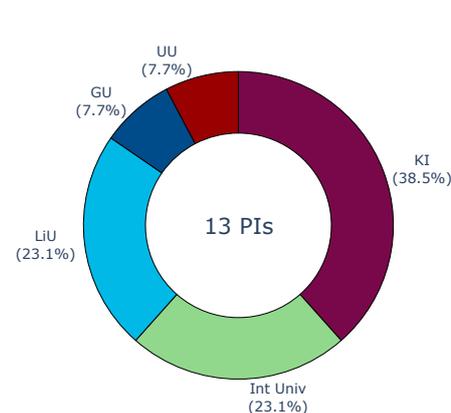
Publication by Journal Impact Factor



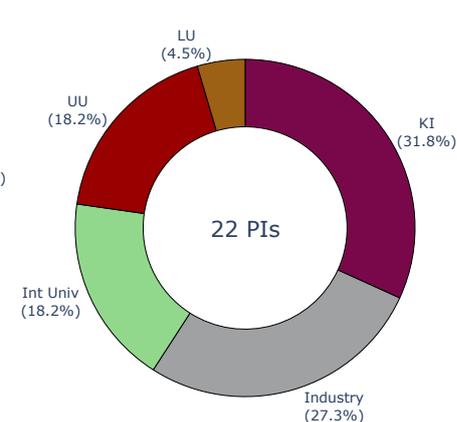
Users 2019



Users 2020



Users 2021





Unit:	Cellular Immunomonitoring
Platform:	Clinical Proteomics and Immunology

Development, Achievements and Plans

The SciLifeLab Cellular Immunomonitoring facility (CIMMR) provides services for phenotyping and functional profiling of immune system from blood, BAL tissue, bone marrow etc. from humans and mice using mass cytometry (CyTOF). The facility has adopted a unique model in running both the experimentation and analysis by the facility staff with long experience thereby enabling better control of all the steps within a project. This is key for overall success given the complexity of such experiments and the instruments. Sample handling is automated to reduce technical variation and improve data quality. There has been successful method development in the facility of a blood stabilizer solution (commercialized by Cytodelics AB), a miniaturized sample preparation (100 uL) for mass cytometry (Olin et al, *Cell*, 2018; Brodin & Quintana-Murci, *Immunity*, 2019) and a deep-learning cell classifier method developed to classify immune populations in an automated and unsupervised manner (Chen et al, *bioRxiv* 2020). Another recent innovation has been in developing a unique buffer solution for stimulation of whole blood keeping the cells viable and responsive to stimulus for long hrs that enables assessment of functional activity of immune cells in blood by multiple downstream methods like CyTOF, flow sorting and transcriptomics, TCR sequencing etc. (Mikes et al., manuscript in preparation; Consiglio et al., manuscript in preparation).

The recent acquisition of 2 new mass cytometers called 'CyTOF XT' (Standard Biotoools, formerly Fluidigm) by our facility have expanded our capabilities owing to the advancements in high throughput with uninterrupted 24hr walk-away acquisition of samples, automation, time to results, and productivity. It provides rich data to help us better understand the complexity in immune systems. Samples are being acquired with more efficiency and most importantly in a less labor-intensive manner enabling efficient workflow with remote operations and instrument monitoring made possible during sample acquisition. Given the expansion in our capabilities in terms of innovation within our facility both experimentally and computationally, Standard Biotoools has signed an agreement with Karolinska Institutet recognizing the Cellular Immunomonitoring facility at SciLifeLab as the reference center for excellence in mass cytometry in Europe. This led to increase in the number of requests and projects from academia/non-academia through Standard Biotoools.

The facility has also begun to work on multiple projects from biotech and pharma industries. Some of the ongoing work has been with iOnctura (manuscript in preparation), Nestle, Janssen, Kancera (manuscript in preparation), and Evolve BioSystems. It's worth highlighting that the study with iOnctura which focused on understanding the immunological parameters of patients with solid tumors using mass cytometry in a dose-escalation trial has led to identifying important changes in different patients, the results of which have been presented upon acceptance of respective abstracts in clinical oncology meetings like ESMO 2021 and ASCO 2022. With Evolve BioSystems, findings from an earlier study (Henrick et al, *Cell*, 2021) has led to establishment of a clinical trial and the investigations are currently ongoing. With Kancera, a phase IIa randomized first-in human trial was done in patients with severe COVID-19 and mass cytometry analysis has shown an immunomodulatory effect of the allosteric antagonist used in this trial. The findings strengthened the continued clinical development of this antagonist against harmful inflammation

[\(https://kancera.com/mfn_news/kancera-reports-top-line-data-from-the-phase-ii-a-study-with-kand567-in-covid-19-patients/\)](https://kancera.com/mfn_news/kancera-reports-top-line-data-from-the-phase-ii-a-study-with-kand567-in-covid-19-patients/).

Our facility has been involved in doing collaborative studies with other units of the CPI platform. One such collaboration is with Affinity proteomics Stockholm unit where an xMAP **assay** for vaccine serology has been established to understand the immune system determinants of infant vaccine responses and the work is currently underway.

With Affinity proteomics Uppsala, a TDP application was made which has been funded this year to establish antibody panels directed against proteins in signaling pathways of interest in oncology and immune cell activation, using a novel multiplex version of in situ proximity ligation assays (isPLA). This project will for the first time provide access to dedicated panels of antibodies that target multiple signaling pathways to monitor changes of importance in oncology and immunology, offering a unique resource for Swedish scientists. Combined with CyTOF, multiplex isPLA analysis will enable powerful analyses of the activation states of immune cells in inflammation and infection.

In the years 2023-2024, our unit will be focusing its efforts in streamlining all the processes for a much smoother and straightforward contracting with biotech and pharma companies as multiple clinical trials and immunomonitoring studies are already ongoing/being planned by the following companies – Nestle, AstraZeneca, Pfizer, Roche, Janssen and Bristol Myers Squibb. We will provide mass cytometry services for immune profiling of subjects recruited to these trials. This will provide very relevant information and would get the focus of our facility closer to precision medicine. We would also work on getting a quick turnaround time and accelerate the therapeutic development arena.

Our unit has recently made an application to VR infrastructure on '*Diagnosing immune system dysregulation to enable precision medicine in patients with inflammatory disorders*'. We know from preliminary experience that measuring key cytokines, immune cell transcriptomes and immune cell states at the single cell level, can provide personalized diagnostics and guide treatments in patients with severe immune dysregulation and we hope with the proposed project for VR, we can ensure that all patients in Sweden can access and benefit from these advances in precision medicine. With the proposed project, we see growing synergies between cross functional units of our platform as in this case with Affinity proteomics Stockholm that we will be collaborating with if the proposal is funded. The proposed project gets multiple teams to work together – SciLifeLab, healthcare, SciLifeLab data center and we will also work closely with the Precision Medicine coordinating group at SciLifeLab aimed at connecting SciLifeLab infrastructure to pharma industry partners and clinical programs and we aim to offer our established and certified assays for future clinical trials in Sweden.

In a recent study (Wahren-Borgström et al., *J Clin. Immunol.* 2022 (in press)) that our facility has contributed with by doing mass cytometry analysis, clinical and immunological changes caused by JAK inhibitor treatment was monitored using plasma proteomics and mass cytometry. This analysis helped in characterizing clinical effects and biomarkers in patients with genetic disorders upon treatment with JAK/STAT inhibitors. This is in line with our VR infrastructure grant proposal as one can tailor treatment to patients based on the understanding of their activating genes and upregulated cytokines.

We wish to see our unit establish a link between SciLifeLab and leading medical centers and clinical experts across Sweden. Such an efficient interface can attract more clinical trials to Sweden and improve the overall clinical academic environment and translational research landscape in Sweden.

Cellular Immunomonitoring

Budget 2022

Costs	2022
Personnel cost	2 441 513
Other personnel costs	18 300
Depreciation	1 572 595
Service and license costs	500 000
Other operating costs	800 000
Premises costs	650 000
Other costs	250 000
Sum costs (kSEK):	6 232 408

Revenues	2022
Funding from SciLifeLab	4 000 000
Funding from financier X	0
Funding from financier Y	0
Funding from financier Z	0
User fees	1 200 000
Sum revenues (kSEK):	5 200 000

Global Proteomics and Proteogenomics

Clinical Proteomics and Immunology Platform ([Web links for Unit: Webpage, Publications](#))

Basic Information

Head(s) of Unit: Maria Pernemalm
PSD(s): Janne Lehtiö
SciLifeLab Unit since: 2017
Host university: KI
FTEs: 8.2
FTEs financed by SciLifeLab: 2.8

Funding in 2021 (kSEK)

SciLifeLab: 3000
SciLifeLab Instrument: 900
KI: 1850
VR: 3832
County council: 3200
University hospital: 1200
Total: 13982

Resource Allocation 2021

Academia (national): 80%
Academia (international): 5%
Internal tech. dev.: 15%
Industry: -
Healthcare: -
Other gov. agencies: -

User Fees 2021

Total (kSEK): 1923
Reagents: 36%
Instrument: 43%
Salaries: 18%
Rent: 3%
Other: -

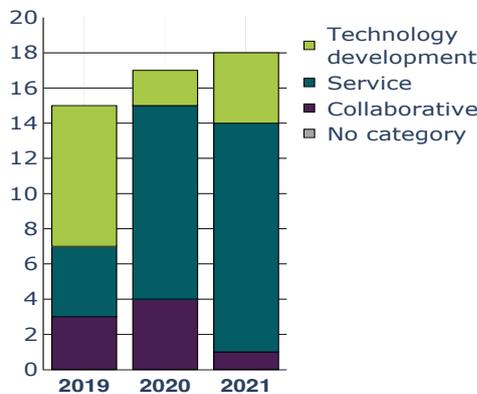
User Fees by Sector 2021

Academia (national): 91%
Academia (international): 6%
Industry: 3%
Healthcare: -
Other gov. agencies: -

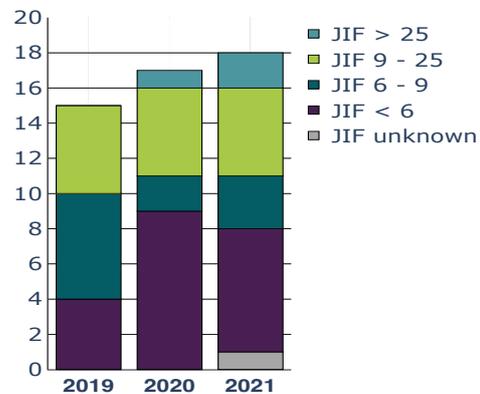
Services

- Unbiased proteogenomics in any species with a sequenced genome
- Personalized proteomics. Variant analysis at the protein level coupled with in-depth quantitative proteome analysis
- Disease state/Variant proteomics. Database supplemented with all known SNPs and disease causing genetic alterations
- In-depth global proteomics
- XenoProteomics

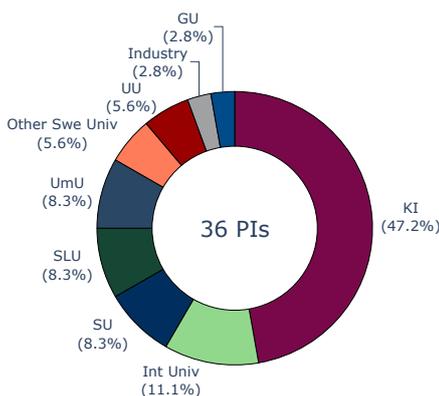
Publication by Category



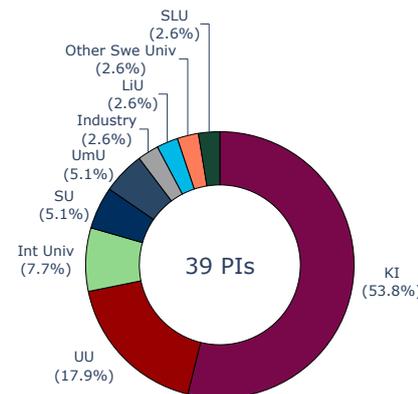
Publication by Journal Impact Factor



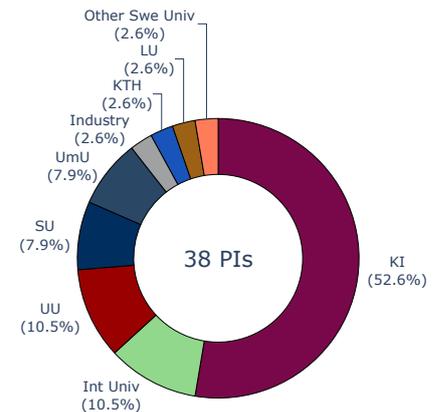
Users 2019



Users 2020



Users 2021





Unit:	Global Proteomics and Proteogenomics
Platform:	Clinical Proteomics and Immunomonitoring

Development, Achievements and Plans

i) ***Development and major achievements 2021–2022***

The GP&PG facility provides high level mass spectrometry (MS) expertise in the area of proteogenomics and related clinical proteomics. Our vision is to offer cutting edge proteogenomics service from environmental meta-proteomics and preclinical models to clinical trials, and therefore we continuously introduce new MS-based technologies and multi-omics data-analysis capabilities into the facility. Clinical proteogenomics is a rapidly developing field taking advantage of the parallel developments in DNA/RNA sequencing, biological MS and bioinformatics. In 2021 our facility was coordinating national application writing for clinical proteomics for VR infrastructure call and the application was successfully funded to form a national clinical proteomics infrastructure including harmonized cutting edge MS and robotics infrastructure between sites together with SciLifeLab and BioMS Lund and Gothenburg facilities. Further, through integration with the regional Clinical Proteomics Facility (headed by Janne Lehtiö, funded by Hospital research budget) as well as collaboration with surrounding research groups, national efforts in genome medicine and the clinical trial units, the Proteogenomics facility has obtained a critical mass of instrumentation and expertise to offer world leading support in clinical proteogenomics.

Over the last two years we have seen an increase in requests of analysis of different blood plasma proteome compartments, especially of extracellular vesicles (EVs), in particular from clinical plasma cohorts. To be able to better advise users we performed an evaluation of different enrichment methods for plasma EVs together with Susanne Gabrielssons group at KI (Veerman. Journal of extracellular Vesicles 2021). We also recently developed a novel method for global in-depth human plasma proteogenomics, enabling quantitative analysis of up to 2000 proteins to assist biomarker discovery (Pernemalm M. eLife 2019) and this workflow has been further improved by using a new type of spin column for high abundant protein depletion (Cao X. Journal of Proteome research 2021). To improve our neoantigen discovery workflow, we have created a new pipeline for immune peptidome analysis which we aim to make available to facility users. Our publication describes direct identification of novel tumor antigens for an aggressive triple-negative breast cancer model. Immunopeptidome profiling revealed 2481 unique antigens, among them a novel ERV antigen originating from an endogenous retrovirus element (Peltonen et al., Cancers 2021). In contrast to in-depth discovery proteogenomics, MS-analysis in Data Independent Acquisition (DIA) mode offers a rapid and reproducible analysis of a proteome using low starting material amount. The method is highly suitable to define the molecular phenotype in clinical studies and has been piloted in a large cancer study (Lehtiö J, Nature Cancer 2021). The turnaround time for DIA analysis/sample is substantially lower than traditional global in-depth proteogenomics, hence a key feature to transition into the clinical setting and for large validation studies and is now offered as a service in the facility. DIA was also lifted as a key development by the international Evaluation committee and supported by a SciLifeLab expensive instrument grant. As a data reporting tool to support clinical decisions, we are currently implementing proteomics data in the Molecular Tumor Board Portal (Tamborero, Nature Cancer. 2022 developed in the Lehtiö research group and is already in use for genomics trials).

We have also worked to improve our pre-clinical assays and developed a combined wet lab and bioinformatics workflow for global subcellular proteome analysis (Arslan T., Nature Protocols, 2022) and added often requested phosphoproteomics to our service portfolio during 2021. Robust phosphoproteomics workflow was co-developed by adapting Broad Institutes Phosphoproteomics workflow funded by the SciLifeLab TDP-funding.

To facilitate the communication with users and improve our project management we have during 2022 set up an iLAB (Agilent) based project portal (https://karolinska.corefacilities.org/service_center/show_external/3726), which is currently being implemented.

ii) ***Development plans for the unit 2023–2024 and beyond***

The facility is currently involved in several projects with impact on future healthcare services, such as development of novel clinical proteomics methods and establishment of a Clinical proteomics unit at the Karolinska University hospital, funded via SciLifeLabs Precision Medicine initiative and Swedish Pandemic Laboratory Preparedness. Through grants from Vinnova, Scilifelab pandemic preparedness and VR (BioMS) we are currently equipping two sample prep labs at the Karolinska University hospital to facilitate the sample prep and analysis of clinical materials both in clinical trial setting, for research, and as a testbed environment for novel technologies. In parallel several IT development projects for secondary use of healthcare data has been initiated both with the hospital IT department as well as the data center at SciLifeLab (as a part of the pandemic preparedness) to connect proteogenomics data with healthcare data in systematic ways.

For future clinical trial use, we are currently developing a workflow for Parallel Reaction Monitoring (PRM) MS. Setting up this service would provide us with a tool to create targeted custom made protein panels based on our proteogenomics discovery analysis, which would provide an important validation tool. In addition, we are also developing a protocol for MS based global protein analysis of FFPE sections, which would make large retrospective sample cohorts available for in-depth global proteomics and proteogenomics analysis. This has traditionally been difficult in MS as the FFPE preparation involves protein crosslinking that needs to be reversed. Preliminary data shows that we can identify a similar number of proteins in FFPE material with our workflow as in fresh frozen tissue using the DIA technology.

The development of spatial- and single-cell genomics and transcriptomics techniques has raised increased interest of studying the global protein expression level in these experiments in parallel. Recently Emma Lundberg at KTH/SciLifeLab and her group developed a method called Deep Visual Proteomics (DVP), which combines artificial-intelligence-driven image analysis of cellular phenotypes with automated single-cell or single-nucleus laser microdissection and ultra-high-sensitivity mass spectrometry (Mundt et al., Nature Biotech 2022). DVP links protein abundance to complex cellular or subcellular phenotypes while preserving spatial context. Together with the Spatial proteomics facility at SciLifeLab and Emma Lundberg's research group, we have now started a collaboration to set this technique up as a service. The VR instrument grant allowed us to purchase a dedicated single cell MS instrument (Bruker TIMS-TOF SCP with Evosep LC system), which is currently being installed in the facility. Moreover, we are currently installing a HTP-proteomics instrument (Bruker TIMS-TOF2 with Evosep LC system, partly financed by VR and SciLifeLab instrument grant). Facilitated by new robotics platform and rapid PRM/DIA analysis we envision to develop clinical trial support with 1–2 weeks turn-around analysis as well as robust QC procedures to allow prospective clinical proteomics as one of the first/if not first proteogenomics core in the world. This effort is done in coordination with other facilities together with SciLifeLabs precision medicine initiative.

We have also generated a proteome data resource for non-bioinformatics experts (Leo IR., Nature Comm) which will us to form a prototype to develop data-portals together with SciLifeLab Data Center. Finally, development of long read sequencing opens up new possibilities to use proteogenomics for variant level analysis and we aim to initiate such technology development project together with researchers and the national genomics platform.

Budget 2022

Global Proteomics and Proteogenomics

Costs	2022
Personnel cost	7 787 755
Other personnel costs	96 025
Depreciation	8 006 338
Service and license costs	905 275
Other operating costs	3 301 375
Premises costs	1 152 208
Other costs	349 125
Sum costs (kSEK):	21 598 101

Revenues	2022
Funding from SciLifeLab	3 000 000
Funding from Funding from Vetenskapsrådet (BioMS)	3 800 000
Funding from KI (BioMS)	1 900 000
Funding from KI/SciLifeLab (Dyr utrustning)	800 000
Funding from Karolinska University Hospital/FoU	3 493 000
Funding from KI/FoU (Dyr Utrustning)	1 200 000
User fees	3 500 000
Sum revenues (kSEK):	17 693 000

Glycoproteomics

Clinical Proteomics and Immunology Platform (Web links for Unit: [Webpage](#), [Publications](#))

Basic Information

Head(s) of Unit: Carina Sihlbom
PSD(s): Elisabet Carlsohn
SciLifeLab Unit since: 2021
Host university: GU
FTEs: 12.0
FTEs financed by SciLifeLab: 1.2

Funding in 2021 (kSEK)

SciLifeLab: 1500
GU: 750
VR: 2400
Total: 4650

Resource Allocation 2021

Academia (national): 35%
Academia (international): 35%
Internal tech. dev.: 30%
Industry: -
Healthcare: -
Other gov. agencies: -

User Fees 2021

Total (kSEK): 450
Reagents: 34%
Instrument: 33%
Salaries: -
Rent: 33%
Other: -

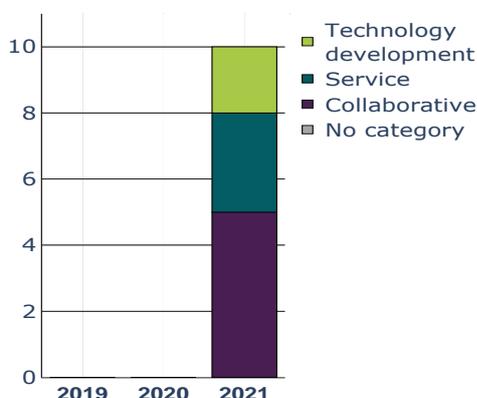
User Fees by Sector 2021

Academia (national): 65%
Academia (international): 25%
Industry: -
Healthcare: 10%
Other gov. agencies: -

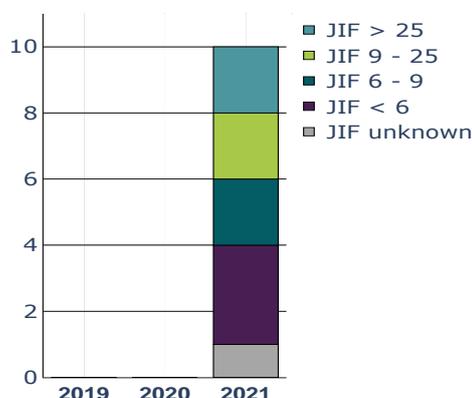
Services

- Protein glycosylation analysis using glycopeptides & nanoLC mass spectrometry (MS/MS) for purified proteins or complex samples, e.g. plasma
- LC-MS/MS of released glycans from biological material
- Analysis of glycosaminoglycans (GAG), chondroitin/heparan sulfate proteoglycans extracted from cells/body fluid
- Multiple post-translational modifications (PTMs) studies e.g. protein glyco- and phosphorylation, including quantification & sample preparation for proteomics

Publication by Category



Publication by Journal Impact Factor



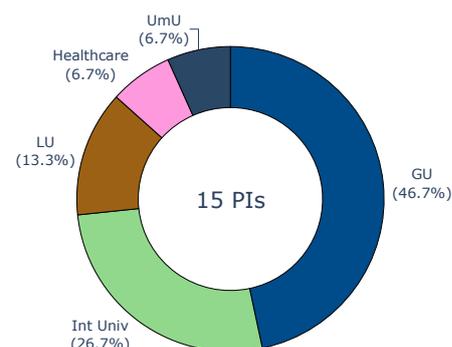
Users 2019

No user information

Users 2020

No user information

Users 2021





Unit:	Glycoproteomics
Platform:	Clinical Proteomics and Immunology
Development, Achievements and Plans	
<p>During 2021 and 2022, we have established data processing workflow for protein glycosylation studies by combining unique features of Byonic™ and Proteome Discoverer™ to facilitate (1) data analysis in large scale glycoproteomic studies and (2) site-specific micro heterogeneity evaluation and quantification (Biol Cell. 2022 Jun;114(6):160–176). The analytical procedures in glycosylation studies were further improved to support the new processing workflows. At present, these include workflows for large scale glycoproteomic projects and deep glycoprofiling projects. Part of this work was published in Nature Methods 18 (11) 1304–1316, Community evaluation of glycoproteomics informatics solutions reveals high-performance search strategies for serum glycopeptide analysis. In another study, a glycoproteomic approach for the identification of novel chondroitin sulfate proteoglycans (CSPGs) using a combination of biochemical enrichments, enzymatic digestions, and nanoscale liquid chromatography tandem mass spectrometry (nLC-MS/MS) analysis, were optimized. This approach has enabled the identification of several novel core proteins and characterization of CS glycopeptides from human cerebrospinal fluid (CSF), (Methods Mol Biol 2022;2303:71–85).</p> <p>To bridge the gap of the limited softwares available for interpretation of glycomics data, we have close collaboration with the Bioinformatic Core Facility at Sahlgrenska Academy. We are developing a custom-made data script to aid in the interpretation of released glycans. This work can be extended to include NBIS and our collaborators in Europe.</p> <p>The Cyclic Ion Mobility Mass Spectrometer from Waters was installed in summer of 2021. After the familiarization of this new system, we are considering research projects that will benefit from the ability to separate fragments from glycoform isomers for structural characterization. In addition to the Waters instrument, an Orbitrap Exploris 480 and an Orbitrap Tribrid Eclipse mass spectrometers have been installed and we are currently transferring and optimizing methods on these new systems.</p> <p>The difference between health and disease in the gut depends largely on the presence and maintenance of a commensal bacterial flora in the mucosal layer of the colon. The colon microbiota utilizes glycans on the mucus glycoproteins as a nutritional source, these glycans are heterogeneous and branched and are heavily sulfated and complex to analyze. In a current project, it was shown that sulfatases produced by <i>Bacteroides Thetaiotaomicon</i>, a dominant member of the human gut microbiota, could collectively degrade all known sulfate linkages in <i>O</i>-glycans. By the use of unique methodology and resources, sulfatase glycan substrates and their end products were characterized using porous graphitized carbon columns connected to mass spectrometry in the negative ion mode. The results were published in 2021, A single sulfatase is required to access colonic mucin by a gut bacterium (Nature 2021; Oct;598(7880):332–337) and the project is expanding.</p> <p>The receptor-binding domain (RBD) of the SARS-CoV-2 spike protein is a conserved domain and a target for neutralizing antibodies. The carbohydrate structures on the spike protein are important for its activity and in one project the carbohydrate content of the recombinant RBD</p>	

produced in different mammalian cells was defined. The carbohydrates on the RBD proteins were enzymatically modulated, and the effect on antibody reactivity was evaluated with serum samples from SARS-CoV-2 positive patients. Removal of all carbohydrates diminished antibody reactivity, while removal of only sialic acids or terminal fucoses improved the reactivity. The results can be of importance for the design of future vaccine candidates, indicating that it is possible to enhance the immunogenicity of recombinant viral proteins. (ACS Infect Dis. 2022 Aug 18)

In 2021 there were three first time users out of the total fifteen PI's using GP-GU and during 2022 eight additionally new user groups utilized our service and support for glycoproteomic studies. The new users are from Umeå, Luleå, Region Östergötland, Stockholm and Denmark. The outreach will continue with assistance from the site coordinator in Gothenburg and together with our CPI platform. GP is part of the PCF course in MS and Proteomics which is announced nationally to all Ph.D students and was given in April 2022 with the next opening in the autumn 2023. We plan to announce national digital workshops in MS-based Proteomics.

GP-GU has attended the HU meetings and CPI Platform meetings. GP-GU is part of Proteomics Core Facility (PCF) and has also been involved in the analysis of archeological bone samples via the Genomics Platform, so called Paleoproteomics. Furthermore, GP-GU, PCF and GPP-KI will work closely within the new VR funding for Clinical Proteomics and Precision Medicine.

The development and technology plans for 2023–2024 and beyond includes:

- Antibody glycosylation studies for biological properties of different patient-derived monoclonal antibodies relevant in molecular medicine of Rheumatology.
- Further development of post-processing scripts to assist data evaluation and presentations will be carried out, which will be conducted by addition to the team by a part-time employed bioinformatician. Validate and adopt new software tools for identifying and assigning glycoconjugates, statistical packages for quantitative glycomics and glycoproteomics, in collaboration with bioinformatic units and two European research groups.
- Establishment of glycoanalytical workflows for samples stored in biobanks, such as FFPE material and low protein amount from tissue biopsies. To aid in this sample preparation, we have acquired a focused-ultrasonicator instrument.
- Exploring the infrared multiple photon dissociation (IRMPD) spectroscopy with mass spectrometry (MS-IR) to differentiate between glycan isomers directly after data-dependent MS/MS in our current ion-trap MS system.
- Setting up analytical workflows for multiple PTM analysis to facilitate PTM cross-talk studies and to use the data already available from phosphorylation studies performed in the Proteomics Core Facility.
- Using cyclic IM-MS to verify glycoanalytical findings in terms of quantitative differentially changed glycans, and the assignment of unknown glycoconjugates, in regards of linkage position and linkage configuration of the glycan part. The pilot project will involve synovial fluid to describe exactly what those differences are. This would allow our users to accurately identify glycoconjugates (glycosyltransferases) that are involved in the transition from a glycostate to another. It would also provide the blue-print for designing synthetic glycoconjugates, to explore how altered glycosylation are influencing the state of a cell or tissue.

Budget 2022

Glycoproteomics

Costs	2022
Personnel cost	2 627 762
Other personnel costs	0
Depreciation	2 940 000
Service and license costs	195 000
Other operating costs	227 500
Premises costs	225 000
Other costs	0
Sum costs (kSEK):	6 215 262

Revenues	2022
Funding from SciLifeLab	2 000 000
Funding from financier X	1 200 000
Funding from financier Y	2 400 000
Funding from financier Z	0
User fees	600 000
Sum revenues (kSEK):	6 200 000

Clinical Genomics platform

Platform Director: Thoas Fioretos, LU

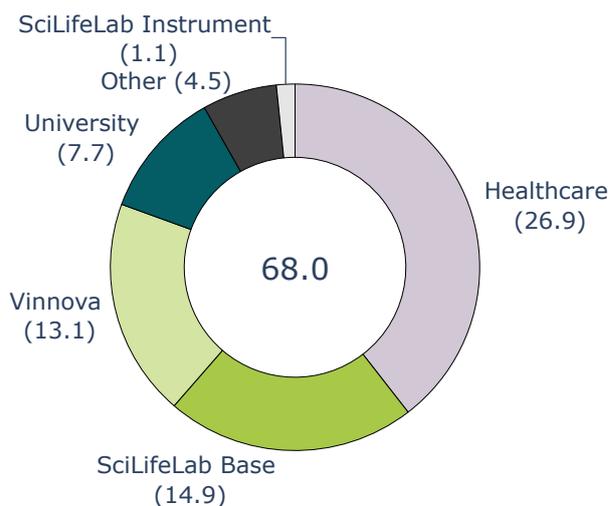
Co-Platform Director: Lucia Cavalier, KI

Platform Coordination Officer: Eva Berglund, UU

Platform and Units SciLifeLab Funding 2021:

Unit	(MSEK)
Clinical Genomics Gothenburg	2.1
Clinical Genomics Linköping	0.8
Clinical Genomics Lund	2.1
Clinical Genomics Stockholm	5.0
Clinical Genomics Umeå	0.8
Clinical Genomics Uppsala	2.5
Clinical Genomics Örebro	0.8
PD, PCO, Platform Strategic Budget	0.8
Sum:	14.9

Total Funding 2021:



Platform Specific Terms and Conditions for Funding - Clinical Genomics

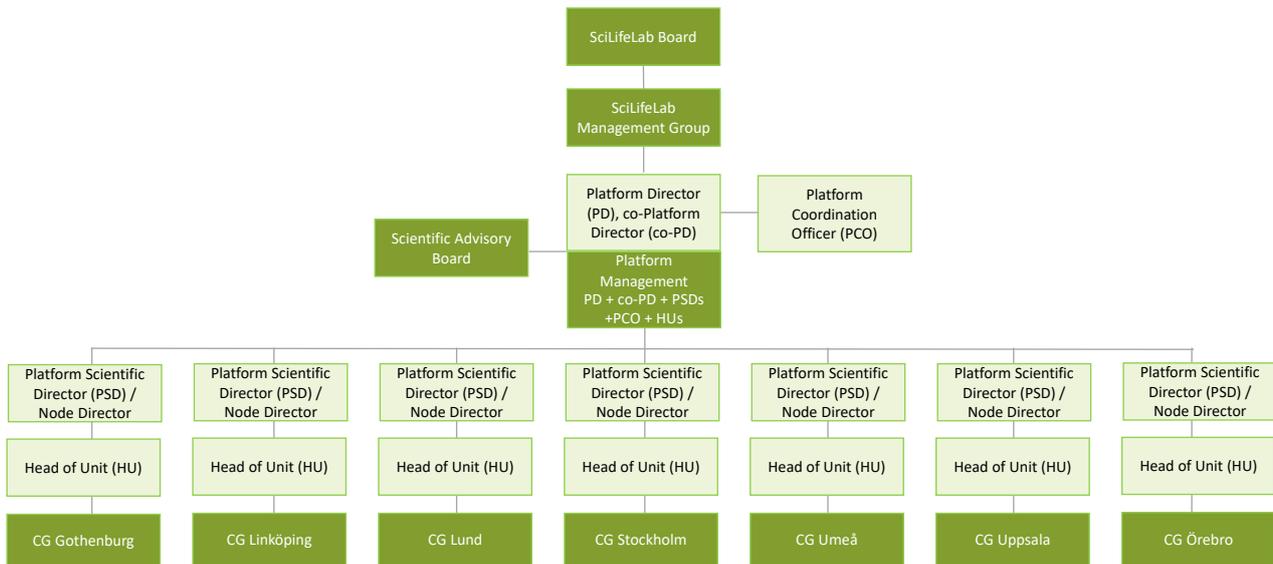
This document concerns the terms and conditions for SciLifeLab funding of the Clinical Genomics Platform and Units from 2021 and onwards and outlines the strategic direction and vision MG wants the platform to take. As a help to follow and measure the progress towards the vision, a separate document outlining specific KPIs for the Clinical Genomics platform has been established (Appendix 1). The mid-term checkup in the middle of the 4-year funding period will focus on how well the Platform and Units have taken into account the items in this document.

- SciLifeLab funding to the Clinical Genomics Platform and Units is meant for:
 - i) collaboration and coordination of Clinical Genomics Units at a national level
 - ii) providing state-of-the-art genomic services for translational research and clinical trials
 - iii) adapting and implementing genomic technologies into clinical utility
 - iv) training and education
 - vi) achieving data sharing
- The platform should actively contribute towards the Government's ambition of making Sweden a leading life science nation
- As a translational Platform with Units at all medical faculties, maintain important links between SciLifeLab, Genomic Medicine Sweden, healthcare, and biobanks, both at national and regional level
- Together with the Clinical Proteomics and Immunology platform and other platforms promote a globally

leading capability for Precision Medicine at SciLifeLab. The capability should be built on and take advantage of existing national initiatives, e.g., Genomic Medicine Sweden.

- The platform is expected to play an important role in the development of Pandemic Laboratory Preparedness, where an important priority is data sharing and data availability of the pandemic in a real-time manner and shared to the public domain
- The platform as well as the SciLifeLab Precision Medicine capability should be closely integrated and engaged in the planned DDLS activities on precision medicine and diagnostics as well as in infection biology and epidemiology
- Together with other platforms, Data Centre and SciLifeLab centrally, support approaches for data sharing for research and society purposes, including more sensitive, clinical data. Also, efforts should be made to promote all users of the Clinical Genomics Platform to have patient consents and ethical permissions for data sharing.
- Substantially enhance the collaboration and synergies with the Genomics platform in technology development and adaptation of new methods for translational research and clinical diagnostics
- Be actively involved in developing national SciLifeLab nodes at each non-host university, primarily built around the Clinical Genomics, Bioinformatics, Spatial and Single Cell Biology and Genomics platforms, along with DDLS activities and WCMM centers

Clinical Genomics platform



Organization

The Clinical Genomics (CG) platform consists of seven nodes, each of which is managed by a Platform Scientific Director/Node Director and a Head of Unit. The founding nodes in 2014 were CG Stockholm and Uppsala, with CG Lund and Gothenburg joining in 2016. In 2019, CG Linköping, Örebro and Umeå became new nodes. With seven nodes, located at all Medical Faculties in Sweden with a university hospital, the platform now has a unique national outreach. In total, 95 FTEs work within our platform. Notably, the nodes differ in size and in services offered (see individual reports) with CG Stockholm, Uppsala, Lund and Göteborg being the largest and CG Linköping, Örebro and Umeå smaller and still in the build up phase. The size of each node is also reflected by the allocated budget from SciLifeLab.

The PD, co-PD and PCO meet every second week to plan platform management group (PMG) meetings and other joint activities/operations at the platform. If necessary, specific HUs are asked to join these meetings. The Scientific Advisory Board (SAB) includes five national and international experts with the first meeting held in April 2022. The SAB will receive the mid-term reports before the next meeting in September and has been asked to make a SWOT analysis and to provide recommendations for future development/actions. The PD and co-PD have regular meetings with the SciLifeLab Infrastructure Director. The PCO has regular meetings with the SciLifeLab Infrastructure Coordinator and other PCOs, as well as with the Communications Manager of Genomic Medicine Sweden (GMS, see below).

Platform Management

PMG meetings with all PSDs and HUs are held monthly to discuss daily operations, new development areas, and strategic issues. Physical PMG meetings are held 1-2 times per year. In March 2022 a physical meeting was held to establish an **operational plan** for the CG platform. This operational plan defines eight main objectives, which reflect the 'general terms and conditions', the 'platform-specific terms and conditions', as well as the 'platform-specific KPIs'. Each objective is broken down into 'key activities', 'target', 'responsible person(s)', 'deadline', and 'follow-up dates'. The operational plan can be accessed through a "Google sheet". At the second physical PMG meeting in September in conjunction with the SAB meeting, the progress will be assessed. To further leverage on specific node capabilities,

we have also prioritized eight **'Technology Focus Areas'** and assigned responsible nodes to lead development in each area (see table below).

Technology Focus Area	Responsible nodes
Informatics/data sharing	Gothenburg, Linköping
Long-read sequencing	Uppsala, Örebro
Optical mapping	Stockholm
Multi-omics	Stockholm, Lund
Ultrasensitive variant detection	Uppsala, Stockholm
Epigenetics	Linköping, Umeå
Single-cell and spatial omics	Lund, Uppsala
Meta-genomics	Örebro, Gothenburg

A first **physical platform retreat** for all personnel was held in October 2021 with 100 participants, to update activities, discuss joint challenges and possible collaborations in thematic groups. The SciLifeLab Facility Forums (October 2019 and October 2022) also gather platform personnel physically. Brief digital updates for all personnel have been held e.g. to introduce the new platform management and present the operational plan.

The platform has a **webinar series** and 10 webinars were held last year, mainly on technologies of our focus areas. The webinars contribute to internal competence development and when International speakers are invited, these webinars are announced to a wider audience. For example, one webinar was organized together with GMS with an invited speaker from the US and Amazon Health talking about AI-driven diagnostics of hematologic malignancies.

At the **cross-platform level**, regular meetings have been held with the Genomics platform, the SciLifeLab capability for Precision Medicine, the SciLifeLab Data Center and the Bioinformatics platform. The CG platform has one member in the R&D group of the Genomics platform,

meeting approximately once a month, as well as several representatives in the different R&D working groups. The close contact with the Genomics platform and the SciLifeLab capability for Precision medicine, resulted in two joint applications for the 'VR Grant for accessibility to infrastructure call'; one focusing on improved support to clinical trials and the other on improved single-cell analysis capabilities.

As the technological backbone of GMS, our platform works closely with **GMS** to promote precision diagnostics and medicine within healthcare of direct impact for patients and the society. Regular meetings between our platform and GMS are held and we participate with expertise and service in all major work packages (e.g., childhood cancer, complex diseases, hematology, solid tumors, infectious diseases, pharmacogenomics, rare diseases, and informatics) of GMS. The successful research-implementation framework established by the CG platform and GMS to promote research and implement precision diagnostics and medicine nationally in Sweden was recently described (Fioretos et al., Nat Med, in press).

Development, Achievements and Plans

Development and achievements 2021-2022

To meet our 'Platform-specific terms and conditions' and the 'platform-specific KPIs', we have developed a joint Operational plan within the platform. Below, the progress within the key objectives of this Operational plan is briefly summarized:

- 1. Increase collaboration and coordination between CG nodes:** The new organization and joint operational plan of the platform has greatly facilitated the collaboration within the platform. By the regular meetings, webinars, joint platform projects, and technology focus areas with dedicated responsible nodes, knowledge and progress is efficiently shared between the nodes.
- 2. Offer broad range of state-of-the-art and end-to-end genomic services with focus towards translational and clinical research and clinical trials**
We have continued developing our service offerings in several key disease areas, including for example rare inherited diseases where our solutions (e.g., clinical decision support system Scout) have now been used to analyse >15,000 whole-genome samples. Several new services have been established during 2021-2022. This includes several modalities of single cell assays with a focus on clinical applications, long-read sequencing (offered together with the Genomics platform), and combined whole-genome and whole-transcriptome sequencing for cancer samples. The platform also supported several clinical trials with services (e.g., MEGALiT, NMDSG14B, ProBio II, Alasca, and iPCM).

For further details, see unit reports.

- 3. Facilitate implementation of new genomics-based methods into clinical use and contribute to demonstrate clinical utility**
In collaboration with our healthcare regions and GMS, we have developed and implemented several new diagnostic tests in clinical routine during 2021-2022. Major tests include the GMS hematology panel (now used broadly in Sweden with >5000 samples analyzed), the GMS solid tumor panel (currently in the validation phase), significant improvements in protocols for WGS for rare disease (see CG Stockholm report), new methods and upscaling of SARS-CoV-2 sequencing, and methylation arrays for improved diagnostics of brain tumors. Currently, we work on a national clinical study aiming to assess whether WGS and whole-transcriptome sequencing can replace current diagnostic methods in acute leukemias (Berglund et al, Frontiers in Medicine, 2022).
- 4. Engage in training and education of the SciLifeLab and healthcare communities**
Through the distributed model of our platform, each node participates in several educational activities. We have contributed to education at undergraduate and graduate level as well as for professional clinical societies (see node reports). In addition, several CG bioinformaticians participate as mentors in the NBIS advisory program, and we have an active dialogue with the SciLifeLab

capability for Precision Medicine regarding contribution to training.

5. **Contribute to DDLS and promote data sharing**

We have regular contacts with GMS, the SciLifeLab Data Center and DDLS regarding synergies in health data sharing. We also contribute to technical development of the National Genomics Platform (NGP), a national data lake of genomics data generated within healthcare across seven hospitals, to enable sharing of sequence data generated within the clinical studies performed within the project. This will be an invaluable research resource within the data-driven precision medicine field. Several nodes are also working with the newly established DDLS data-nodes to understand how healthcare data can be made available to the DDLS project through the Clinical Genomics platform links to the healthcare community.

6. **Promote the SciLifeLab capability for Precision Medicine**

We have an active dialogue with the SciLifeLab capability for Precision Medicine, and engage continuously in establishing and maintaining important links between SciLifeLab and key stakeholders in precision medicine at a national and regional level, including GMS, healthcare and biobanks. We are a partner in the Vinnova-funded project TestBed Sweden to promote the establishment of clinical trials in Sweden. We have also been active

in discussions regarding establishment of centers for precision medicine at the different university hospitals.

7. **Strengthen national preparedness for future pandemics**

We lead the PLP project Genomic Pandemic Preparedness Portfolio (G3P) that coordinates the development of a genomics-based preparedness, covering aspects related to data generation, bioinformatic analysis, and aggregation and visualization of results, and we will also contribute to all Technology Development Projects at Clinical Microbiology laboratories funded by SciLifeLab.

8. **Increase SciLifeLab and CG platform visibility**

We work actively with increasing the visibility of our platform and SciLifeLab, and have established a communication plan with activities. For example, we have set up a LinkedIn account for the platform and contributed several articles about CG platform news to the SciLifeLab website/newsletter. We have also presented the platform at several conferences, such as the NMMP meeting in Ystad 2022 and the Nordic Precision Medicine Forum 2022 (see node reports for further details). Many communication activities are performed in conjunction with GMS, and a joint communication plan will underline the role of each organization and visualize synergies. We have been involved in the establishment of SciLifeLab nodes at non-host universities (Lund, Gothenburg, Umeå and Linköping).

Plans for 2023-2024

We aim to continue along the route taken and to further increase and align our intra- and cross-platform activities to meet the ambitious objectives set out. We aim to reach a point where all services offered are harmonized and easily accessed, with some nodes taking the responsibility for a 'Technology Focus Area', followed by distribution of expertise and technology to the other nodes depending on the overall national demand for such services. To increase harmonization, we would like to strengthen the platform with additional resources for administrative and scientific coordination.

We will also engage fully in promoting the DDLS program, and we foresee that there is a need to structure and streamline our work to contribute with FAIR scientific data to the DDLS-initiative. To realize data sharing, we have identified the need for a dedicated platform-specific research data manager.

Another major focus of the platform will be to support the

Plans for beyond 2023-2024

During 2023-2024, we will continue the work towards our vision to operate as an **internationally leading infrastructure supporting translational and clinical research, and develop tomorrow's diagnostics within healthcare**. This includes

SciLifeLab precision medicine capability. If our VR application on support for clinical trials is funded, activities related to this will be highly prioritized. Likewise, if the single-cell application is funded, we will intensify the development of clinical applications of single-cell sequencing.

Regarding international collaborations, we plan to continue with a strong dedication to lead and contribute to various bioinformatic pipelines using the international nf-co.re workflow collaboration. We are also active partners in the Nordic Alliance for Clinical Genomics, and through GMS strongly linked to several national programs for implementation of genomic medicine and precision medicine in Europe (including Genomics England, Danish Genome Center, ZPM Center for Personalised Medicine in Germany). These international collaborations will help driving further international harmonization within clinical genomics and precision medicine.

further advancing our expertise and services in genomics-based methods to make a strong national impact for Swedish precision medicine research. In addition, by working close with our Regional healthcare partners and GMS, we will

continue our work to make a direct impact on genomics-based precision diagnostics and medicine within healthcare. The specific goals and activities will be set in dialogue within

the platform and with the SciLifeLab Management Group and will be form the basis for our Operational plan(s) in 2023/2024.

Questions/comments to reviewer

Many nodes within the platform face challenges in recruiting and retaining highly skilled bioinformaticians. Here, we would like to see a closer collaboration with NBIS, who could have bioinformaticians affiliated/embedded in the unit to help develop the services offered at the unit and cross-unit level.

For the platform to fully contribute to the DDLS-program, there is a need to work on legislative issues centrally at SciLifeLab to enable data sharing in a structured way. A Strategic plan for how the different platforms, including the CG platform, can contribute to DDLS would be beneficial

(address challenges, possible solutions, resources needed. etc)

For the CG platform and other platforms within SciLifeLab to provide services to clinical trials from the industry, thereby promoting the Swedish life science sector, there is likely a need for some nodes/platforms to become ISO certified or accredited (e.g. ISO 17025). Within the CG platform, CG Stockholm has an ISO 17025 accreditation for selected analyses. It would be important for SciLifeLab to discuss the need and format for obtaining accreditation of relevant services to support clinical trials.

Request for additional funding 2023–2024

Coordination at the platform level

To reach our first objective “Increase collaboration and coordination between CG nodes”, we have identified a great need for resources for coordination at the platform level. We have extended the PCO role from 20% to 40%, however, this is not sufficient for full harmonization of services. With seven nodes at different universities, coordination of meetings as well as clear and transparent communication requires a lot of effort. In addition, the limited budget from SciLifeLab (14.8 MSEK) for a platform with 95 FTEs requires constant activity in attracting external funding. We propose to add two new part time roles at the platform level, that will be combined with other assignments at the individual nodes.

1. Administrative coordinator (0,25 FTE). Assignments will include to support planning, organization and documentation of meetings and events, internal and external communication as well as ensure good routines for document handling and storage. The cost is estimated to 140 kSEK for 2023 (9 months) 187 kSEK for 2024 (12 months).
2. Scientific coordinator (0,25 FTE). Assignments will include to support coordination and writing of grant applications and joint scientific articles. The cost is estimated to 187 kSEK for 2023 (9 months) 250 kSEK for 2024 (12 months).

Contribution to DDLS and data sharing

We have discussed with Johan Rung at the SciLifeLab Data Center how we best can contribute to DDLS and reach our fifth objective “Contribute to DDLS and promote data sharing”. We have jointly identified the need to recruit a platform-specific Data Research Manager (1 FTE).

Assignments will include support with structuring our data handling processes and IT-infrastructures, as well as being a contact person with the Data Center, the DDLS Data area nodes, and GMS. The cost is estimated to 600 kSEK for 2023 (6 months) and 1200 kSEK for 2024 (12 months).

Request for additional funding 2023–2024

Specify all costs in kSEK

Unit	SciLifeLab funding 2022 (kSEK)	Requested Scilifel.ab funding 2023 (kSEK)	Requested SciLifeLab funding 2024 (kSEK)
CG platform	14800	15727	16437

Clinical Genomics Gothenburg

Clinical Genomics Platform (Web links for Unit: [Webpage](#), [Publications](#))

Basic Information

Head(s) of Unit: Per Sikora, Marcela Davila
PSD(s): Lars Palmqvist
SciLifeLab Unit since: 2016
Host university: GU
FTEs: 12.2
FTEs financed by SciLifeLab: 3.0

Funding in 2021 (kSEK)

SciLifeLab: 2100
GU: 550
Vinnova: 3713
University hospital: 2500
Other: 750
Total: 9613

Resource Allocation 2021

Academia (national): 10%
Academia (international): -
Internal tech. dev.: 10%
Industry: -
Healthcare: 80%
Other gov. agencies: -

User Fees 2021

Total (kSEK): 3600
Reagents: -
Instrument: 10%
Salaries: 85%
Rent: -
Other: 5%

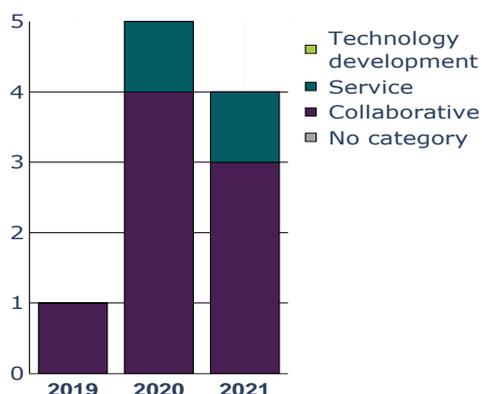
User Fees by Sector 2021

Academia (national): 10%
Academia (international): -
Industry: -
Healthcare: 90%
Other gov. agencies: -

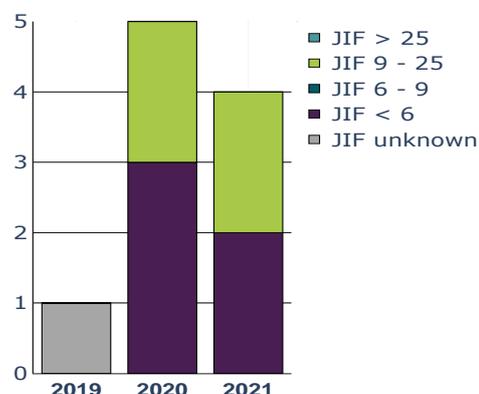
Services

Sequencing and bioinformatics support for clinical research and implementation projects with a focus on NGS. Support on a wide range of NGS applications including WGS for clinical applications. The sequencing facility performs RNA-seq, exome sequencing, panels, metagenomics and bacterial genome sequencing locally, including 10x single-cell, exome and WGS. General consulting and support on cluster hardware and software infrastructure development and storage for NGS applications.

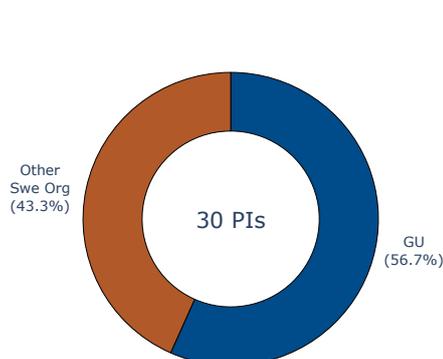
Publication by Category



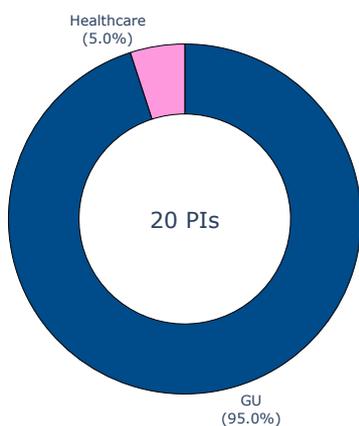
Publication by Journal Impact Factor



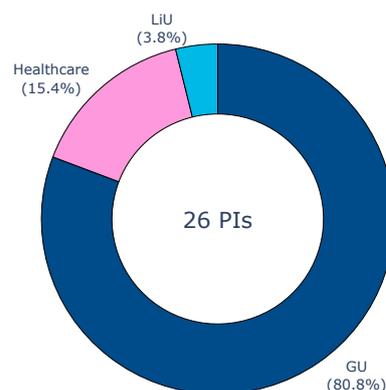
Users 2019



Users 2020



Users 2021





Unit:	Clinical Genomics Gothenburg
Platform:	Clinical Genomics

Development, Achievements and Plans

Clinical Genomics Gothenburg (CGG) became a node (unit) to the Clinical Genomics platform in 2016. The node is organized within the Core Facilities at the University of Gothenburg and collaborates closely with the Center for Medical Genomics (CMG) which is part of the Sahlgrenska university hospital. CMG also provides laboratory services within routine healthcare. CGG employs a total of 10 bioinformatics FTEs and 3.5 laboratory FTEs. CGG offers a wide variety of genomic services, with a focus on bioinformatics and data sharing as well as metagenomics and epigenetics for translational and clinical research projects. In addition, there is a strong focus on developing and adapting new technologies for clinical diagnostic use. In 2021, 4195 samples were processed in 29 different research projects from 25 individual users. In addition, the unit sequenced 8795 SARS-CoV2 samples. The unit contributed to 7 scientific articles during 2021–2022.

i) Development and major achievements 2021-2022:

Increase collaboration and coordination between CG nodes and other SciLife platforms. CGG has been working closely with other CG-facilities and the GMS project to develop a national rare disease pipeline based on the NF-core framework. This pipeline will help unifying the analysis of rare disease samples across the platform as well as provide a single pipeline for implementation in healthcare. Furthermore, we are developing a unified pediatric cancer pipeline together with several other sites. This work is funded by the Swedish Pediatric Cancer biobank. CGG is locally connected to newly established SciLifelab units, where CGG's efforts together with the Clinical Proteomics and Immunology unit have resulted in the development of analysis tools and pipelines for proteomics data, crucial for several multi-omics approaches. CGG has started a dialogue with NGI to establish a seamless support for researchers using both platforms and provide local bioinformatics expertise, storage and project management combined for projects that are too big to handle within the node. CGG is also involved in the NBIS advisory program, representing the platform. Finally, CGG is actively coordinating with other national CG nodes for meeting the needs of the local research community in terms of sequencing and bioinformatics services.

Offer broad range of state-of-the-art and end-to-end genomic services with focus towards translational and clinical research and clinical trials. The facility has recruited a research coordinator, who has surveyed the local research community in order to map the existing and future NGS needs. The generated report will form the basis of further investment and development projects within the node. During 2022 CGG has expanded the sequencing infrastructure with an additional NovaSeq, doubling the sequencing capacity and increasing resilience for instrument breakdowns. Matching the additional sequencer, there has also been expansions in the the robotics park with a Tecan NGS robot as well as in the IT infrastructure, doubling the storage capacity to 1 pb and quadrupling the compute resources to approximately 2000 cores. In order to organize data and samples, ensuring a high standard of service CGG is implementing a common LIMS system together with CMG. This new system will simplify ordering for research groups and research data delivery, as well as ensure an easy transition of developed methods, from clinical utility trials to clinical routine.

Facilitate implementation of new genomics-based methods into clinical use and contribute to demonstrate clinical utility. During 2020 and 2021 CGG has implemented a workflow for

methylation arrays for prognostic stratification of CNS tumors in both children and adults and this service is now available at national level at CMG at Sahlgrenska. Together with CGL we are exploring the possibility of developing a joint classifier for methylation profiles in tumors. Furthermore, the clinical feasibility of introducing whole genome and transcriptome sequencing including all acute myeloid and lymphoblastic leukemias is currently being tested. We have also developed and implemented a joint analysis pipeline for COVID analysis within the national GMS network. CGG is working to replace the existing analysis pipeline for whole genome sequencing in rare disease and the cancer panel with pipelines developed nationally and jointly with other CG nodes. Lastly ultrasensitive detection of circulating DNA is currently implemented for several clinical uses together with Professor Anders Ståhlberg at Sahlgrenska Center for Cancer Research.

Engage in training and education of the SciLifeLab and healthcare communities. During the past years, the node has organized seven different courses at the PhD level in the fields of bioinformatics and programming. The basic courses aim to introduce wetlab students, scientists and clinicians to various webtools in the analysis of biological data with a focus on the interpretation of NGS data analyses. The more advanced courses, allow students to develop their practical skills in the analysis of data obtained from different techniques. In 2021, we organized and offered a masters level course, *Analysis of NGS data with clinical applications*, aiming to build-up the knowledge needed within this area at an early stage. In terms of supervision, we have co-supervised a total of 6 students, a masters student and four PhD students (Gothenbur University, Linnaeus Universtity, Uppsala University and University of Lyon).

Contribute to DDLS and promote data sharing. The node has had an active role in the application process for DDLS and worked with the Wallenberg Center for Molecular and Translational Medicine and Chalmers E-commons on the Molecular Biology. CGG is represented in the DDLS data-reference group and is also building collaborations with the KI DDLS-data node on precision medicine. The close collaboration with GMS and our deep understanding of healthcare data structures puts CGG in a unique position to develop data brokerage applications between the National Genomics Platform of GMS and the DDLS program in the future, opening the door for an immense wealth of data.

Strengthen national preparedness for future pandemics. The node worked within the SciLifeLab platform and GMS to establish an analysis pipeline for SARS-CoV-2 WGS analysis and have sequenced 16090 samples during 2021-2022. We have also worked with SciLifeLab Data Office in order to investigate the possibilities of data sharing between healthcare, GMS and SciLifeLab in an automated and organized fashion.

ii) Development plans for the unit 2023–2024 and beyond:

The developmental plans at CGG for the near future (2023–2024) include but are not restricted to:

- There have been two bioinformatics units within Core Facilities, the Bioinformatics Core Facility and CGG. These units will be merged into the Bioinformatics and Data Center (BDC) to provide a united bioinformatics hub with complementing areas of expertise and improved access for researchers.
- At the technical level we will:
 - Introduce long-read sequencing capability
 - Design a virtual research environment (VRE) for the University of Gothenburg
 - Develop a metagenomics pipeline in close collaboration with Örebro and Stockholm (a highly prioritized project)
- In terms of education and training, we are planning to start a master program in clinical genomics and bioinformatics at the Sahlgrenska Academy.

iii) Specific questions or comments for the reviewers:

There have been occasions where we have not being able to hire the best candidate due to geographical reasons and the University's guidelines to work within the premises. This is an issue that should be addressed to be able to build a strong unit with the best people. Establishing a common agreement between Universities where we can share premises and staff would be beneficial in the long run, since this will also contribute to the integration and collaboration amongst units.

Clinical Genomics Gothenburg

Budget 2022

Costs	2022
Personnel cost	12 533 981
Other personnel costs	0
Depreciation	2 533 333
Service and license costs	254 000
Other operating costs	635 000
Premises costs	0
Other costs	0
Sum costs (kSEK):	15 956 314

Revenues	2022
Funding from SciLifeLab	2 100 000
University Co-Financing	1 650 000
University Hospital Co-Financing	2 700 000
Barntumörbanken Funding	750 000
GMS-Vinnova Funding	5 622 000
User fees	3 500 000
Sum revenues (kSEK):	16 322 000

Clinical Genomics Linköping

Clinical Genomics Platform (Web links for Unit: [Webpage](#), [Publications](#))

Basic Information

Head(s) of Unit: Tobias Strid
PSD(s): Peter Söderkvist
SciLifeLab Unit since: 2019
Host university: LiU
FTEs: 3.0
FTEs financed by SciLifeLab: 1.0

Funding in 2021 (kSEK)

SciLifeLab: 800
Vinnova: 900
ALF: 300
Total: 2000

Resource Allocation 2021

Academia (national): 70%
Academia (international): -
Internal tech. dev.: 20%
Industry: -
Healthcare: 10%
Other gov. agencies: -

User Fees 2021

Total (kSEK): 398
Reagents: -
Instrument: -
Salaries: -
Rent: -
Other: -

User Fees by Sector 2021

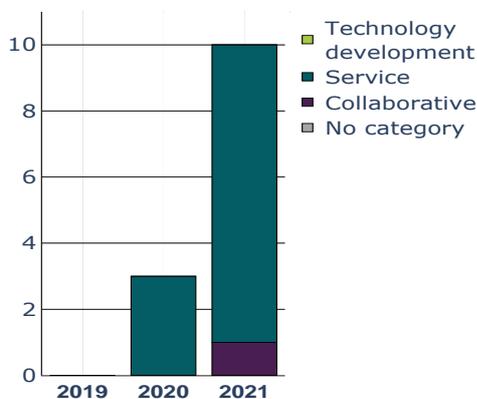
Academia (national): 90%
Academia (international): -
Industry: -
Healthcare: 10%
Other gov. agencies: -

Services

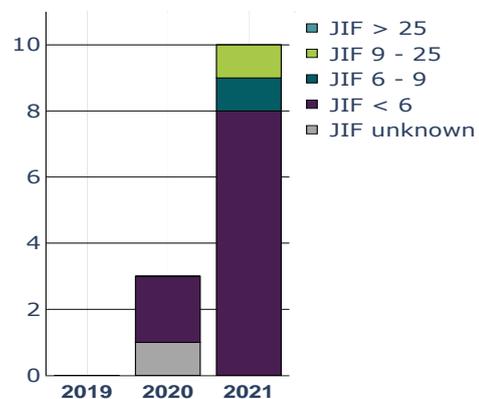
Sequencing, molecular assays and bioinformatics service/support on a wide range of applications:

- DNA Exome-sequencing
- DNA-sequencing using targeted panels
- Microbial whole-genome sequencing
- SARS-CoV2-whole genome sequencing
- Gene expression and methylation arrays (Affymetrix, Illumina)
- Molecular genetic analysis (genotyping and RNA expression)

Publication by Category



Publication by Journal Impact Factor



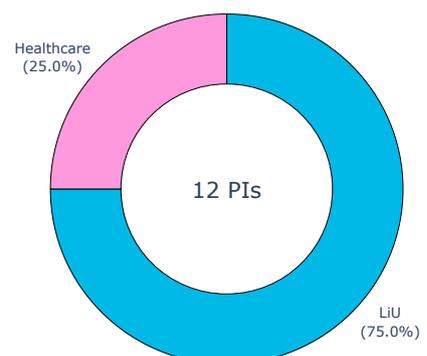
Users 2019

No user information

Users 2020



Users 2021





Unit:	Clinical Genomics Linköping
Platform:	Clinical Genomics

Development, Achievements and Plans

Clinical Genomics Linköping (CGLi) is a recently established unit within the Clinical Genomics platform that started in a planning stadium in 2020 and became an operative unit during 2021. The platform is organized under the Medical Faculty at Linköping University, integrated with the existing core facility (CF) and collaborates closely with the Departments of Clinical Pathology, Genetics and the Clinical Unit for Molecular Biology that are parts of the university hospital. CGLi employs a total of 4 FTEs and offers a wide variety of genomic services, with a focus on molecular analysis (e.g., DNA/RNA sequencing) for translational and clinical research projects. In addition, there is a strong focus on developing and adapting new technologies for clinical diagnostic use. In 2021, 1778 samples were processed in 15+ different research projects from 10 individual users. The unit contributed to 10 scientific articles during 2021–2022.

- i) Since the startup of CGLi, financing and recruitment of staff has been the main focus and one bioinformatician, 1 molecular biologist and 1 lab technician have been employed to complement the existing CF bioinformatician and lab technician for molecular analysis. Besides standard laboratory equipment, including PCR and qPCR machines for molecular biology, the CF/CGLi is relatively well equipped with instruments for most state-of-the-art molecular technologies, including Sanger, Illumina and Nanopore DNA/RNA sequencing, gene expression and methylation array analysis, isolation of single cells and digital PCR for ultrasensitive detection. The establishment of CGLi has meant a transition of CF from a technical based to a more project oriented end-to-end service including bioinformatic analysis. We presently offer service for bioinformatic analysis and provide DNA/RNA sequencing, array and digital PCR analyses for specific projects. Currently, we are providing start to end exome sequencing service, including analysis and interpretation, for a larger national project on SCAD (Spontaneous Coronary Artery Dissection), and during our first year we have experienced an increased demand of our services among local, both basic and clinical researchers and we are currently running 14 parallel projects mainly from LiU but also from outside of the organization. Both our bioinformaticians do also participate in several work packages within Genomic Medicine Sweden.

As a part of a cross platform activity, we have recently established co-operations project together with CG Göteborg and Umeå on methylation profiling in cancer, which represents a common focus area, “Epigenetics”. This originates from research projects that shows epigenetic profiling as a potential and promising diagnostic tool and clinically methylation data is a predictor for treatment decisions for brain tumors. We are currently working on developing the bioinformatic analyses of methylation data and improving the methylation analyses from array based to direct Nanopore sequencing.

We are also heavily involved in cross platform activities connected to the Pandemic Preparedness Program related to data sharing in-between CG nodes, with other SciLifeLab platforms and with healthcare through GMS.

The unit is engaged in educational activities related to NGS based precision diagnostics in several educational programs. We are also involved in the establishment of the master program for Genetic Counseling and has been granted budget to establish a PhD/master course in precision medicine during the 2023 spring semester.

As our level of services just has been established, we have initiated reach out activities initially in regional networks for strategic research areas, e.g., LiU Strategic research areas, an activity that will be further developed and intensified.

- ii) Plans for 2023–2024 involves consolidation and expansion of the platform to be able to offer a broader spectrum of more general services, but also to speed up turnaround times for projects and to lead the development of special focus areas of CGLi, e.g., epigenetics and data sharing. We are currently in the process to increase our short read sequencing capacity by a purchase of a new, mid- to-high output sequencer and additional technological focus areas during this time period will be in the fields of epigenetics, long-read sequencing and single cell sequencing. When it comes to organizational plans are we still in the process of establishing the best suitable organization for the unit and an ongoing work to increase co-operability between CGLi and the diagnostic unit for molecular biology at the Linköping University hospital will be intensified during this period, including both an increased organizational as well as locational co-operation.
- iii) It is noteworthy that the home university of CGLi, LiU, is and has been the main financial supporter in the establishment of CGLi rather than ScilifeLab. The transformation from the previous core facility for molecular biology into a Clinical Genomics platform has put demands both on investments in both technology and, mainly, in personal, which is the limiting factor and the obstacle to enable full-service projects offered by a SciLifeLab unit/platform. So far, this has resulted in recruitment of a 50% head of unit, 100% molecular biologist, 100% lab technician and 2 x 100% bioinformaticians and the budget of 800 kSEK annually granted by SciLifeLab does only cover a minor part of establishing a Clinical Genomics platform.

Clinical Genomics Linköping

Budget 2022

Costs	2022
Personnel cost	3 755 981
Other personnel costs	66 000
Depreciation	1 060 000
Service and license costs	272 000
Other operating costs	200 000
Premises costs	0
Other costs	50 000
Sum costs (kSEK):	5 403 981

Revenues	2022
Funding from SciLifeLab	800 000
University Co-Financing	560 000
University Hospital Co-Financing	1 600 000
Barntumörbanken Funding	750 000
GMS-Vinnova Funding	1 000 000
User fees	800 000
Sum revenues (kSEK):	5 510 000

Clinical Genomics Lund

Clinical Genomics Platform (Web links for Unit: [Webpage](#), [Publications](#))

Basic Information

Head(s) of Unit: Markus Heidenblad
PSD(s): Thoas Fioretos
SciLifeLab Unit since: 2016
Host university: LU
FTEs: 11.0
FTEs financed by SciLifeLab: 3.0

Funding in 2021 (kSEK)

SciLifeLab: 2100
LU: 4480
Vinnova: 2744
ALF: 3650
Other: 2100
Total: 15074

Resource Allocation 2021

Academia (national): 70%
Academia (international): -
Internal tech. dev.: 15%
Industry: -
Healthcare: 15%
Other gov. agencies: -

User Fees 2021

Total (kSEK): 14900
Reagents: 75%
Instrument: 15%
Salaries: -
Rent: -
Other: 10%

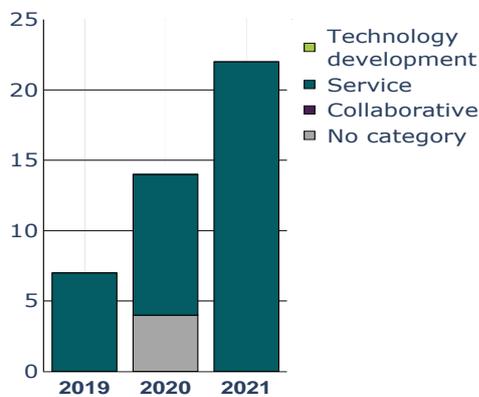
User Fees by Sector 2021

Academia (national): 82%
Academia (international): 2%
Industry: -
Healthcare: 16%
Other gov. agencies: -

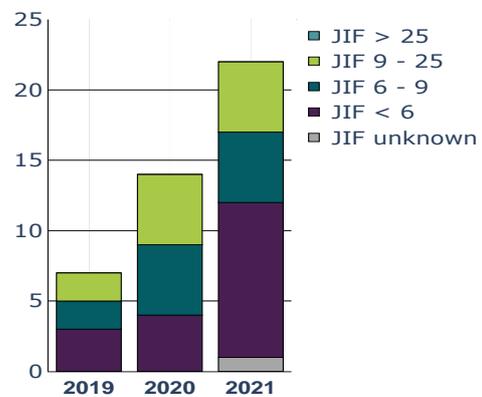
Services

Service in NGS-based technologies for investigators at Lund University and Region Skåne in projects with a strong translational edge or aiming at clinical implementation of new diagnostics assays. National services within specific high-profile areas of the facility.

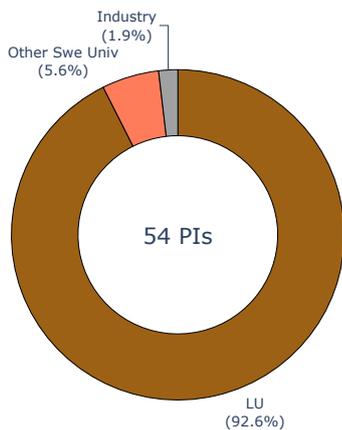
Publication by Category



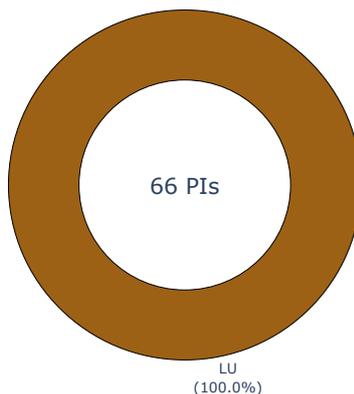
Publication by Journal Impact Factor



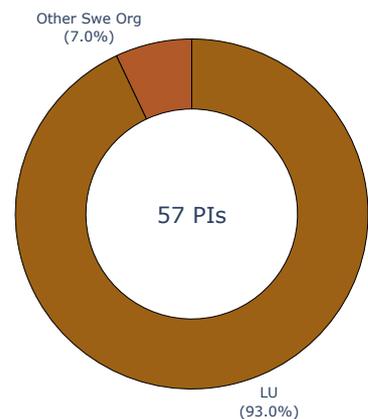
Users 2019



Users 2020



Users 2021





Unit:	Clinical Genomics Lund
Platform:	Clinical Genomics

Development, Achievements and Plans

Clinical Genomics (CG) Lund became a node (unit) within the Clinical Genomics platform in 2016. The platform is organized under Lund University (LU) and collaborates closely with the Center for Molecular Diagnostics (CMD, Region Skåne) that is a part of the University Hospital. CG Lund employs a total of 11 FTEs and offers a wide variety of genomic services, with a focus on single-cell sequencing, for translational and clinical research projects. In addition, there is a strong focus on developing and adapting new technologies for clinical diagnostic use. In 2021, 2565 samples were processed in 107 different research projects from 63 individual users. The unit contributed to 23 scientific articles during 2021.

i) Development and major achievements

A major event in 2021 was the move to new state-of-the-art facilities at the Bio Medical Center (BMC) at LU. Through the new location CG Lund is nicely embedded in strong research and infrastructure environments (including the new SciLifeLab Site), and yet close to CMD, facilitating a smooth transition of new research methods into routine diagnostics.

CG Lund and CMD work closely together in several development projects, particularly within Genomic Medicine Sweden (GMS), where the two units lead or contribute to several working groups. In another collaborative project, following recommendations from the Public Health Agency with regards to the covid-19 pandemic, coworkers at CG Lund and CMD implemented a high-throughput method for SARS-CoV-2 whole genome sequencing, demonstrating the major **societal impact** that units within the CG platform is having. The bioinformatics workflows and data analysis tools developed at CG Lund and CMD are currently being further improved and expanded for more viral agnostic use in the G3P cross-platform project, part of SciLifeLab's Pandemic Laboratory Preparedness (PLP) program. In addition, CG Lund is working together with Prof. Patrik Medstrand in a separate PLP project (part of the Clinical Microbiology call), aiming at developing new NGS-based diagnostics for other viruses (e.g. RS virus, influenza, and Hepatitis C).

During 2021-2022, major **technology development** within CG Lund was focused on new sc applications. The CG platform envisions that sc technologies will play an essential role in future diagnostics and has assigned CG Lund to spearhead this development. To adapt sc sequencing for diagnostic use, CG Lund has received both local and national grants. Several new methods were launched in 2021 (e.g. multiome based on the 10x Genomics platform, and full-length mRNA sequencing and DLP+ for genomic CNV analysis, based on the Takara iCell8 platform) and the unit was first in Sweden to become a certified service provider (CSP) for 10x Genomics. Additional sc development is ongoing in several areas, including;

- *spatial transcriptomics* (Visium, 10x Genomics) in collaboration with the Dept. of Pathology
- *fixation protocols*, for more feasible sample treatment and batching possibilities, enabling new clinical applications as well as the chance to provide service to users outside LU
- additional methods for *genomic sc interrogation* (e.g. for SNV and indel detection)

Several procurements were also completed in 2021-2022, mainly to enable development of additional sc methods (e.g. CellenONE v1.4 and Chromium X) and to increase the sequencing capacity (NextSeq 2000), but also to improve and streamline project management within the unit (iLAB, Agilent).

As to **scientific achievements**, CG Lund contributed to 23 original research articles in 2021, a more than 300% increase compared to 2019 and 2020. Related to its leading sc development role, a review article, entitled “*Single-cell sequencing in translational cancer research and challenges to meet clinical diagnostic needs*”, was also published by scientists within CG Lund.

In 2021, all users were affiliated with LU. However, in 2022 new **user groups** were also served, e.g. from other universities and from the life sciences industry. To further extend the user base, several **outreach activities** have been organized, both locally (e.g. at other LU faculties) and nationally (e.g. the Molecular Medicine Fellows Program meeting in Ystad in May 2022). Additional activities will, furthermore, be organized with the newly formed SciLifeLab site at Lund University.

CG Lund participated in several **cross-unit and cross-platform collaborations**. At the cross-unit level, meetings are held regularly to exchange knowledge and to harmonize methods offered by the platform. At the cross-platform level, CG Lund collaborates with the Eukaryotic Single Cell Genomics unit to establish new sc methods for coming clinical needs. In addition, CG Lund is currently working with NGI, the Single-Cell and Spatial Biology platform, and NBIS in a VR call to build a national infrastructure for sc technologies. CG Lund is also part of the G3P project (see above) and was instrumental in establishing the SciLifeLab Site at Lund.

ii) Development plans for 2023 and beyond

In the coming years CG Lund envisions a continued strong development in several fields;

At the unit/platform-level

- Further *consolidation, standardization and automation* of today’s genomics and transcriptomics services (e.g. WGS, WES and RNA-seq).
- *New single-cell and spatial omics applications*; lower cell amounts, higher cell numbers, new fixation protocols, interrogation of additional genomic alterations, spatial transcriptomics etc.
- *New omics modalities* – introduce new modalities where sequencing can be used as a read-out, e.g. epigenomics, proteomics, fragmentomics.

At the SciLifeLab-level

- Continued work to *promote precision diagnostics and medicine*. CG Lund by its close collaboration with the separate clinical diagnostic unit (CMD) has a long-standing experience in how novel technologies can be adapted and introduced into healthcare
- Continued work to *promote the DDLS-initiative*, which will require joint efforts to establish a framework to enable data sharing of sensitive clinical data (see also iii).
- Strengthened *data analysis, management, and IT support* – activities to bring our platform closer to NBIS and the Data Centre.
- Facilitate and *promote SciLifeLab’s Precision Medicine* capability, modelled on the successful collaboration between the CG platform and GMS.

iii) Specific questions or comments for the reviewers

- With the trend to establish nodes at the larger universities, there is a need to harmonize IT systems as well as the computational and data storage infrastructure. In the future, data will also be increasingly generated within healthcare. The DDLS initiative has formed national Data Area Nodes, but such nodes/resources were not allocated to LU. For CG Lund and the SciLifeLab site at Lund to fully contribute to the DDLS-initiative, there is a need to have IT systems engineers employed/embedded to help aligning with the national DDLS initiative

Clinical Genomics Lund

Budget 2022

Costs	2022
Personnel cost	14 011 196
Other personnel costs	248 000
Depreciation	2 681 097
Service and license costs	2 374 600
Other operating costs	16 568 498
Premises costs	1 650 000
Other costs	140 000
Sum costs (kSEK):	37 673 390

Revenues	2022
Funding from SciLifeLab	2 250 000
Funding from financier MedFak	2 600 000
Funding from LU-Stemtherapy	1 550 000
Funding from Vinnova GMS	1 656 000
Funding from Lundbergs stiftelse	2 700 000
Funding from Scilife	1 800 000
Funding from financier Medfak	480 000
Funding ALF for rent	1 650 000
Funding from financier FoU (RS)	2 000 000
User fees	17 856 000
Sum revenues (kSEK):	34 542 000

Clinical Genomics Stockholm

Clinical Genomics Platform (Web links for Unit: [Webpage](#), [Publications](#))

Basic Information

Head(s) of Unit: Valtteri Wirta
PSD(s): Valtteri Wirta
SciLifeLab Unit since: 2014
Host university: KI, KTH
FTEs: 36.7
FTEs financed by SciLifeLab: 6.2

Funding in 2021 (kSEK)

SciLifeLab: 5000
SciLifeLab Instrument: 999
KI: 1498
Vinnova: 3479
University hospital: 5000
Total: 15976

Resource Allocation 2021

Academia (national): 24%
Academia (international): -
Internal tech. dev.: 17%
Industry: -
Healthcare: 59%
Other gov. agencies: -

User Fees 2021

Total (kSEK): 69000
Reagents: 61%
Instrument: 17%
Salaries: 19%
Rent: 3%
Other: -

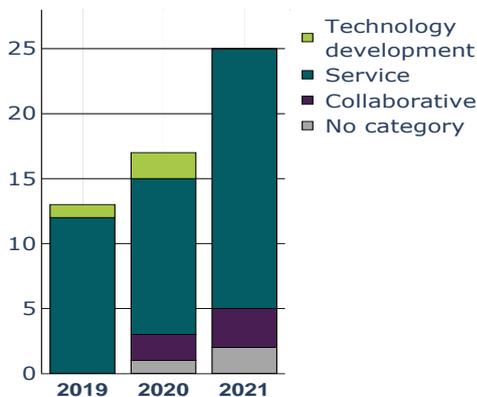
User Fees by Sector 2021

Academia (national): 15%
Academia (international): -
Industry: -
Healthcare: 85%
Other gov. agencies: -

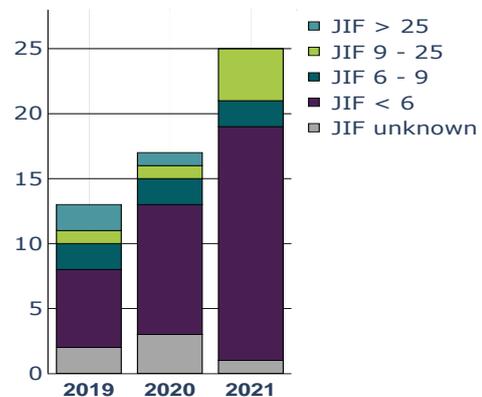
Services

- DNA sequencing
- Clinical exome and whole-genome sequencing
- Microbial whole-genome sequencing
- Targeted panels using various bait sets (contact for detailed information)
- RNA Seq using both poly A and random priming
- Ready-made libraries (prepared by collaborator)

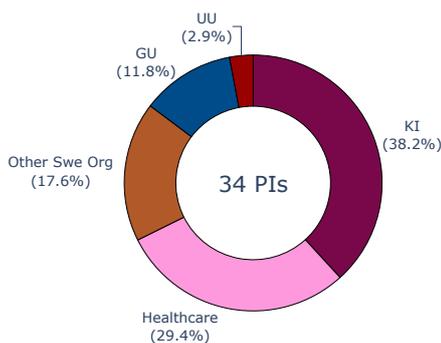
Publication by Category



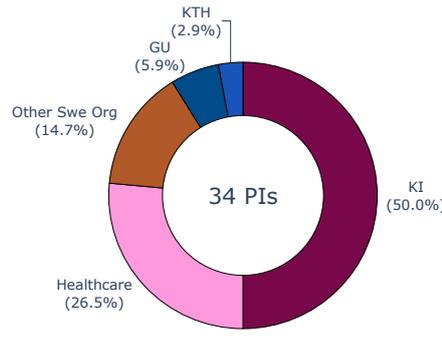
Publication by Journal Impact Factor



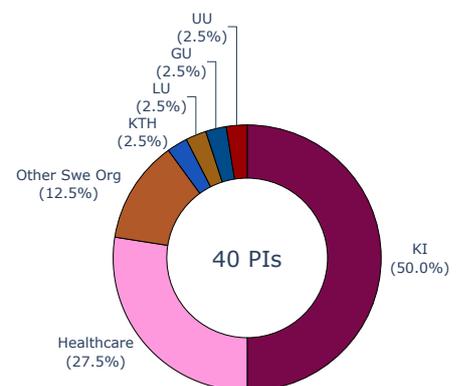
Users 2019



Users 2020



Users 2021





Unit:	Clinical Genomics Stockholm
Platform:	Clinical Genomics

Development, Achievements and Plans

Clinical Genomics (CG) Stockholm was one of the founding nodes (units) to the Clinical Genomics platform in 2013. The platform is organized under Karolinska Institutet and KTH Royal Institute of Technology and collaborates closely with the Karolinska University Hospital. CG employs a total of 40 FTEs. CG Stockholm offers a wide variety of genomic services, with a focus on large-scale sequencing, for translational and clinical research projects with rare inherited diseases, cancer and infectious diseases. In addition, there is a strong focus on developing and adapting new technologies for clinical diagnostic use. In 2021, more than 40,000 samples were processed in different research projects, origination from at least 40 individual users. The unit contributed to 25 scientific articles.

i) Development and major achievements 2021–2022: Development of **open-source bioinformatic tools** across the different disease areas has been a continued major focus. This includes continued migration towards modular Nextflow-based workflows and increased national and international collaborations. In rare diseases we have continued to drive the development of a comprehensive workflow extracting the maximum information from short-read sequencing data, moving into a multi-omics analysis using combined genome sequencing and transcriptome analysis, we are in the process of migrating the workflow to nf-core (nf-co.re/raredisease). For cancer applications we have focused on improving the calling of copy number and structural variation using whole-genome data in order to maximise the potential of genome-based analysis in understanding events driving tumour progress. Within infectious diseases we initially implemented SARS-CoV-2 sequencing for short-read data, and later expanded to also enable analysis of long-read nanopore data, and continued development of the diagnostic metagenomics pipeline (nf-co.re/taxprofiler). Bioinformatic development work is done in a collaborative manner with both national and international collaborators, as well as often in close collaboration with users within academia and healthcare. **Within the Platform**, CG Stockholm coordinates development activities within multi-omics and genome structure analysis using optical mapping. Towards **multi-omics**, we are developing transcriptome-based analyses for both rare diseases (in national collaboration via CG Platform and GMS) and cancer (e.g., nf-co.re/rnafusion). **Optical mapping** technology is being implemented as a complement to long-read sequencing based structural variant detection. This is important in addressing genetic variation in repetitive regions, and currently bioinformatic development is ongoing and service offerings directed towards external users will be initiated towards end of 2022. **Infrastructure development** - CG Stockholm operates a high-capacity NGS lab and informatics environment, tailored for supporting research projects with prospective patient recruitment with need for rapid return of results. During 2021–2022 we expanded our liquid handling infrastructure (now consisting of five large liquid handling systems) as well as together with NGI Stockholm purchased a fourth NovaSeq 6000 to our jointly operated sequencer installation base. To support the increasing number of samples, we have also scaled up our IT and are in the process of virtualizing and containerizing all workflows and IT systems. This allows for deployment in other infrastructures, to increase capacity and reduce turnaround times.

Achievements and milestones in our rare disease track includes expanding to new disease groups and achieving in Dec 2021 a milestone of 10,000 samples analysed using WGS. A scientific

summary of the first approximately 5000 samples was published in May 2021 (Stranneheim et al, Genome Biology). In cancer, a specific focus has been on maximizing the value of prospective, real-time, whole-genome sequencing in parallel with standard of care diagnostics in specific disease areas, including hematological malignancies and pediatric cancers (GMS-linked projects), as well as in sarcomas. In total, more than 300 cancer patients have been analysed using this approach in 2021–2022. CG Stockholm is also providing patient stratification services to several clinical trials and clinical implementation projects using nationally and custom-designed targeted assays. To support the regional and national public health authorities during the pandemic, we have since January 2021 carried out the SARS-CoV-2 sequencing for the Region Stockholm and Gotland in collaboration with the Karolinska university hospital. Data is being made in real-time available to the research community through the international data sharing repository GISAD. The sequencing effort has also provided weekly updates on the relative representation of SARS-CoV-2 strains.

Outreach and dissemination activities CG Stockholm's employees have been involved as lecturers at several courses aimed for master and PhD students, and physicians. We also receive on a regular basis external visitors to SciLifeLab, including scientific visitors, politicians and various other international delegations. CG Stockholm is also one of the founding members of the Nordic Alliance for Clinical Genomics (NACG), a network of Nordic research and clinical laboratories utilizing genomics-based tools to address challenges related to human health and disease. During Jan 2023 CG Stockholm will be hosting the next workshop for NACG, with >100 attendees expected from 20-30 different organisations across the Nordics. **Activities cross-units and cross-platform** within SciLifeLab have been carried out as often as possible. Examples include the numerous technology development activities carried out by CG Platform in the GMS initiative (joint development of bioinformatic workflows for rare disease, cancer, SARS-CoV-2 and metagenomics), development of clinical decision support system Scout together with CG Lund. In addition, CG Stockholm is actively involved in the Pandemic Laboratory Preparedness program (PI: Wirta, CG Stockholm) where all CG units, NGI and National Pandemic Center collaborate. NGI Stockholm and CG Stockholm share the sequencer infrastructure and have been jointly investing in additional sequencers for the last eight years. Internationally, CG Stockholm collaborates with other clinical genomics labs through Cancer Core Europe network of comprehensive cancer centers, as well as with external bioinformaticians and software developers on individual tools.

ii) Development plans for the unit 2023–2024 and beyond: A continued focus is expected on maximizing the value of whole-genome sequencing for different clinical applications to continue driving precision diagnostics and precision medicine into healthcare. This includes continued further development of the wetlab methods and bioinformatic workflows, as well as continued work on clinical decision support systems to support the clinical interpretation of the data. A special focus will be on the development activities coordinated by Stockholm (multi-omics and optical mapping). As the cost of sequencing continues to drop and the analytical solutions mature, we expect to be involved in several new prospective studies assessing the value of comprehensive WGS (or other NGS techniques) versus current standard of care diagnostics. We also expect these studies to provide insights into new disease mechanisms and therapy options. To extend beyond short-read sequencing, we have during 2022 intensified the work with long-read sequencing (nanopores) with initial focus on development of bioinformatic analysis workflows. We will follow this path during upcoming years to address the gaps in short read sequencing. The **optical mapper** (Saphyr) for addressing large structural aberrations that cannot be successfully resolved using either short-read or current long-read sequencing will be launched as a service for the Swedish research community during 2023 (pilots may start earlier). Towards **multi-omic analyses** our initial focus during 2023-2024 will be on implementing the bioinformatic workflows and decision support systems for data interpretation, while leveraging on other SciLifeLab infrastructures for the initial data generation needs. This approach provides a cost efficient approach towards development and implementation, as well as allows utilisation of existing expertise within the SciLifeLab environment. To support the **increasing number of samples** and projects, we are addressing all steps in the workflow to increase level of automation and harmonization between protocols. This includes wetlab, bioinformatics and preparing IT infrastructure for operation across multiple different server infrastructures.

Clinical Genomics Stockholm

Budget 2022

Costs	2022
Personnel cost	35 120 988
Other personnel costs	655 375
Depreciation	5 557 027
Service and license costs	5 020 015
Other operating costs	23 172 557
Premises costs	3 741 901
Other costs	467 400
Sum costs (kSEK):	73 735 263

Revenues	2022
Funding from SciLifeLab	5 000 000
Funding from financier X	750 000
Funding from financier Y	816 000
Funding from financier Z	2 000 000
User fees	65 000 000
Sum revenues (kSEK):	73 566 000

Clinical Genomics Umeå

Clinical Genomics Platform (Web links for Unit: [Webpage](#), [Publications](#))

Basic Information

Head(s) of Unit: Per Larsson
PSD(s): Richard Palmqvist
SciLifeLab Unit since: 2019
Host university: UmU
FTEs: 2.0
FTEs financed by SciLifeLab: 1.2

Funding in 2021 (kSEK)

SciLifeLab: 800
County council: 200
Total: 1000

Resource Allocation 2021

Academia (national): 55%
Academia (international): 5%
Internal tech. dev.: 20%
Industry: -
Healthcare: 20%
Other gov. agencies: -

User Fees 2021

Total (kSEK): 300
Reagents: 60%
Instrument: 10%
Salaries: 30%
Rent: -
Other: -

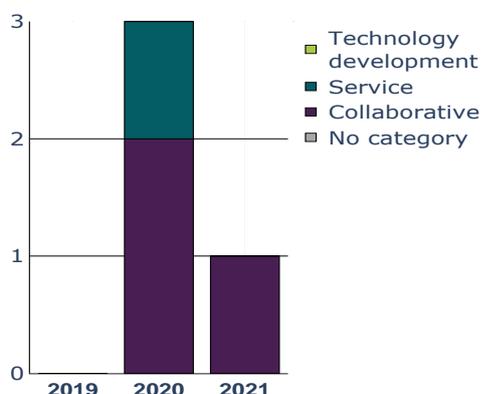
User Fees by Sector 2021

Academia (national): 80%
Academia (international): -
Industry: -
Healthcare: 20%
Other gov. agencies: -

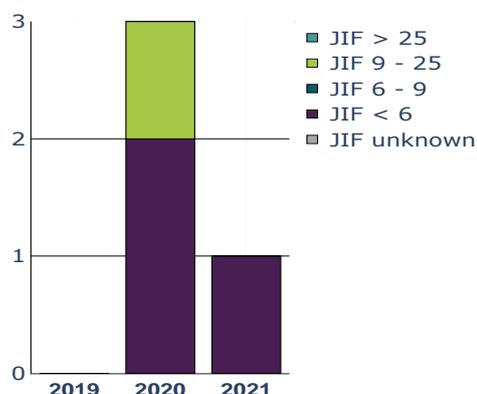
Services

- Meta-, microbial, human genomics
- Archer Analysis server
- Guppy and R-studio server
- Microarray
- Telomer length analysis
- Digital PCR
- Fusion gene detection
- Myeloid, Solid tumor, cardiogenetics panels
- Custom sequencing (illumina, nanopore)
- Data storage / backup and Linux accounts to users for supported projects

Publication by Category



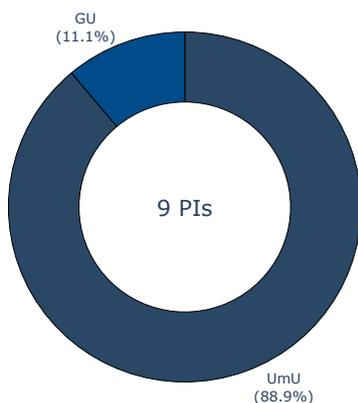
Publication by Journal Impact Factor



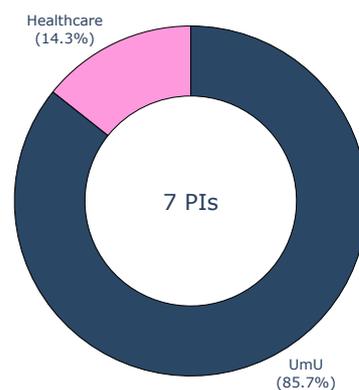
Users 2019

No user information

Users 2020



Users 2021





Unit:	Clinical Genomics Umeå
Platform:	Clinical Genomics

Development, Achievements and Plans

Clinical Genomics (CG) Umeå became a unit to the Clinical Genomics platform in 2019 and fully operational in 2021. The platform is organized under Umeå University and collaborates closely with the clinical genetics department that is a part of the Umeå university hospital and GMC Norr that is organized under both the hospital and the university. CG Umeå employs a total of **2.8 FTEs**, consisting of head of unit, 1 molecular biologist/coordinator, 1 lab technician, 1 senior and 1 junior bioinformatician. Not employed, CG Umeå can also put into service 3 senior bioinformaticians, 2 molecular biologists, 1 developer and one IT-project manager employed by Region Västerbotten (genetics development group at clinical genetics, also involved in various Genomic Medicine Sweden projects). Achieving significant synergies, CG Umeå is tightly integrated with the genetics development group with common meetings held on a weekly basis. The tight integration creates a buffer where personnel and other resources as can be borrowed/purchased between organizations.

CG Umeå offers a variety of genomic services with a wet lab focus on Archer panels for translational and clinical research projects. In addition, there is a strong focus on developing and adapting new technologies for clinical diagnostic use. In 2021, 1550 samples were processed in 14 different research projects from 18 individual users. The unit contributed to 11 scientific articles during 2021-2022.

i) Development and majors achievements 2021–2022:

Comment in the following order as per instructions: Technology development, scientific achievements, new user groups, outreach efforts, training and education, contribution to cross-unit and cross-platform initiatives etc., of the unit 2021–2022.

1. Supported by the SciLifeLab Pandemic Preparedness grant, CG Umeå has been instrumental in implementing nanopore-based sars-cov-2 monitoring at Umeå university hospital (G3P project).
2. Within the G3P project CG Umeå has developed *poresamples*, a GUI tool for user-friendly setup of nanopore sequencing runs. CG Umeå has also developed *CoVIZ*, a prototypic web-based clinical assessment tool for sars-cov-2 sequence data that explores new assessment concepts.
3. CG Umeå has developed *teloplot*, a GUI tool for interactive analysis of telomer length data to support clinical interpretations. Currently used in production at clinical genetics and in research.
4. CG Umeå was awarded a 4-year 2 Mkr grant from TUA for GENOMIC DENTISTRY
5. CG Umeå has initiated work to develop diagnostics for telomere-related diseases based on NGS (SciLifeLab TDP grant.)
6. Participation in education/teaching: supervision of an undergraduate project and co-supervision of doctoral students.

ii) Development plans for the unit 2023–2024 and beyond:

Future plans for CG Umeå.

- a. A future prioritized focus area in Umeå is array-based DNA methylation analysis, where CG Umeå will collaborate closely with CG Linköping and CG Gothenburg on national level. In Umeå, the work will be headed by assoc prof Sofie Degerman with an extensive research experience of epigenetics. Local clients will include several research groups in Umeå within the EpiCon consortium (<http://www.epicon.nu>, focusing on epigenetics) as well as the ALLTogether consortium, comprised of research groups from 14 European countries and focusing on acute lymphatic leukemia (ALL). One aim for the platform is to be the European reference laboratory for the ALLTogether consortium.
 - b. CG Umeå recently obtained funding from TUA, which supports research and education within the odontological sciences similar to ALF for medical research and education. The funds will be used to support a project in which 5 000 bacterial strains will be sequenced and genotyping/targeted sequencing of a cohort of up to 1 500 dental patients. The work will be conducted in collaboration with research groups at the faculties of odontology in Umeå and Gothenburg and internationally. This project is of significant importance as a ground-breaker for future odontological projects.
 - c. Telomere analysis methods is a major focus area. The SciLifeLab TDP grant awarded to CG Umeå will enable continued method development in this area and support our Nordic reference lab status for telomere analysis.
 - d. Funding was recently secured for procurement of an industrial-scale sequencing instrument and complementary IT infrastructure. This will enable Clinical Genomics to provide timely WGS services.
 - e. Within Region Västerbotten purchase of an optical genomic mapping instrument, such as the Bionano Genomics Saphyr, is scheduled for 2024 at clinical genetics (hospital) and will be available also for service through CG Umeå.
 - f. Further increase integration with the Umeå SciLifeLab Site. Among other things plans exist for collaboration on IT administration to reduce administrative overhead.
 - g. Increase teaching and outreach activities.
- ii) Starting a new unit such as Clinical Genomics Umeå is not without challenges. A general issue is securing sufficient long-term funding to enable the unit to bridge the productivity drop when hiring new personnel.

Clinical Genomics Umeå

Budget 2022

Costs	2022
Personnel cost	2 606 519
Other personnel costs	0
Depreciation	46 667
Service and license costs	0
Other operating costs	0
Premises costs	0
Other costs	0
Sum costs (kSEK):	2 653 186

Revenues	2022
Funding from SciLifeLab	800 000
Funding Pandemic Preparedness	500 000
Consultations, bioinformatics	475 000
Funding TDP telomers	200 000
Funding TDP PLP ClinMicro	200 000
Funding Clinical Study Amgen	300 000
User fees	300 000
Sum revenues (kSEK):	2 775 000

Clinical Genomics Uppsala

Clinical Genomics Platform (Web links for Unit: [Webpage](#), [Publications](#))

Basic Information

Head(s) of Unit: Malin Melin
PSD(s): Ulf Gyllensten
SciLifeLab Unit since: 2014
Host university: UU
FTEs: 17.4
FTEs financed by SciLifeLab: 4.4

Funding in 2021 (kSEK)

SciLifeLab: 2500
SciLifeLab Instrument: 300
UU: 500
Vinnova: 1571
ALF: 4900
University hospital: 3960
Total: 13731

Resource Allocation 2021

Academia (national): 35%
Academia (international): 2%
Internal tech. dev.: 20%
Industry: 5%
Healthcare: 38%
Other gov. agencies: -

User Fees 2021

Total (kSEK): 9200
Reagents: 63%
Instrument: -
Salaries: 37%
Rent: -
Other: -

User Fees by Sector 2021

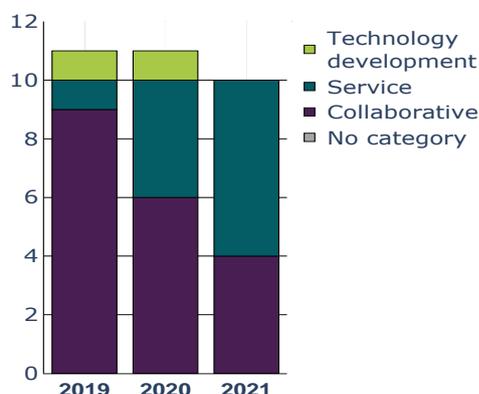
Academia (national): 44%
Academia (international): 3%
Industry: -
Healthcare: 53%
Other gov. agencies: -

Services

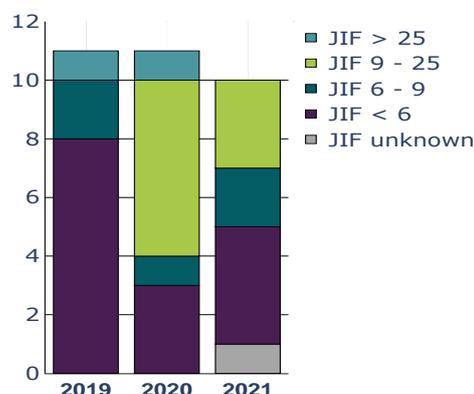
Fully tailored support with translational research projects. Development and clinical implementation of new diagnostic tests. Examples of applications:

- Gene panel to whole-genome sequencing
- Gene expression and gene fusion analysis with NGS and NanoString
- Mutation detection with digital PCR
- Single-cell multi-omics with Mission Bio

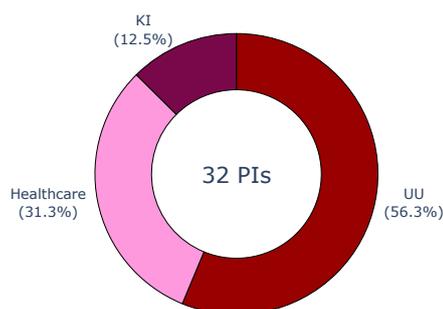
Publication by Category



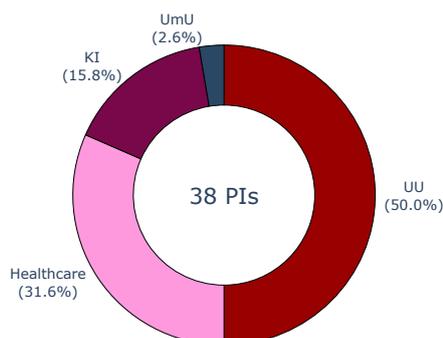
Publication by Journal Impact Factor



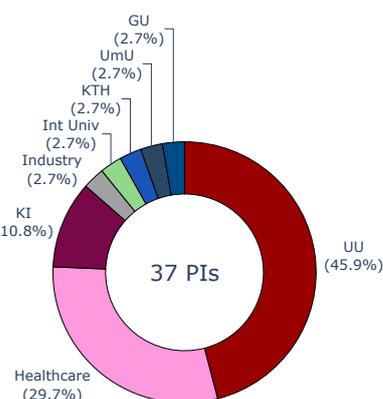
Users 2019



Users 2020



Users 2021





Unit:	Clinical Genomics Uppsala
Platform:	Clinical Genomics

Development, Achievements and Plans

The Clinical Genomics Uppsala (CGU) node (unit) was formed in 2014. CGU is a collaboration between Uppsala University and Uppsala University Hospital, and is fully integrated within the hospital clinics. CGU employs 19 FTEs and focus on developing and adapting new genomic technologies for clinical diagnostic use. A range of genomic services have been validated for clinical research projects and implemented in clinical routine, with a focus on solid tumors, hematology, inherited diseases, microbiology and bioinformatics. During 2021, 4800 patient samples were analyzed using clinical assays implemented by CGU; an increase by 41% compared to 2020. In 2021, 2200 samples were processed in 86 research/development projects from 37 individual PIs. CGU contributed to 13 scientific articles during 2021. The increasing income from operations reflects the clear increase in demand (increased 37% 2021 compared to 2020).

i) Development and major achievements 2021–2022:

Technology developments

- CGU has implemented 70 advanced molecular tests into routine healthcare, of which 10 new tests were added in 2021. CGU offers the clinically validated tests as a service to researchers, but also tailor methods according to the needs of each research project using NGS (short-read and long-read), Nanostring, digital PCR and Mission Bio single-cell multi-omics.
- Several new technologies have been implemented, including single-cell multi-omics, whole-genome and whole-transcriptome sequencing of cancer samples, and 23 new clinical *in silico* gene panels for inherited diseases 2022 (e.g. inherited breast cancer and epilepsy).

Scientific achievements

- CGU has contributed key methodology to several important publications. For instance, a study demonstrated that molecular analysis is necessary before treatment with recently approved NTRK inhibitors (Elfvig et al, Lung Cancer 2021).
- Of note is also our collaboration with Prof Ulf Landegren regarding the Super Rolling-Circle Amplification (superRCA) method for clinical use of low frequency cancer mutations. This project, funded by SciLifeLab TDP and Vinnova, has resulted in new services and a recent publication in Nature Communications (Chen et al, Nat Commun 2022). The start-up company Rarity Bioscience was formed 2021.

- CGU provides a unique environment for industry collaborations. We have collaborated with companies such as Bristol-Myers Squibb, Illumina, Oncodia and Incyte.

New user groups

- Incorporation of clinical microbiology as a new diagnostic focus area. CGU will support research, innovation and healthcare related to Covid and future diagnostic tests for virus, bacteria and parasites.

Outreach efforts

- CGU has performed several outreach activities, including two webinars with Mission Bio, and contributed to newsletters.

Training and education

- CGU has contributed with lectures, participated as mentors in NBIS bioinformatics advisory program and arranged site visits during 2021/2022. A new Masters program in Precision Medicine will be launched at UU, and CGU will have a key role in teaching and training.

Contribution to cross-unit and cross-platform initiatives

- CGU has launched several cross-platform collaboration projects focusing on long-read sequencing with NGI (UGC), and is also collaborating with NGI (SNP&SEQ) for whole-genome and whole-transcriptome sequencing. CGU is an active part of Genomic Medicine Sweden (GMS), including several cross-unit collaborations, and in the SciLifeLab G3P Pandemic Laboratory Preparedness project by coordinating long-read activities across units/platforms.

ii) Development plans for the unit 2023–2024 and beyond:

CGU is a technology-driving accelerator and test bed for molecular diagnostics in translational research and for clinical assay implementation. Our goal is to expand the operations to meet the increasing needs and offer researchers an opportunity to perform projects ranging from services based on existing validated clinical methods to research collaborations, involving new technologies and innovations that are developed and validated for routine diagnostics. We continuously expand and improve the catalogue of methods in order to offer cutting-edge technologies. We are responsible for driving development of long-read and ultrasensitive detection methods within the CG platform.

Ongoing and planned projects include:

1. Long-read sequencing techniques are already used today for diagnostic applications in Uppsala (SARS-CoV-2, BCR::ABL1 mutation analysis), and we plan to participate in new clinical trials based on these methods. CGU leads a national collaboration with NGI (UGC) and GMS to evaluate the use of long-read sequencing to identify and characterize structural variants and repeat expansions in various hereditary diseases. We are also collaborating with NGI on WGS and targeted long-read sequencing of cancer samples.

2. Ultra-sensitive detection of patient-specific variants can be used to monitor the level of remaining cancer cells after treatment, and for early detection of relapse. We have recently completed a proof-of-principle study in which the usefulness of droplet digital PCR (ddPCR), as a minimum residual disease (MRD) assay, was evaluated in a retrospective Nordic cohort of MDS patients. The goal for the coming years is to implement ddPCR as a clinical MRD assay for hematological malignancies. Furthermore, in collaboration with Rarity Biosciences, we evaluate the clinical benefits of the superRCA technology.

3. Establish methods for whole genome and transcriptome analysis for haematological and hereditary diseases, with the aim to replace current standard-of-care methods (FISH, karyotyping, array).

4. We have recently established single-cell multi-omics (Mission Bio Tapestri), combining DNA and protein analysis, and anticipate that both research and clinical diagnostic applications will grow significantly in the coming years.

5. A milestone achieved during autumn 2022 is the clinical implementation of a Comprehensive Genomic Profiling Panel (GMS560) for solid tumors. This panel will be a cornerstone for molecular profiling of solid cancer and a key application in clinical studies in precision oncology.

6. A goal is to increase focus on diagnostics for clinical trials, including the clinical research and development unit at the University Hospital. Comprehensive genomic profiling (DNA + RNA) with GMS560 of solid tumors will be an integrated part of molecular screening in the national clinical studies MEGALiT and START-NET.

7. Establish novel diagnostic assays in the recently incorporated microbiology area. This includes analyses of multi-resistant bacteria (MRSA), Chlamydia and parasites.

The goal is to also include additional diagnostic areas, such as immunology and pharmacogenomics in CGU, and to be continuously active in Genomic Medicine Sweden (GMS) and other national and international networks.

iii) Specific questions or comments for the reviewers:

The organization of CGU in relation to the Uppsala University Hospital clinics is presently being reviewed. A CGU Director with a joint appointment at the University and Hospital will have a key role in the new organization. At present, we receive limited funding from Uppsala University (500 kSEK SFO yearly), and will request additional support from both the University and Uppsala University Hospital for this key position.

Clinical Genomics Uppsala

Budget 2022

Costs	2022
Personnel cost	10 738 397
Other personnel costs	1 200 000
Depreciation	1 099 889
Service and license costs	320 000
Other operating costs	4 900 000
Premises costs	225 000
Other costs	0
Sum costs (kSEK):	18 483 286

Revenues	2022
Funding from SciLifeLab (N + SFO)	3 000 000
Funding SciLifeLab depreciation ddPCR instrument	278 859
Funding from SciLifeLab pandemic preparedness	750 000
Funding from ALF (infrastructure)	3 000 000
Funding for depreciation cluster/IT infra (ALF and other sources)	710 000
Funding for service cost, Miseq, Akademiska sjukhuset	60 000
Funding from Vinnova for GMS	1 632 000
User fees	9 000 000
Sum revenues (kSEK):	18 430 859
Sum funding at Akademiska sjukhuset	3 900 000
Sum funding at Akademiska sjukhuset	3 900 000

Clinical Genomics Örebro

Clinical Genomics Platform (Web links for Unit: [Webpage](#), [Publications](#))

Basic Information

Head(s) of Unit: Bianca Stenmark
PSD(s): Gisela Helenius
SciLifeLab Unit since: 2019
Host university: ÖRU
FTEs: 5.0
FTEs financed by SciLifeLab: 0.0

Funding in 2021 (kSEK)

SciLifeLab: 800
ÖRU: 208
University hospital: 5880
Total: 6888

Resource Allocation 2021

Academia (national): 80%
Academia (international): -
Internal tech. dev.: 10%
Industry: -
Healthcare: 10%
Other gov. agencies: -

User Fees 2021

Total (kSEK): 3077
Reagents: 80%
Instrument: -
Salaries: 20%
Rent: -
Other: -

User Fees by Sector 2021

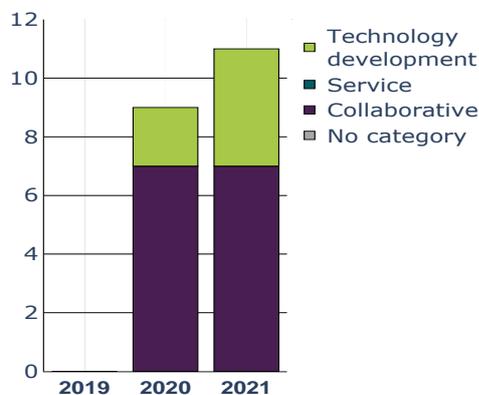
Academia (national): 90%
Academia (international): -
Industry: -
Healthcare: 10%
Other gov. agencies: -

Services

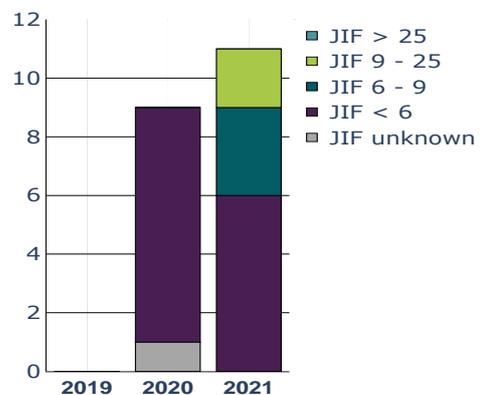
Support with translational research projects from design to clinical interpretation. Development of new diagnostic tests. Examples of applications:

- Microbial whole-genome sequencing
- Metagenomic sequencing
- Exome sequencing
- Targeted sequencing using panels
- Ultrasensitive detection of genetic variants using digital droplet PCR

Publication by Category



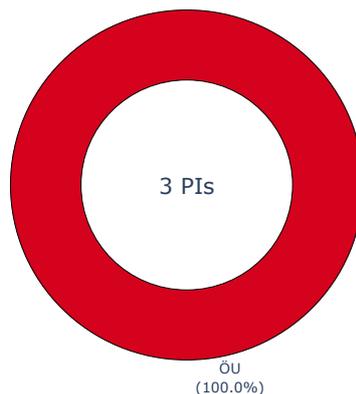
Publication by Journal Impact Factor



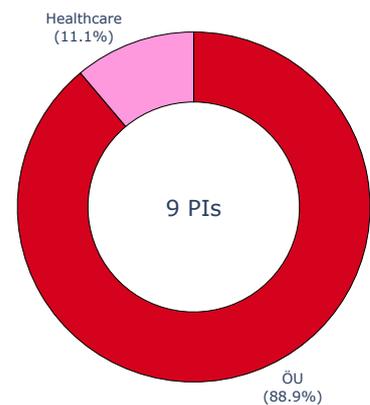
Users 2019

No user information

Users 2020



Users 2021





Unit:	Clinical Genomics Örebro
Platform:	Clinical Genomics

Development, Achievements and Plans

Clinical Genomics (CG) Örebro became a node (unit) to the Clinical Genomics platform in 2019. The platform is organized under Örebro University and collaborates closely with Laboratory Medicine that is a part of the university hospital. In total, 19 persons work part time in CG Örebro depending on service demands, this corresponds to an average of 5 FTEs. CG Örebro offers a wide variety of genomic services, with a focus on metagenomics and long-read sequencing, for translational and clinical research projects. In addition, there is a strong focus on developing and adapting new technologies for clinical diagnostic use. In 2021, 2 697 samples were processed in 19 different research projects from 9 individual users. The unit contributed to 13 scientific articles during 2021–2022.

i) Development and majors achievements 2021–2022:

Technology development

CG Örebro develops clinical testing for exome sequencing, microbial whole-genome sequencing, metagenomics, RNAseq, ultrasensitive detection and targeted panels. In 2021, we established a long-read sequencing protocol for SARS-CoV-2 for health care that was taken into clinical use. CG Örebro also contributed to the development of a national bioinformatic pipeline for SARS-CoV-2 data that is established on the National Genomic Platform for clinical use in Genomic Medicine Sweden (GMS). The focus area of CG Örebro is metagenomics, specifically with long-read sequencing. Within the national pandemic laboratory preparedness G3P project, Örebro together with NGI is responsible for the metagenomic pilot. CG Örebro also develops a service for amplicon-based and shotgun metagenomics for diagnosis of infections, focusing on sepsis and joint infections as well as clinical applications of microbiome studies. 16S amplicon-based metagenomics is under development for implementation into clinical use in 2022. CG Örebro serves as the technical backbone for the validation of the targeted panel for comprehensive genomic profiling of solid tumors at the Genomic Medicine Center Örebro. Additionally, a targeted panel for pharmacogenomics has been designed and validation is ongoing together with CG Linköping. The assay will be used in a clinical trial that is planned to start early 2023.

Scientific achievements

In 2020, CG Örebro contributed to 9 publications, which increased to 11 in 2021. In 2021 we had 18 ongoing projects and as of August 2022 we have 24, 18 of which are focused on microbiology.

New user groups

Due to the technology development in metagenomics with clinical applications we have initiated new collaborations with two different centras at Örebro University, the Nutrition-Gut-Brain - Interactions research centre and Inflammatory Response and Infection Susceptibility Centre. These collaborative projects have focused on further development of 16S and shotgun metagenomics in sterile and non-sterile sites, where the issues of contamination, especially from the host, have been approached.

CG Örebro will also serve the Pandemic Preparedness ClinMicro Örebro project on pre-analytics for pandemic preparedness with staff and technical expertise.

Outreach efforts

Several outreach activities have been organized, during Clinical Trials Day at Örebro University Hospital, 20 May 2022, the CG platform was presented both with an oral presentation and a showcase booth of provided services, ongoing projects and possibilities for new collaborations. Additionally, we arranged a CG Örebro symposium, 19 November 2021, with a program including a presentation of the platform by the PD and short presentations of ongoing projects with the aim to show the possibilities within CG for researchers at Örebro university and University hospital.

Training and education

HU planned and executed the course “Molekylärdiagnostik med NGS” 24–25 January 2022 via the Institute for biomedical laboratory sciences (IBL). The course focused on clinical use of NGS and staff from CG Örebro lectured on laboratory and bioinformatics aspects.

Contribution to cross-unit and cross-platform initiatives

At the cross-unit level, monthly meetings are held to exchange knowledge and to harmonize methods offered by the platform. The national pandemic laboratory preparedness G3P project is an example of cross-unit collaboration with true national coverage including all GC units, where one work package is coordinated from CG Örebro through Paula Mölling. Another example of a cross-unit collaboration between two CG units is the targeted panel for pharmacogenomics developed by Anna Green, CG Örebro, and evaluated together with Clinical Genomics Linköping. Presently, CG Örebro is involved in the G3P metagenomics pilot together with NGL.

ii) Development plans for the unit 2023–2024 and beyond

- The development of service for metagenomics studies using long-read sequencing will be further developed to include both DNA and RNA microbial genomes and the service will also be optimized for more sample types that are of clinical relevance. We are also planning to set up a service for metatranscriptomics to obtain whole gene expression profiling of complex microbial communities which we believe will be in demand for researchers working on gut microbiota and in the future other pathological conditions.
- For the coming years we will continue to establish methods for ultrasensitive detection of solid tumors in plasma. Initially for detection of recurrent disease but also as a diagnostic and prognostic tool for mainly breast-, lung-, colorectal- and oropharyngeal cancer. The techniques include both sequencing and digital droplet PCR (ddPCR). We aim to implement ddPCR targeting circulating tumor HPV-DNA as a clinical minimum residual disease analysis for squamous cell oropharyngeal cancer in the coming years.
- Establishing a suitable organizational structure for CG Örebro with premises specifically designated for CG Örebro. The unit is planned to be a part of the Precision Medicine Örebro center that will be a shared facility between the Örebro University hospital and Örebro University. The new location will serve as a meeting point for translational and clinical research together with clinical diagnostics and education/training.
- Budgetary means for 2023-2024 will focus on new staff including 1 staff scientist and 1 bioinformatician dedicated to serve CG Örebro as well as improved sequencing capacity in the form of a new mid output sequencing instrument planned for 2023. Funding from Örebro University has also been confirmed for additional laboratory equipment for pre-sequencing procedures.
- Improved IT-infrastructure for 2023 include a project management system and electronic lab notebook. Shared storage and compute power at Örebro University is planned for 2024.

iii) Additional comments

Due to the uncertainties with long-term funding, Örebro University has been hesitant to employ staff dedicated to the work within CG Örebro. After the initial years of setting up the new unit the faculty has become convinced of its relevance and can trust the continuous demands of our services. Another challenge with establishing the new unit has been the co-operative organization between the hospital and the university that the work within the CG platform requires.

Clinical Genomics Örebro

Budget 2022

Costs	2022
Personnel cost	4 160 511
Other personnel costs	300 000
Depreciation	1 557 114
Service and license costs	915 764
Other operating costs	3 630 860
Premises costs	479 595
Other costs	378 595
Sum costs (kSEK):	11 421 843

Revenues	2022
Funding from SciLifeLab	800 000
Funding from financier X	372 678
Funding from financier Y	6 695 480
Funding from financier Z	416 909
User fees	3 077 000
Sum revenues (kSEK):	11 362 066

Bioinformatics Platform

Platform Director: Bengt Persson, UU

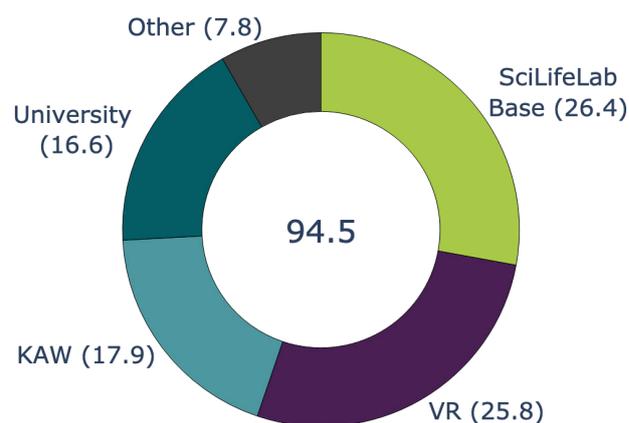
Co-Platform Director: Björn Nystedt, UU

Platform Coordination Officer: Björn Nystedt, UU

Platform and Units SciLifeLab Funding 2021:

Unit	(MSEK)
Support, Infrastructure and Training	17.0
Compute and Storage	3.4
BioImage Informatics	3.6
AIDA Data Hub	1.0
PD, PCO, Platform Strategic Budget	1.4
Sum:	26.4

Total Funding 2021:



Platform Specific Terms and Conditions for Funding - Bioinformatics

This document concerns the terms and conditions for SciLifeLab funding of the Bioinformatics Platform and Units from 2021 and onwards and outlines the strategic direction MG wants the platform to take. The mid-term checkup in the middle of the 4-year funding period will focus on how well the Platform and Units have taken into account the following items:

- Ensure that SciLifeLab funds are used in the platform in a manner that will align with the priorities and goals of the entire SciLifeLab organization
- Ensure that SciLifeLab funds are used in the platform in a manner that will align with the priorities and goals of the entire SciLifeLab organization
- Provide resources within the SciLifeLab platform funding to engage in the SciLifeLab capabilities, integrating data and know-how from several different platforms
- Require supported projects to commit to FAIR data sharing
- Together with the SciLifeLab management suggest a platform governance and steering structure in line with the general policy for SciLifeLab platforms and the NBIS consortium agreement
- Brand itself in line with the SciLifeLab policy on platform branding, while taking into account that the Platform is funded from multiple sources
- Work as an integral part of the SciLifeLab infrastructures, facilitating the combination of technology-driven and data-driven research services
- Contribute to the Spatial and Single Cell Biology capability with resources from BioImage Informatics Unit
- Support projects with data produced at SciLifeLab, and in mining existing datasets that can feed validation projects for the laboratory infrastructure, to a degree that matches the SciLifeLab platform funding
- Dedicate one responsible contact person for each SciLifeLab laboratory platform to jointly improve user consultation and support
- When needed, participate in user planning meetings together with the laboratory platforms to evaluate project feasibility, improve study design, and promote data sharing
- Collaborate with the Data Centre to enable good data management practices according to the Open Science and FAIR principles for users of the SciLifeLab infrastructures
- Contribute to the planned concept of SciLifeLab national nodes at non-host universities, where multiple platforms can integrate their national actions and links to the national SciLifeLab organization as well as to the local user base and local infrastructures
- Aid the Data Centre and SNIC/SUNET to develop a prospective plan for the storage and compute requirements, needed by the life science users, at SNIC/SUNET and other sites for high-performance computing
- Provide the necessary infrastructure for sensitive human data storage, e.g. EGA-SE, to support translational and clinical research, clinical diagnostics, and health data mining, enabling the necessary support for the Swedish participation in the European 1+ Million Genome project (1 + MG)
- Together with the SciLifeLab management and the DDLS steering group develop a plan for the use of AI and machine learning as part of the bioinformatics platform and for the SciLifeLab infrastructures as a

whole

- Aid the research community as a whole to carry out data-driven mining of existing data sets and resources, to build data-driven hypotheses, and to promote efficient usage of SciLifeLab wet lab infrastructures to validate these
- Continue to be a key driver in providing advanced training and Ph.D./post-doc course work at SciLifeLab and in collaboration with the DDLS training initiatives
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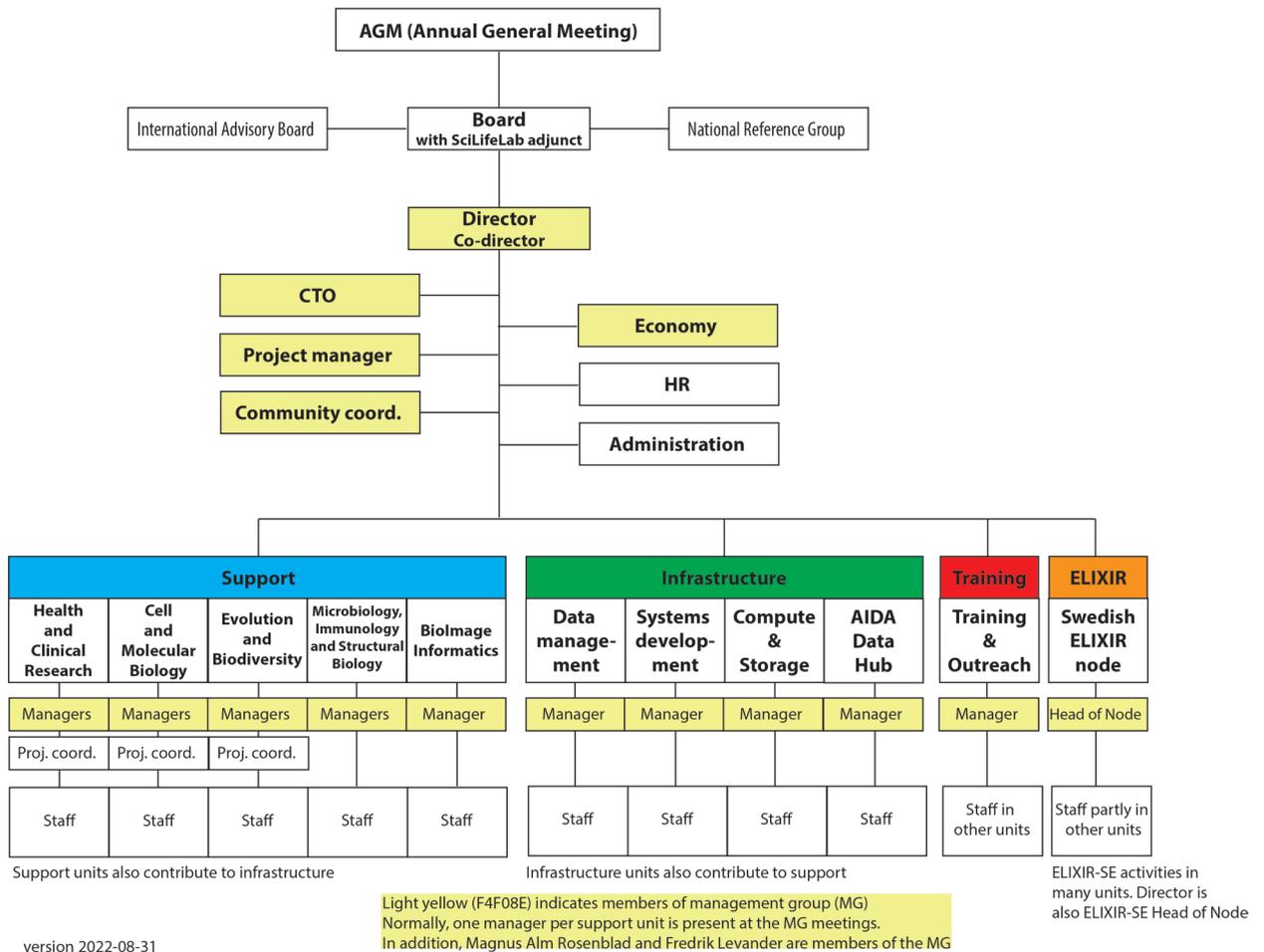
Organization and Management

Organization

NBIS (Bioinformatics platform) is a consortium of 11 members – UU (host), Chalmers, GU, KI, KTH, LiU, LU, NRM, SLU, SU and UmU. These meet annually at the Annual

General Meeting (AGM; Stämman). These 11 members are the same as those engaged in the DDLS initiative.

NBIS organisational chart



The **NBIS Annual General Meeting (stämman)** is the highest decision body, where university representatives are taking decisions on co-funding, strategic issues, and appointment of Board and Reference group. The **NBIS Board (styrgrupp)** is the strategic and scientific leading organ taking decisions on annual work plan, activities and budget. It has an International Advisory Board to its help. It continuously follows that NBIS functions properly and has the power to suggest changes of support and infrastructure functions.

The board meets 3–4 times a year and consists of 8 members. The director, the CTO, the SciLifeLab infrastructure director, and the Reference Group chair participate in these board meetings, but without voting rights. **The International Advisory Board** supports the NBIS board in decision making, especially regarding strategic issues. The **Reference group** secures contact between board/director and each participating university.

Platform Management

NBIS is divided into **organisational units**, as depicted in the figure above. The managers and ELIXIR-SE head of node together with the director and co-director form

the **management team** that have monthly video meetings to coordinate activities and discuss operational matters. Important questions of policy, strategy and economy are

put forward to the Board for decision.

Each support team / unit has regular meetings with their respective staff to coordinate and optimise their support and infrastructure activities. In addition, there are regular training meetings with representatives from all relevant units to coordinate our training activities.

Our economy administration provides material for budget decisions, monitors the financial status, handles distribution of money from NBIS to and from the respective university and invoicing of user fees.

NBIS has a web site (<https://nbis.se>) for providing up-to-date information both to our users and for internal purposes. NBIS also has a project management system

Future improvements of the organisation

From 2023 and onwards, NBIS would very much prefer to receive our SciLifeLab funding at the platform level instead of divided into 4 parts. Our economy is run on the platform level in order to enable flexibility and rapid responses to changes in user needs. If SciLifeLab would like to “ earmark ” targeted investments, this could be done in the decision letter. In reality, NBIS often adds resources from other funds to enable necessary staffing in our units.

Since the establishment of SciLifeLab Data Centre (DC) we have been closely collaborating and coordinating our activities in order to optimally utilise our respective resources. This has worked very well and from the beginning there was a clear distinction between our respective target users – NBIS provided support to end users and DC provided support to SciLifeLab platforms.

Development, Achievements and Plans

Items listed in the Platform Specific Terms and Conditions for Funding

Ensure that SciLifeLab funds are used in the platform in a manner that will align with the priorities and goals of the entire SciLifeLab organization: Recent major re-organisation to better align our support teams with SciLifeLab platforms and DDLS efforts. Ongoing expansion to cover support in structural biology, both experimental and structure prediction analyses. Continuous dialogue and coordination with DC regarding user support for DDLS.

When needed, participate in user planning meetings together with the laboratory platforms to evaluate project feasibility, improve study design, and promote data sharing: Laboratory platforms can contact NBIS at usermeeting@nbis.se for joint user meetings, alternatively turn to their assigned NBIS platform contact person, or NBIS PCO.

Dedicate one responsible contact person for each SciLifeLab laboratory platform to jointly improve user consultation and support: Implemented during spring

facilitating tracking of projects and allowing for NBIS staff to easily share data and information with their users. For larger support projects, a project workspace is set up for joint documentation and planning together with each research group in a private wiki.

In order to ensure a continuous competence development of the NBIS staff, they are given time (up to 20%) for education and professional development, e.g. when engaging in support tasks needing additional competence. As bioinformatics is a rapidly evolving discipline and new areas emerge, over time NBIS staff might move between different areas, depending on user needs and their own interests.

The last years, this distinction has become fuzzier as the DDLS activities were initiated and DC started additional activities that also target end users. We still solve this by close coordination between our respective organisations. The DC director is adjunct member of the NBIS management team and there is close collaboration between NBIS and DC, especially within the areas of data management and compute & storage.

For the future, it would be beneficial if SciLifeLab in order to avoid the “dual instructions” in the bioinformatics area could give mandate to NBIS for new tasks that are within our operations, instead of only giving new tasks to DC. Both NBIS and DC are SciLifeLab entities.

2022.

Work as an integral part of the SciLifeLab infrastructures, facilitating the combination of technology-driven and data-driven research services: Our SciLifeLab contact persons, our new support organisation, and the establishment of DDLS Data Science Nodes together with Data Centre will enable improved integration with the other SciLifeLab infrastructures and promote optimal data use and re-use.

Provide resources within the SciLifeLab platform funding to engage in the SciLifeLab capabilities, integrating data and know-how from several different platforms: NBIS is heavily engaged in Precision medicine, Pandemic Laboratory Preparedness, and Planetary biology, where we provide infrastructure, tools and bioinformatics competence.

Contribute to the Spatial and Single Cell Biology capability with resources from BioImage Informatics Unit: The BioImage Informatics Unit has contributed to the Spatial and Single Cell Biology capabilities by the GPU-accelerated viewer TissUUmapi, and providing advanced support, see <https://tissuumaps.github.io/>. Enabling hosting, viewing

and sharing of large spatial omics research projects via the SciLifeLab DC, e.g. the results of the Human Developmental Lung Cell Atlas. Together with the Human Developmental Cell Atlas and other NBIS staff organising a workshop on Spatial Omics Data Analysis 2022 that provides resources to advanced tools for analysis of spatial datasets via a series of online lectures and computer practicals.

Continue to be a key driver in providing advanced training and Ph.D./ post-doc course work at SciLifeLab and in collaboration with the DDLS training initiatives: NBIS delivered 8 courses in bioinformatics with 177 participants during the first half of 2022 in addition to delivering a Train-the-Trainer course to increase pedagogic expertise within SciLifeLab. NBIS training promotes Open Science and FAIR with training materials openly available. The Swedish Bioinformatics Advisory program has now included advisors from other SciLifeLab platforms, extending collaboration and knowledge transfer across SciLifeLab. The inclusion of additional trainers and experts across other platforms is part of the new NBIS Training co-production model, to collaboratively meet the increasing training demands seen from the community. NBIS Training is involved in the InfraLife project creating the Structural Biology course. NBIS leads the establishment of a central national Training Hub at SciLifeLab and is engaged in DDLS education and training, including preparations for the DDLS research school. Together with DC, NBIS training is collecting and establishing a collection of Open and FAIR training tools and materials within the foundational topics of DDLS, e.g. data science, research data management, statistics, ethics in data, Open and FAIR. AIDA Data Hub has held training sessions on GDPR and sensitive personal data management at the regular AIDA AI courses for radiologists and pathologists, aiming to increase availability of clinical AI training data for research, and has also organised a well-received AIDA DGX-2 advanced user training workshop in collaboration with ENCCS and Nvidia, where a follow-up event is planned for this fall.

Require supported projects to commit to FAIR data sharing: NBIS promotes OS and FAIR in our projects, actively supporting early data deposition to international repositories.

Collaborate with the Data Centre to enable good data management practices according to the Open Science and FAIR principles for users of the SciLifeLab infrastructures: Together with DC established a joint access point for data management support for researchers and infrastructure platforms, including best practice guidelines. Provided training in good data management practices.

Aid the Data Centre and SNIC/SUNET to develop a prospective plan for the storage and compute requirements, needed by the life science users, at SNIC/SUNET and other sites for high-performance computing: NBIS platform

director and Compute & Storage manager have, together with the DC director, taken an active role in shaping the VR application for the SNIC successor NAIS. We are also engaged in discussion about the future role of UPPMAX, as the de facto standard large-scale bioinformatics compute centre, and provider for DDLS infrastructure.

Provide the necessary infrastructure for sensitive human data storage, e.g. EGA-SE, to support translational and clinical research, clinical diagnostics, and health data mining, enabling the necessary support for the Swedish participation in the European 1+ Million Genome project (1+MG): NBIS together with CSC in Finland leads the European infrastructure work in 1+MG. Recently the EU project GDI (Genomic Data Infrastructure) was funded, where NBIS has a key role. NBIS also engaged in the new EU project EHDS Pilot 2 to coordinate with the European Health Data Space. NBIS has performed an EGA-SE end-to-end demonstration of the full process of submitting data as well as accessing it, in collaboration with central EGA. Legal agreement between central EGA and NBIS was recently signed enabling our federated services for sensitive data to become operational. NBIS leads development of the Bigpicture repository infrastructure, which uses/extends Federated EGA technology for use in European digital pathology AI.

Together with the SciLifeLab management and the DDLS steering group develop a plan for the use of AI and machine learning as part of the bioinformatics platform and for the SciLifeLab infrastructures as a whole: AI is an important part of NBIS future activities. The AIDA Data Hub provides sharing, processing, and policy support for AI training data, primarily in medical imaging, and plans to expand service offering with application expertise. As a first step, we focus on internal and external education. This consists of an ongoing internal journal club in the area and a national course. AI and machine learning is already widely used with the BioImage Informatics Unit.

Aid the research community as a whole to carry out data-driven mining of existing data sets and resources, to build data-driven hypotheses, and to promote efficient usage of SciLifeLab wet lab infrastructures to validate these

Jointly with the Data Centre establishing four DDLS Data Science nodes (DSN) to strengthen bioinformatics support and service provision, as well as developing content at the DDLS Data Platform to aid the research community to carry out data-driven mining of existing data sets and resources, to build data-driven hypotheses and promote validation at SciLifeLab wet lab infrastructures. The DSN will provide additional user interfaces that will help us to deliver the services needed by the communities.

Contribute to the planned concept of SciLifeLab national nodes at non-host universities, where multiple platforms can integrate their national actions and links to the national SciLifeLab organization as well as to the local

user base and local infrastructures: NBIS has since 2010 successful activities at all six sites. NBIS is supporting the establishment of upcoming SciLifeLab nodes, such as in Linköping, where AIDA Data Hub is planned to participate in the node steering group.

Together with the SciLifeLab management suggest a platform governance and steering structure in line with the general policy for SciLifeLab platforms and the NBIS consortium agreement: NBIS organisation is described on page 1 and 2.

Support projects with data produced at SciLifeLab, and in mining existing datasets that can feed validation projects for the laboratory infrastructure, to a degree that matches

the SciLifeLab platform funding: Will be initiated in 2023.

Brand itself in line with the SciLifeLab policy on platform branding, while taking into account that the Platform is funded from multiple sources: NBIS has a visual identity in line with SciLifeLabs visual identity to promote recognition through similarity. SciLifeLab brand is represented in materials where applicable in adherence with SciLifeLab visual identity guidelines. NBIS and SciLifeLab logos are shown together.

For space reasons, this text is provided on our unit descriptions.

D

Request for additional funding 2023–2024

NBIS herewith applies for additional funding 2023–2024 for three new activities:

1. Increased coordination between NBIS and Data Centre, especially in the area of data submission brokering. We apply for 0.5 FTE.
2. Artificial Intelligence (AI) in drug discovery and chemical biology is an important area and requires integration of activities at DDD, CBCS, NBIS and Data Centre. The emergence of huge make-on-demand chemical libraries and DNA-encoded chemical libraries (DECL) with several billions of compounds per library requires AI-based methods to make in silico screening more efficient, and a supporting infrastructure at SciLifeLab for this type of hybrid screening technologies combining wet lab data with in silico predictions is urgently required. NBIS together with prof. Jens Carlsson (UU, former SciLifeLab fellow) has in the last two years piloted bioinformatics support in computational structural and chemical biology, and we are also jointly driving an ongoing TDP to better facilitate novel AI-based screening methods. As these and other AI-related applications are becoming increasingly important in this context, discussions are currently ongoing on how to best establish strong capabilities jointly across the SciLifeLab platforms. NBIS

therefore now applies for 1 FTE to increase our efforts in this area and to further strengthen collaborations with DDD, CBCS and SciLifeLab Data Centre, as well as with Jens Carlsson and other relevant research groups.

3. We plan to extend the AIDA Data Hub with application expertise (2 FTE) in AI for medical imaging diagnostics, to provide advanced support and training to researchers in the AIDA community, with primary focus on projects with a clear connection to the broader SciLifeLab aims, including precision medicine and multi-omics. This would help realise a part of the original proposal to incorporate AIDA Data Hub into SciLifeLab (2–8 MSEK/yr) that has thus far not been possible to achieve within current unit budget (2 MSEK/yr). These application experts are envisioned to contribute as an integrated part of BioImage Informatics unit activities, and are expected to help realise synergies springing from increased operational collaboration between AIDA Data Hub and other SciLifeLab units that currently offer training and support in imaging and machine learning, especially at the Bioinformatics platform and in particular the BioImage Informatics unit. These synergies are described in further detail in the unit reports for AIDA Data Hub and the BioImage Informatics.

Requests for expanded funding 2023–2024

Specify all costs in kSEK

Unit	SciLifeLab funding 2022 (kSEK)	Requested ScilifeLab funding 2023 (kSEK)	Requested SciLifeLab funding 2024 (kSEK)
SIT (#1 and #2 above)	18 000	19 500	19 500
AIDA Data Hub (#3 above)	2 000	4 000	4 000

Support, Infrastructure and Training

Bioinformatics Platform (Web links for Unit: [Webpage](#), [Publications](#))

Basic Information

Head(s) of Unit: Bengt Persson
(Bioinformatics PD) + 9 Co-heads
PSD(s): Gunnar von Hejine
SciLifeLab Unit since: 2013
Host university: Chalmers, GU, LiU, LU, KI, KTH, NRM, SLU, SU, UmU, UU
FTEs: 72.0
FTEs financed by SciLifeLab: 17.0

Funding in 2021 (kSEK)

SciLifeLab: 17000
University: 15815
VR: 20000
KAW: 19500
Elixir: 1000
EU: 4615
Nordforsk: 1300
Total: 79230

Resource Allocation 2021

Academia (national): 82%
Academia (international): 1%
Internal tech. dev.: 15%
Industry: 1%
Healthcare: 1%
Other gov. agencies: -

User Fees 2021

Total (kSEK): 10300
Reagents: -
Instrument: -
Salaries: 100%
Rent: -
Other: -

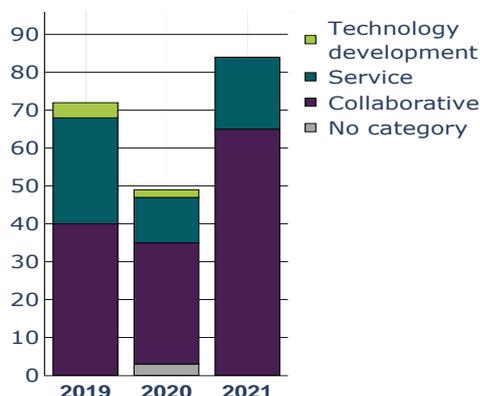
User Fees by Sector 2021

Academia (national): 100%
Academia (international): -
Industry: -
Healthcare: -
Other gov. agencies: -

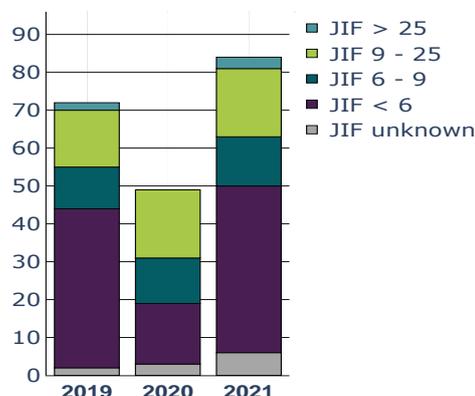
Services

- Short-, medium-, and long-term bioinformatics support in all life science areas
- Drop-in sessions and consultation meetings
- Data management support
- Infrastructure development and maintenance
- Tool and pipeline development
- Advanced training at national and international level

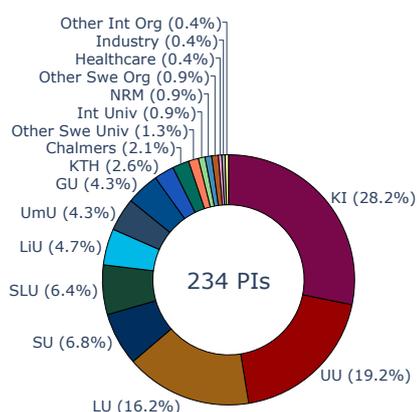
Publication by Category



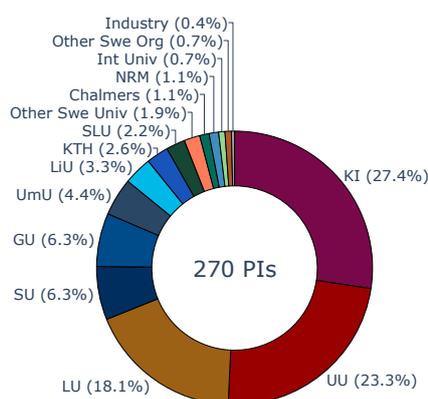
Publication by Journal Impact Factor



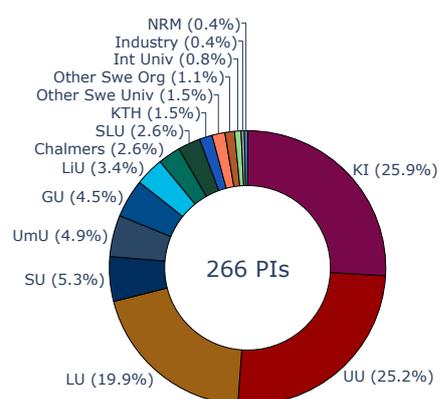
Users 2019



Users 2020



Users 2021



Unit:	Support, Infrastructure and Training
Platform:	Bioinformatics

Development, Achievements and Plans

i) DEVELOPMENT AND MAJOR ACHIEVEMENTS 2021–2022

Support re-organised to best meet the DDLS/SciLifeLab goals

NBIS Support staff helps researchers with advanced bioinformatics tasks, now **providing support to almost 300 PIs annually** (40% female, 60% male) resulting in 93 publications in 2021. Our staff is nationally distributed and connected to all emerging SciLifeLab local nodes. The three largest universities in NBIS usage are KI, UU, and LU, and about half of all support is provided from one university to another, emphasising the importance of a national infrastructure. We have strong domain knowledge in all four thematic areas of the DDLS programme, and have recently performed **a major re-organisation of the Support teams to better meet future challenges** in line with the DDLS and SciLifeLab goals. We provide national drop-in sessions via Zoom (total 44 in 2021; since these are now organised nationally, the total number becomes less compared to when they were run at each site) enabling smooth contact between researchers and our experts, which many times is the first contact in a support case.

Improved capabilities and cross-platform interactions

We have broadened our activities to **better support users from all SciLifeLab platforms**, including Bioimaging (mainly at the BIIF unit), proteogenomics (embedded staff rotating at SciLifeLab units), structural biology (recruiting Cryo-EM staff), and computational chemistry (pilot support and TDP with Jens Carlsson (UU)). We recently **assigned contact persons for each SciLifeLab platform** to further improve and facilitate interactions and joint strategic efforts, and the platforms can reach us at usermeeting@nbis.se for **joint user meetings**. We lead two current TDPs “*BeyondFold*” and “*AI-enabled virtual screening for chemical probes*”, targeting users of the ISB, CBGE, and DDD platforms.

Together with the Genomics platform we **promote evolutionary and biodiversity research** through a VR accessibility project (“*A Swedish Earth Biogenome Project platform*”), and a recently granted EU project (“*ERGA*”), and by interacting with the Planetary Biology Capability.

We provide **key infrastructure and data management for the Precision Medicine Capability**, including being the Swedish node in the Federated European Genome-phenome Archive (EGA-SE) and together with CSC in Finland leading the infrastructure work for the European 1+ Million Genomes project (1+MG). NBIS is WP lead in the EU project GDI (Genomic Data Infrastructure) for the European onboarding to the 1+MG infrastructure. We also participate in a recently granted EU project for EHDS2 Pilot (European Health Data Space). NBIS is leading the Nordic Heilsa Tryggvedottir project on sensitive data.

During 2021, we started the large EU IMI project **Bigpicture aiming at creating the future European digital pathology platform**. NBIS provides systems development support to improve the Sensitive Data Archive (SDA, formerly Local EGA), and we have adapted the software stack for the Bigpicture project (<https://bigpicture.eu/>) to enable access to sensitive pathology images. In Bigpicture we have piloted services for data mirroring between archives and also a federated discovery service. Related to Bigpicture, NBIS recently received EU funding for the project EUCAIM to build a European cancer image infrastructure. Furthermore, we are in contact with the Pandemic Laboratory Preparedness Capability regarding recruitments of NBIS Support staff within the DDLS programme.

Increased efforts in Open Science and FAIR data management

By recruiting Data Stewards, we have **increased our efforts to promote OS and FAIR practices, and with the Data Centre we have established a joint access point for data management support for researchers and infrastructure platforms.** We have also engaged internationally with **a leading role in the pan-European ELIXIR-CONVERGE project** to deliver sustainable FAIR life science data management services, such as improved/extended guidelines at the [ELIXIR RDMKit web resource](#) and provision of training. We have recently engaged in the EOSC advisory group [Metadata and data quality](#). Our systems development team provides support in deploying tools so that they can be used by the entire life science community, and not just by bioinformaticians. We also facilitate large scale analyses by the development of stable and user-friendly pipelines. NBIS works strategically with Reproducible Research, actively promoting and deploying stable workflow systems and reproducible compute environments, both for internal tools development and for supported research projects.

Training a new generation of life science researchers

In 2021, NBIS had ~600 participants in the 36 training events we supported. Of these, 18 workshops are part of the NBIS course catalogue and 18 are collaborative efforts with others e.g. infrastructure platforms, international research groups, ELIXIR etc. Since 2015 we also provide a highly appreciated PhD advisory mentor programme in bioinformatics where PhD students get mentorship guidance from NBIS experts over a period of 2 years, totalling >110 PhD students so far. **From 2022, we have expanded to engage expert advisors from other SciLifeLab platforms in the bioinformatics mentoring programme as well.** In addition to providing national advanced bioinformatics training, NBIS training, as the Swedish node of ELIXIR, is involved on the international arena such as **leading the ELIXIR Training Platform (Executive Committee member) and chairing a Task Force within the EOSC advisory group** [Research careers and curricula](#), and NBIS experts engage in ELIXIR Community work transferring both state-of-the-art knowledge and training activities to a wider stakeholder user group outside of Sweden.

ii) DEVELOPMENT PLANS 2023–2024

In addition to continuing the ongoing developments described above, we plan efforts to further develop the following areas during 2023–2024. (Also see the [NBIS Strategic Plan 2022-2026](#).)

Data-Driven Life Science: Jointly with the Data Centre establish four DDLS Data Science Nodes (DSN) to strengthen bioinformatics support and service provision, as well as developing content at the DDLS Data Platform to aid the research community to carry out data-driven mining of existing data sets and resources, to build data-driven hypotheses and promote validation at SciLifeLab wet lab infrastructures. The DSN will also add user interfaces that will help us to provide the services needed by the communities.

AI and Machine Learning: Together with the SciLifeLab management and the DDLS steering group develop a plan for the use of AI and machine learning as part of the bioinformatics platform and for the SciLifeLab infrastructures as a whole. This is expected to have an impact across multiple research areas and technologies currently supported by us, but potentially also open up NBIS services in new domains like drug discovery and chemical biology (see suggested additional funding below).

Training Hub: Drive the establishment of a SciLifeLab Training Hub to meet the continuously increasing training needs as a fundamental pillar to reach the strategic goals of DDLS/SciLifeLab.

Finally, we apply for additional funding in 2023–2024 for a) 0.5 FTE for coordination between NBIS and Data Centre (especially in the area of data submission brokering), and b) 1 FTE for establishing SciLifeLab capabilities in AI-based methods related to chemical biology and drug development in collaboration with DDD, CBCS, Data Centre and others.

Support, Infrastructure and Training

Budget 2022*

Numbers show current budget and within parentheses the budget in the VR application 2019 (updated version November 2019)

INCOMES

VR	20 000	(20 000)	
VR EGA-SE	2 268		
SciLifeLab	25 550	(22 000)	
SciLifeLab TDP	2 000		
KAW	19 596	(17 000)	
Universities	16 558	(16 350)	
ELIXIR	1 000	(4 000)	
EU projects	5 550		
NeIC	1 550	(1 000)	
User fees	10 100	(14 000)	
Surplus from 2021	1 155		

TOTAL	105 327	(94 350)	
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EXPENSES

Module 1 - Management	7 400	(9 486)	5.95 FTE
Module 2A - Bioinformatics support (SMS) including PartnerProjects	29 767	(22 690)	25.55 FTE
Module 2B - Bioinformatics support (LTS) including "Big Data" at SU	25 950	(20 400)	25.35 FTE
Module 2C - Bioinformatics support (Sysbio)	3 400	(5 100)	3 FTE
Module 3 - Data management and data publication	4 550	(10 396)	4.3 FTE
Module 4 - Systems development, tools & infrastructure	14 000	(12 442)	13.35 FTE
Module 5 - Compute and storage support that is not funded by SNIC	4 970	(6 120)	4.8 FTE
Module 6 - Training and National Networking		included in other modules	
Module 7A - International - Swedish ELIXIR node	8 290	(6 732)	5.9 FTE
Module 8A - BioImage Informatics Facility	3 800		4 FTE
Module 8B - AIDA Data Hub	3 200		3 FTE

TOTAL	105 327	(93 366)	
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Comments:

Module 8 is new, formed by BioImage Informatics Facility and AIDA Data Hub, which became parts of NBIS from 2021.

*Budget for the entire Bioinformatics platform.

Compute and Storage

Bioinformatics Platform (Web links for Unit: [Webpage](#), [Publications](#))

Basic Information

Head(s) of Unit: Marcus Lundberg
SciLifeLab Unit since: 2013
Host university: UU
FTEs: 3.45
FTEs financed by SciLifeLab: 2.65

Funding in 2021 (kSEK)

SciLifeLab: 3400
UU: 800
Total: 4200

Resource Allocation 2021

Academia (national): 80%
Academia (international): -
Internal tech. dev.: 20%
Industry: -
Healthcare: -
Other gov. agencies: -

User Fees 2021

Total (kSEK): 0
Reagents: -
Instrument: -
Salaries: -
Rent: -
Other: -

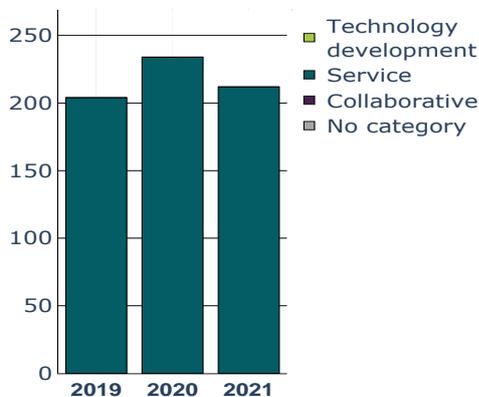
User Fees by Sector 2021

Academia (national): -
Academia (international): -
Industry: -
Healthcare: -
Other gov. agencies: 100%

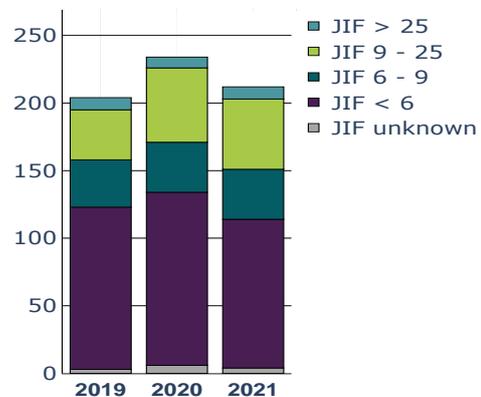
Services

High-performance computing and storage resources, maintenance of relevant bioinformatics software and data (e.g. reference genomes), and associated user support. The facility is hosted at Uppsala Multidisciplinary Center for Advanced Computational Science (SNIC-UPPMAX), which is Uppsala University's resource for high-performance computing and related know-how.

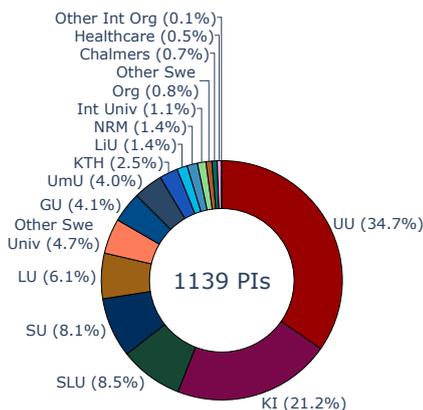
Publication by Category



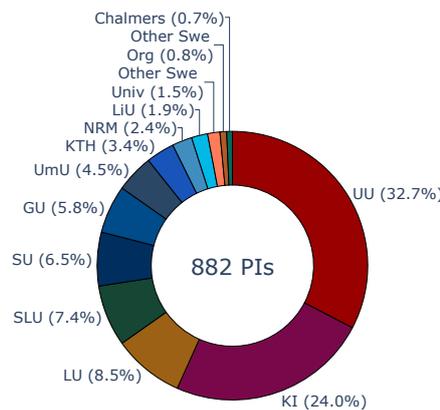
Publication by Journal Impact Factor



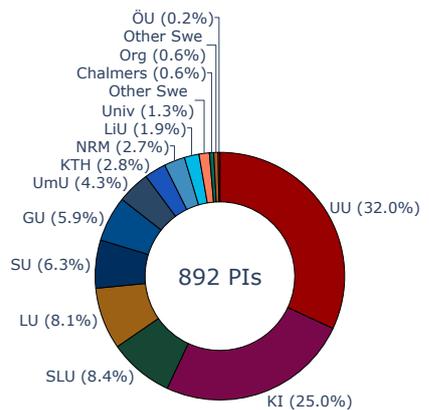
Users 2019



Users 2020



Users 2021





Unit:	Compute and Storage
Platform:	Bioinformatics

Development, Achievements and Plans

i) The community that Compute and Storage supports has, in the past two years, grown by about 20% per year in number of projects and users. A small number of new user groups have come to us from organisations that traditionally did not use us, including Örebro and Jönköping universities. Meanwhile, the resources that we support have grown in size and complexity — notably GPU resources on the sensitive data system. The software library has grown considerably as well, especially in the domain of machine learning but also more traditional Next-Generation-Sequencing analysis tools.

A significant proportion of the user support effort in 2021 was directed at helping users manage problems that arose with the Crex storage system, which is mounted on the general-purpose compute cluster, Rackham. The demand for storage space outstripped the capacity of the system, which led to performance degradation, instability, and a need for users to be more selective with data retention on the system.

Addition of new staff has allowed Compute and Storage to improve support in a couple of key areas – workflow managers and container-based software deployment. These are important technologies that dramatically improve user productivity. Additionally, a significant effort is spent on supporting users in navigating the judicial issues related to sensitive data processing, e.g. performing Data Protection Impact Assessments and writing Personal Processing Agreements.

Compute and Storage management was directly involved with helping UPPMAX secure funding from SNIC to extend Crex as well as invest in GPU capability on Bianca. Additional investments in Bianca, designed to improve usability and extend its lifetime, were also made. Together, these initiatives have ensured continued access and relevance to key resources, enabling hundreds of research projects.

ii) The sudden end of the SNIC organisation entails many changes and a large degree of uncertainty. The SNIC advanced user support activity with which Compute and Storage has collaborated will cease to exist, and it is unclear whether this will be replaced at all. Additionally, it is not known whether the new organisation will provide a competent replacement for the UPPMAX systems, which are currently funded until the end of 2024.

Therefore, NBIS is taking steps to ensure that our very much appreciated user support continues and that we do not lose any competence. From 1 January 2023, NBIS (unit Compute and Storage) will take over relevant SNIC-funded application experts at UPPMAX, taking responsibility for the national advanced user support needs for life science users of SNIC/NAIS/UPPMAX systems (and their successors). This will increase the size of the Compute and Storage unit in NBIS with 2–3 FTEs. The costs for this increase are taken within NBIS.

Our user support will be closely coordinated with that of SciLifeLab Data Centre, which is in the process of starting its own user support service for DDLS systems that they are setting up. A desired

Unit Report 2022

outcome is a single point of entry for support for SciLifeLab users for support on any DDLS or SNIC/NAIS/UPPMAX system.

Compute and Storage will take steps to continue to give support for our users on nationally available compute and storage resources even after 2024, wherever these systems might be located. If there will be a shift from UPPMAX systems, then the focus in 2024 must be to ensure that users will have access to the complete software library and reference databases that they need.

In order to meet these challenges, Compute and Storage is making an effort during the autumn 2022 to align its vision, goals, and strategy to the current situation through a series of meetings. Since its inception in 2016, the organisation has grown and the landscape has evolved considerably. Now is the time to take stock and make sure that we can continue to provide life science researchers with the digital research environment and support they need.

Compute and Storage

Budget 2022

Costs	2022
Personnel cost	3 313 202
Other personnel costs	13 200
Depreciation	0
Service and license costs	0
Other operating costs	6 600
Premises costs	29 301
Other costs	37 400
Sum costs (kSEK):	3 399 703

Revenues	2022
Funding from SciLifeLab	3 130 000
Funding from financier X	0
Funding from financier Y	0
Funding from financier Z	0
User fees	0
Sum revenues (kSEK):	3 130 000

Biolmage Informatics

Bioinformatics Platform (Web links for Unit: [Webpage](#), [Publications](#))

Basic Information

Head(s) of Unit: Anna Klemm
PSD(s): Carolina Wählby, Kevin Smith
SciLifeLab Unit since: 2016
Host university: UU, KTH
FTEs: 4.3
FTEs financed by SciLifeLab: 1.6

Funding in 2021 (kSEK)

SciLifeLab: 3600
VR: 750
Other: 1000
Total: 5350

Resource Allocation 2021

Academia (national): 60%
Academia (international): -
Internal tech. dev.: 40%
Industry: -
Healthcare: -
Other gov. agencies: -

User Fees 2021

Total (kSEK): 35
Reagents: -
Instrument: -
Salaries: 96%
Rent: 4%
Other: -

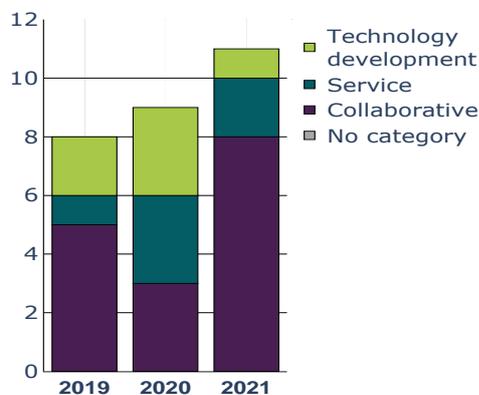
User Fees by Sector 2021

Academia (national): 100%
Academia (international): -
Industry: -
Healthcare: -
Other gov. agencies: -

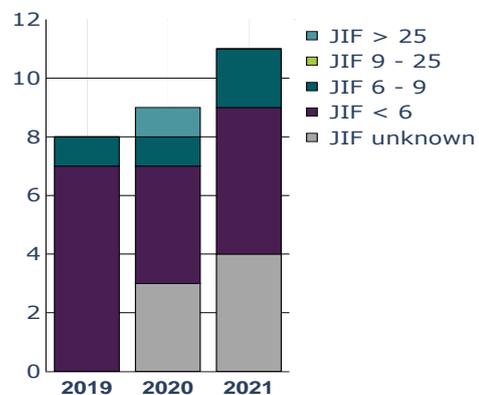
Services

- Microscopy imaging and quantitative data analysis
- Image analysis assay development and image processing algorithm development and software engineering
- High throughput/large-scale image processing using computing clusters, including data transfer and storage.
- Large-scale data analysis and visualization

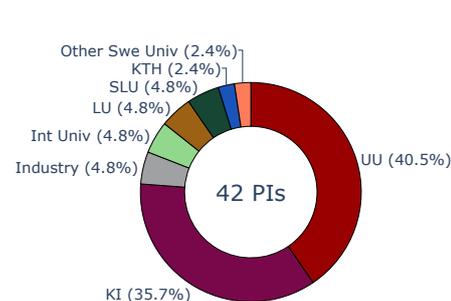
Publication by Category



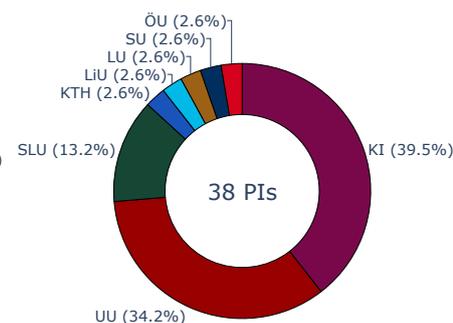
Publication by Journal Impact Factor



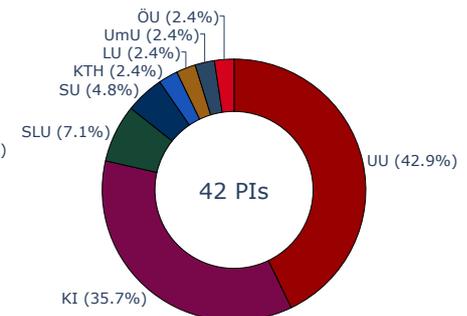
Users 2019



Users 2020



Users 2021





Unit:	Biolmage Informatics
Platform:	Bioinformatics

Development, Achievements and Plans

i) Development and major achievements of the unit 2021–2022

The BioImage Informatics Unit (BIIF) provides support and training to perform state-of-the-art analysis on image data. In 2021, we supported 41 PIs and contributed actively in 10 training events. Next to this, in 2021 and 2022 BIIF had/is having a special focus on AI-based image analysis (DCNNs) in combination with Spatial and Single Cell Biology capabilities. BIIF contributed to the capability by the following activities:

- Releasing GPU-accelerated viewer TissUUmmaps, and providing support, facilitating a range of spatial omics projects by enabling large-scale data viewing and sharing, see <https://tissuumaps.github.io/>
- Enabling hosting, viewing and sharing of large spatial omics research projects via the SciLifeLab data center, e.g. the results of the Human Developmental Lung Cell Atlas (<https://tissuumaps.dckube.scilifelab.se/web/private/HDCA/index.html>)
- Together with the Human Developmental Cell Atlas and other NBIS staff organizing a workshop on Spatial Omics Data Analysis. The workshop, taking place August 29 – September 3, 2022, provides resources to advanced tools for analysis of spatial datasets via a series of online lectures and computer practicals. See more info here: <https://www.scilifelab.se/event/spatial-omics-data-analysis/> The course had 120 applicants, showing the great interest for these techniques.
- Ongoing efforts with the spatial proteomics unit (Charlotte Stadler) and the research groups of Arne Östman (KI) and Patrick Micke (UU) to establish workflows for segmentation and learning-based approaches for classification of cells and detection of cell-niches in multiplexed fluorescence microscopy image data. Next to the ongoing work, we published the collaborative technology development together with Carolina Wählby's research group (<https://doi.org/10.1002/cyto.a.24467>) and also created training material (<https://www.youtube.com/watch?v=WTAgXpuuqNY>).

In 2021 and 2022 until now we have also published 16 journal papers, involving state-of-the-art image analysis techniques and their applications in the life sciences. Here we would like to highlight a deep-learning based tool for the automated detection of vascular remodeling in lymph node tissue images (<https://onlinelibrary.wiley.com/doi/10.1002/path.5981>), and a novel method for spatiotemporal modeling of cell-type signatures using graph convolutional neural networks (<https://doi.org/10.1371/journal.pcbi.1010366>).

We have also published several overview articles together with the international bioimage analysis community, e.g. a glossary of current bio-image analysis tools (<https://doi.org/10.1002/1873-3468.14451>), which contribute to the outreach in the field.

Other training and educational efforts include the organization of the EMBO Practical Course “Advanced Methods in Bioimage Analysis” and participation in the teaching of several PhD-level image analysis courses (in Sweden and outside).

ii) Development plans 2023–2024 and beyond

We will focus on further developing advanced (often AI and learning-based) methods for analysis of spatial omics techniques (spatial omics and multiplexed fluorescence data analysis). This development is coordinated with other NBIS experts within a specialized technology group, in collaboration with the Spatial Omics platform, and together with the TissUUmmaps team. We are working on streamlining the analysis of ISS data as much as possible, and current workflows are being used and evaluated in the ongoing workshop on Spatial Omics Data Analysis (<https://www.scilifelab.se/event/spatial-omics-data-analysis/>).

Another focus is on the analysis of quantitative phase imaging data in a collaboration with Lars Behrendt, UU. This will be used to monitor the effect of drugs and pharmaceuticals on bacteria using microfluidic technologies.

As a third focus we will continue our collaboration with the new DDLS fellow, Wei Ouyang (KTH) in using the ImJoy server to bring deep-learning tools to our users.

We just submitted the application for the second edition of the EMBO practical course “Advanced Methods in Bioimage Analysis” and expect a positive reply, given the interest and feedback to the first edition, and we plan to run more instances of the current workshop on Spatial Omics Data Analysis, further tuned and improved based on input from the participants.

We will continue to be active in the Nordic and European Bioimage Analysis community and plans are to further shape these communities, expanding our network of experts and keeping up with the latest developments in the field. Gisele Miranda from BIIF is funded as Imaging Scientist by the Chan-Zuckerberg Initiative (CZI) and is actively involved in their network worldwide. CZI has developed into a major funding resource in the last years with a special focus on funding open-source tools and networks connected to bioimaging.

We are already collaborating closely with the AIDA Data Hub, and see great potential for development by closer integration and physical placement of expertise at LiU. This would help us provide the best possible support for projects with a strong clinical component and special requests for secure data handling close to computational power.

iii) Specific questions or comments for the reviewers

For maintaining and further developing our unit, we ask the reviewers to consider securing national long-term funding for the FTE currently funded by time-limited SLL-UU-SFO funding. We further strongly support funding for 2 FTEs working as application experts at the AIDA data hub, LiU. These application experts would primarily focus on projects with a clear connection to the broader SciLifeLab aims, including precision medicine and multi-omics, and be an integrated part of BIIF, as described above.

Biolmage Informatics

Unit Budget 2022

Costs	2022
Personnel cost	7 293 935
Other personnel costs	112 400
Depreciation	75 667
Service and license costs	0
Other operating costs	0
Premises costs	135 000
Other costs	0
Sum costs (kSEK):	7 617 002

Revenues	2022
Funding from SciLifeLab	3 600 000
Funding from SciLifeLab-UU SFO	1 000 000
Funding from CZI	1 000 000
Funding from VR NMI	750 000
Funding from Swiss National Science Foundation	485 000
User fees	800 159
Sum revenues (kSEK):	7 635 159

AIDA Data Hub

Bioinformatics Platform (Web links for Unit: [Webpage](#), [Publications](#))

Basic Information

Head(s) of Unit: Joel Hedlund
PSD(s): Claes Lundström
SciLifeLab Unit since: 2021
Host university: LiU
FTEs: 0.7
FTEs financed by SciLifeLab: 0.7

Funding in 2021 (kSEK)

SciLifeLab: 1000
Total: 1000

Resource Allocation 2021

Academia (national): 45%
Academia (international): 10%
Internal tech. dev.: 10%
Industry: 15%
Healthcare: 20%
Other gov. agencies: -

User Fees 2021

Total (kSEK): 0
Reagents: -
Instrument: -
Salaries: -
Rent: -
Other: -

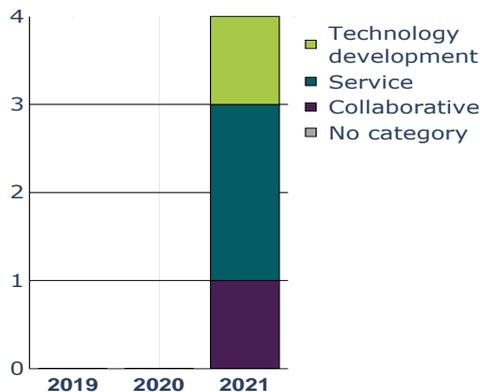
User Fees by Sector 2021

Academia (national): -
Academia (international): -
Industry: -
Healthcare: -
Other gov. agencies: 100%

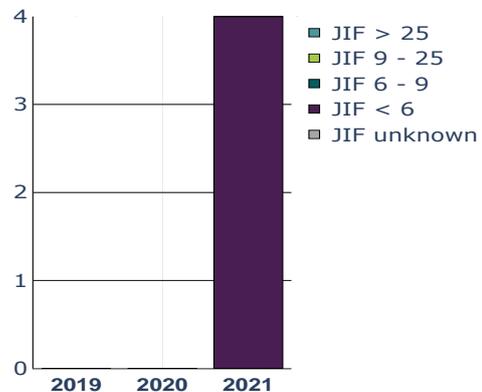
Services

- Policy support for sensitive personal research data.
- Data sharing.
- GPU compute.
- Picture Archive and Communication System (PACS).
- Code collaboration.
- Training and community building.

Publication by Category



Publication by Journal Impact Factor



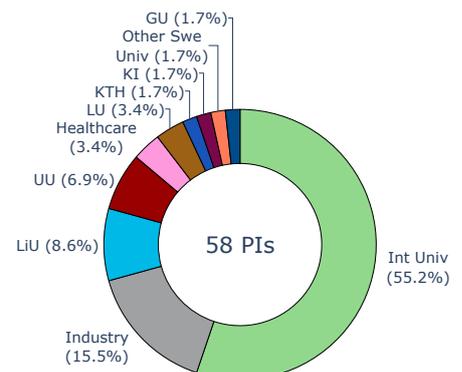
Users 2019

No user information

Users 2020

No user information

Users 2021





Unit:	AIDA Data Hub
Platform:	Bioinformatics

Development, Achievements and Plans

[AIDA Data Hub](#) is a data infrastructure established to support the national AIDA community with services in data sharing, processing, and policy support. [AIDA](#) itself is a national collaboration arena for research and innovation in medical imaging diagnostics AI, funded by [Medtech4Health](#) and engaging [~50 partners](#) from academia, healthcare, and industry (up from ~35 at the start of the strategy period). The AIDA Data Hub is fully funded by SciLifeLab since its incorporation into the [Bioinformatics](#) (NBIS) platform in July 2021, and participates actively in platform management and group leader activities, workshops and retreats. [Services](#) include the [DGX-2](#) secure compute service, which at the time of incorporation was the largest national GPU resource secure enough for sensitive personal data. We collaborate with the [Data Centre](#) to operate the [AIDA wiki](#), and the [AIDA Nextcloud](#) for data sharing with AIDA and the world. We also use the Bioinformatics platform [GitHub](#) and [Slack](#) for code sharing, and community technical support and announcements.

i) Development and major achievements 2021–2022

AIDA Data Hub is now [sharing 5.75 TB AI training data](#) for medical imaging research ([metrics](#): 30233 scans, in 18 datasets, from 5 modalities). We have now facilitated ethical and legal data sharing with researchers in 27 countries on 5 continents, up from 8 and 3 respectively, in 92 external sharing events since the start of 2021 (internal sharing point-to-point among AIDA partners not tracked). In this strategy period, our DGX-2 secure compute service has had a 96% utilization, and has had its storage capacity extended. We also collaborated with [SCAPIS](#) to set up a [VINNOVA](#) funded data lab on this system, where AI researchers can securely process multimodal SCAPIS personal data for research. We have also established a devops scrum team for operating the services, that interacts daily with other devops scrum teams in the Bioinformatics platform to develop services for processing sensitive personal data for research.

We attribute much of our success to our [AIDA Data Sharing Policy \(Sci Data, OpenAccess\)](#) which we developed in collaboration with the AIDA community and stakeholders, in order to provide succinct and understandable guidelines for best practices in using and sharing clinical imaging data for research in Sweden and similar countries, which make it easier to demonstrate that the activities are in fact ethical and legal. This policy is being [continuously updated](#), as further needs for guidance are identified. In this strategy period, we added support for data sharing on delegation using DTAs, and for processing personal data using DPAs, which are now in place with research groups at GU, KI, and KTH. We have also added decision support in data access request evaluation. Furthermore, we contributed to the national health data working group in the government collaboration program for health and life science ([summary report](#), [more info](#)). We have also published guidance on how to effectively present machine learning results to clinicians and healthcare stakeholders ([Acta Orthop, OpenAccess](#)), and on proactive construction of an annotated imaging database for AI training ([J Digit Imaging, OpenAccess](#)).

We also contribute to major European efforts, such as [Bigpicture](#), which is a flagship EU-IMI project that entered execution phase in Feb 2021 with the aim to establish a Petabyte platform for European digital pathology AI. Here, we lead the repository infrastructure development, which is carried out in collaboration with the sensitive data services teams at the NBIS Systems

Development unit and [CSC.fi](#) (i.e. the [ELIXIR-SE](#) and [ELIXIR-FI](#) nodes). Selected AIDA Data Hub [pathology datasets](#) were used as pilot data for repository development. The pilot system is now in operation, based on ELIXIR technologies developed for genetics: [Federated EGA](#), [Life Science AAI](#), [REMS](#), and [ELIXIR Beacon](#). The repository has received its first three clinical datasets, from [Region Östergötland](#), [Medical University of Vienna](#), and [University Medical Center Utrecht](#). Large scale archive operations are planned to commence Feb 2023.

We also plan to set up similar infrastructure for the planned Federated European Infrastructure for Cancer Images Data (the recently granted EU project EUCAIM, analogous to GDI). Here, we contributed to the SciLifeLab efforts to prepare and coordinate the Swedish parts of the application, and participated in the three-person writer group that finalized the Swedish contributions to the application. Our contribution to EUCAIM is planned to consist of deploying essentially a Bigpicture federated node on [Berzelius](#) sensitive (a planned [DDLS](#) enabling extension of the Swedish flagship GPU resource, secure enough for processing sensitive personal data), opening it up also for other cancer imaging techniques, such as in radiology. This is indeed also one of the driving use cases included by the DDLS [data platform](#) planning group, where we participate, in part in the role of the LiU appointed DDLS data contact. It is also a component of our support to the [LiU/CMIV](#) health tripod strategy, where our DGX-2 system constitutes the first realized part of the implementation of interfacing double data lakes for facilitated use of clinical- and research health data at Region Östergötland and LiU. It is also a part of our support to the establishment of the Linköping SciLifeLab node, where we are planned to participate in the node steering group.

We have presented our activities for example to the [Nordic e-Infrastructure Collaboration all-hands meeting](#), and to the [e-health agency](#), and VINNOVA presented our activities for the European Commission Federated European infrastructure for cancer images data [information and networking session](#). We have also held training events for example on GDPR and data management at the regular AIDA AI courses for clinicians, with the aim to increase availability of clinical AI training data for research. We also organized a well-received [AIDA DGX-2 advanced user training workshop](#) in collaboration with ENCCS and Nvidia. A follow-up event is planned for this fall.

ii) Development plans 2023–2024 and beyond

In the coming period we plan to continue the activities and plans as described above, and in addition we plan to extend the AIDA Data Hub with application expertise (2 FTE) in AI for medical imaging diagnostics, to provide advanced support and training to researchers in the AIDA community, with primary focus on projects with a clear connection to the broader SciLifeLab aims, including precision medicine and multi-omics. This would add support and training to the AIDA Data Hub service offering (currently purely a data and processing infrastructure unit), and would help realize an important part of the original proposal to incorporate AIDA Data Hub into SciLifeLab (2–8 MSEK/yr) that has thus far not been possible to achieve within current unit budget (2 MSEK/yr). These application experts are expected to facilitate knowledge transfer between AIDA Data Hub user groups, help reduce startup latencies in new fellowships and innovation projects supported by AIDA Data Hub, and by enabling bringing in more fellowships and junior researchers, by providing a core resource with deep technical expertise (as supervisor availability is an identified current limiting factor). We see that this effort can help build SciLifeLab synergies, in the form of increasing operational collaboration between AIDA Data Hub and other SciLifeLab units that currently offer training and support in imaging and machine learning, especially at the Bioinformatics platform and in particular the BioImage Informatics unit. We also foresee that this effort will increase knowledge sharing between SciLifeLab units and between user communities, and help facilitate user mobility and ensure broad uptake of new techniques and technologies.

iii) Specific questions or comments for the reviewers

In order to realize the application expert expansion described above, we propose an increase of the AIDA Data Hub budget by an additional 2 MSEK/yr during 2023–2024.

AIDA Data Hub

Budget 2022

Costs	2022
Personnel cost	1 066 464
Other personnel costs	29 500
Depreciation	823 708
Service and license costs	0
Other operating costs	52 328
Premises costs	28 000
Other costs	0
Sum costs (kSEK):	2 000 000

Revenues	2022
Funding from SciLifeLab	2 000 000
User fees	0
Sum revenues (kSEK):	2 000 000

► Chemical Biology and Genome Engineering Platform

Platform Director: Anna-Lena Gustavsson, KI

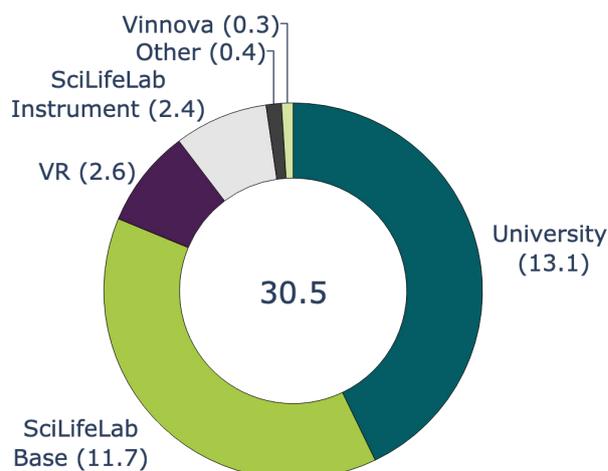
Co-Platform Director: Berhard Schmierer, KI

Platform Coordination Officer: Berhard Schmierer, KI

Platform and Units SciLifeLab Funding 2021:

Unit	(MSEK)
Chemical Biology Consortium Sweden	6.0
Chemical Proteomics	1.7
CRISPR Functional Genomics	3.2
PD, PCO, Platform Strategic Budget	0.8
Sum:	11.7

Total Funding 2021:

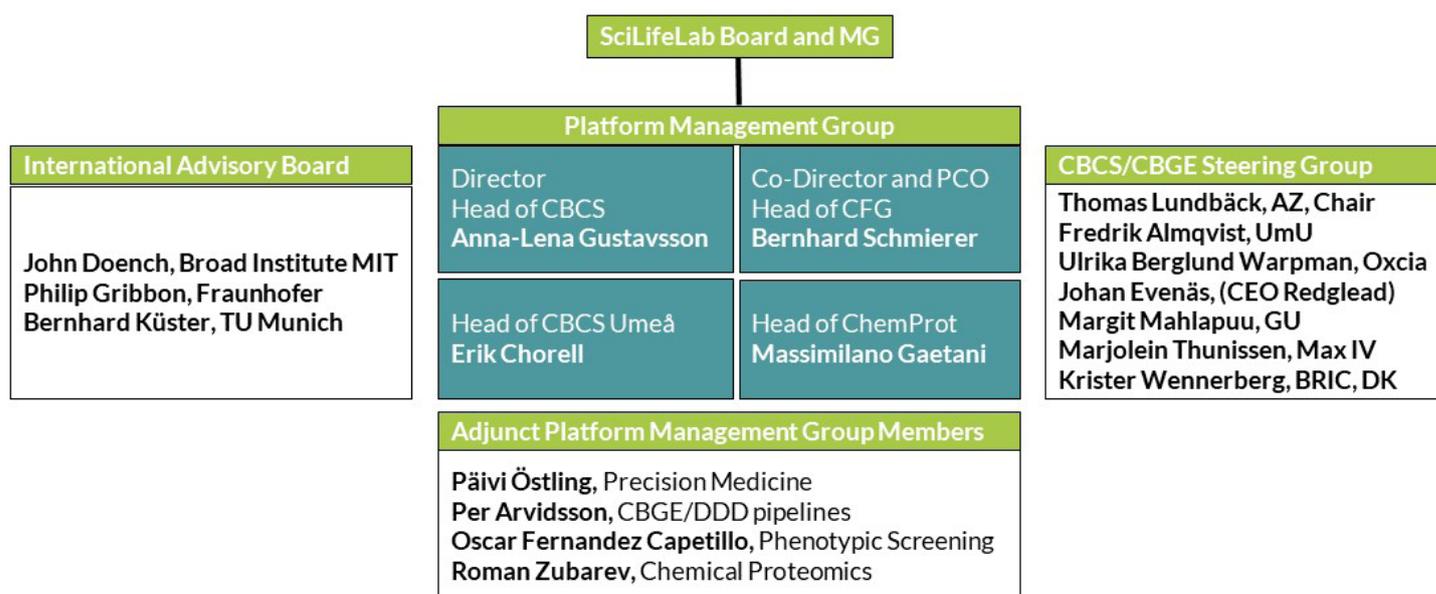


Platform Specific Terms and Conditions for Funding - Chemical Biology and Genome Engineering

This document concerns the terms and conditions for SciLifeLab funding of the Chemical Biology and Genome Engineering Platform and Units from 2021 and onwards outlines the strategic direction MG wants the platform to take. The mid-term checkup in the middle of the 4-year funding period will focus on how well the Platform and Units have taken into account the items in this document.

- SciLifeLab funding to the Chemical Biology and Genome Engineering Platform and Units is meant for providing nationally unique technologies and services within chemical biology, chemical proteomics and CRISPR-based functional genomics
- Ensure that SciLifeLab funds are used in the platform in a manner that aligns with the priorities and goals of the entire SciLifeLab organization
- Together with the SciLifeLab management suggest a clear platform governance and steering structure according to the suggested general policy for governance and steering of SciLifeLab infrastructure.
- Create a plan for the development and integrated services for the new platform in the next four-year period, involving the research community, considering renewal at the international cutting edge with e.g. information management. For example, information management at all levels is essential in order to reach to the level of data-driven SciLifeLab operation.
- Consider how CBGE can join the set-up of cross-platform capabilities, such as Pandemic Laboratory Preparedness, Precision Medicine, Planetary Biology, and Integrated Structural Biology.
- The platform, and in particular CBCS, should further strengthen links with the DDD platform and improve the ability to feed projects for the DDD. Work on things that are not part of the DDD; but also acquire capabilities from DDD for chemical biology work.
- CBCS should continue to provide multidisciplinary approaches for chemical biology studies of biological processes as well as for target identification and mechanism of action determination of drugs. The services should make use of the HTGE and Chemical Proteomics Units in a coordinated fashion.
- When CBCS is applying to VR infra funding, please consider how to best distinguish the SciLifeLab and VR funded components. Platforms can be jointly funded, but SciLifeLab funds should not be used to simply co-fund VR infrastructure activities (or vice versa). There will need to be a good and logical role for both funds that can support each other, but not directly overlap.
- In collaboration with the Bioinformatics platform and Data Centre, continue to develop chemoinformatics and data-driven capabilities, such as open science and FAIR data bases
- Consider interactions with external sites and strategic partnerships, such as with SGC Stockholm node, EU-ESFRI programs, etc

Organization and Management



Organization

The CBGE platform is governed by the platform management group (PMG), who are supported by adjunct PMG members. The Platform Steering Group (PSG) appointed by SciLifeLab is identical to the VR-appointed steering group for CBCS, and thus has two roles with two distinct mandates. As a Platform Steering Group, the role is to advise on policy issues and on long-term strategies, with the aim to keep platform

services relevant for Swedish industry and academia. The members also act as platform ambassadors to help improve national recognition and spread. The PSG is complemented by a second body, the International Advisory Board, which consists of world-class experts in CBGE's technologies. The platform IAB brings in an even broader, and, importantly, international, perspective.

CBGE Management

PMG meetings. The PMG meets every second week for 1.5 hours to discuss platform-relevant topics and make strategic decisions. Adjunct members, representatives from other platforms or from the research community are invited to these PMG meeting as needed. Meeting minutes are kept and stored on Nextcloud, as are all other

platform-relevant documents. The PSG meets 2-3 times per semester, and the first meeting took place at the end of August 2022. The platform IAB will be called upon annually, with the first in-person meeting scheduled for May/June 2023.

Interactions with other platforms.

CBGE/DDD interactions. Anna-Lena Gustavsson and Bernhard Schmierer have monthly meetings with Per Arvidsson and Kristian Sandberg from DDD to discuss interaction and novel developments of interest to both platforms. A DDD/CBGE webinar was held in August 2022. During the SciLifeLab Outreach Day in January 2022, CBGE and DDD hosted a joint session, where previous platform users presented their experience. Projects that are not

mature enough for DDD are referred to CBGE, and options are discussed. **CBGE/NBIS interactions.** CBGE has been assigned a dedicated contact person at NBIS (Sebastian Kapell). **Others.** Most interactions with other platforms occur at the unit level, including cross-platform TDPs. These interactions are described in the unit reports of CBCS, CFG and Chemical Proteomics.

Development, Achievements and Plans

Development of the platform 2021-2022

Mission. The three units of the platform have a diverse service portfolio spread across several fields. This multi-

disciplinary setting provides unique opportunities for customers in target discovery and mechanism-of-action (MoA) elucidation downstream of chemical screens. CBGE offers chemical, genetic, and proteomic methods to home in on targets of small compounds. The platform aims at bridging the gap between phenotypic observation and mechanistic insight, which is a prerequisite for further development of a compound by DDD.

Establishing integrated service pipelines. All units are experts in their respective technologies; however, the platform is still learning how to precisely combine the orthogonal approaches in the most effective manner. Platform strategic funding is key for this endeavour. The 2021/2022 strategic funding was thus predominantly used to attract suitable platform pilot projects (PPPs), which were then given increased subsidy. An open call attracted 15 applications, four of which were chosen by the platform management group for additional subsidy and are currently executed or scheduled to be executed (Daniel Öhlund, UmU; Margareta Wilhelm, Sean Rudd and Arne Östman, KI). Within these PPPs, we are establishing workflows for integrated platform services in MoA studies, and are harmonizing and streamlining our support. Moreover, additional projects from the call are run by the units as standard service projects without additional subsidy.

Data and computation. Artificial Intelligence (AI) in drug discovery and chemical biology is an important area and integration of activities at DDD, CBGE, NBIS and SciLifeLab Data Center is currently ongoing within a TDP, also involving Jens Carlsson (UU) and other relevant research groups. Making data available in a FAIR format is a priority, and CBGE is currently exploring the best options for different types of data (ChemDepot, SciLifeLab Data Repository, CoVid Portal, CRISPR screen databases such as BioGRID ORCS, PRIDE database, etc.)

Contribution to SciLifeLab Capabilities. CBGE contributes actively to Precision Medicine (Päivi Östling, Janne Lehtiö

Development plans for 2023-2024

Integrated platform services and tech development at the unit level. The establishment of integrated platform pipelines and full use of platform synergies in target discovery and MoA elucidation remains a major priority during 2023-2024, both at the experimental and computational level. In parallel, these efforts are accompanied by and coordinated with continuous renewal at the cutting edge at the unit level. This second focus on the individual units' tech development is important, as many projects do not benefit from integrated platform pipelines but require state-of-the-art competence in a specific area. Both the Platform Strategic Funding, as well as TDP funding and Expensive Instrument funding are crucial for the CBGE platform and its units and should be continued in the future. All units are active in one or several

and others) with genetic and chemical screens in patient-derived cells, iPSCs and ESCs), to Pandemic Laboratory Preparedness (Marjo Puumalainen: BSL3 compound screens), and to Planetary Biology (Björn Hellman, UU: environmental toxicology on fish reporter cell lines; Magnus Engwall, Örebro: cell painting for toxic compound profiling; Adrian Dauphinee, SLU-UU: screening for compounds modulating plant autophagy and chemical proteomics on selected compounds; Anna Linusson, UmU: HTS of metacaspases (MC) from Arabidopsis and Trypano-soma; Per-Olof Syrén, KTH: HDX-MS on catalysis of polymers in an aqueous environment.)

National and international interactions. Internationally, CBGE is one of the main players in the Horizon Europe-funded drug repurposing consortium "Building a sustainable European innovation platform for the repurposing of medicinal products, REMEDI4ALL". CBGE will contribute to WP6 - "Preclinical development and validation for drug repurposing", which provides a fantastic opportunity to further develop workflows for MoA elucidation within drug repurposing projects. Through CBCS, the platform represents Sweden in the European Research Infrastructure Consortium EU-OPENSREEN, and is part of EUbOPEN, an Innovative Medicines Initiative (IMI)-funded project. Nationally, all units of CBGE play an active role in PhenoTarget, a Swedish network in phenotypic drug discovery.

Industry connections. CBGE has strong connections with industry, most prominently collaborative interactions with AstraZeneca (access to compound libraries, exchanges in CRISPR screening experience, organization of scientific meetings). Other collaborations are in place with Countagen AB and Moligo AB, two Swedish start-ups. Fee-for-service projects exist with Pelago Biosciences AB, Alzecure Pharma AB, Oncorena AB, Beactica Therapeutics AB, Glyxogen Therapeutics (Israel), Byondis (the Netherlands), Elikya Therapeutics (France), OM Pharma (Switzerland) and MOMA Therapeutics, US.

of six TDPs awarded to CBGE in the recent years, and these efforts will be continued in the future.

Outreach activities. Outreach was severely limited by the pandemic. CBGE is committed to step up outreach activities in the future. The platform will tour universities in Sweden, to advertise and explain our services. The newly established nodes at GU, LU, UU and LiU will be important to advertise these events, which will include showcases, such as the currently active Platform Pilot Projects. In 2023, the platform will organize and host a European Chemical Biology Symposium 2023 and a CRISPR Symposium. CBGE's involvement in national (PhenoTarget, BioMS) and international consortia (EU-OPENSREEN, EUbOpen, REMEDI4ALL) provides a forum for outreach and

collaboration within Sweden and Europe.

Increased interaction with companies. CBGE has many contacts with the private sector and will continue to establish collaborations. One quickly developing area at AstraZeneca is gene-editing and genetic screening, and the platform will establish closer ties with AZ also in this space. A recurring issue is the lack of clear procedures for running company projects at full cost. CBGE will actively work with SciLifeLab's OO and the host universities to find solutions to this important issue.

Contribution to Scilifelab capabilities. Modification of our existing technologies to facilitate application within the major capability areas precision medicine, pandemic laboratory preparedness and planetary biology is already ongoing, and a platform priority for the next two years. This includes miniaturizing chemical, genetic and proteomic experiments to limited numbers of patient derived cells,

adapting these procedures to iPSCs, spheroids and organoids, and to enable screens in a BSL3 environment.

Promotion of data driven science. CBGE not only generates big data (next generation sequencing data, MS-based proteomics data, imaging data, multivariate data from phenotypic screens), but our methods are instrumental in data-driven hypothesis generation and validation of initial results. Each platform unit will actively support users in making their data publicly Findable and Accessible, while striving to deliver standardized data in an Inter-operable and Reusable format (FAIR criteria). In a diverse platform like CBGE, a major challenge is understanding each other's datasets and finding ways for integrative data-mining and data interpretation. The pilot projects we are currently running will highlight both problems and inform solutions to these challenges.

Request for additional funding 2023–2024

Additional funding requests.

CFG. CBGE's integrated platform pipelines crucially depend on precision gene editing expertise for the KO of suspected drug targets for target validation, and the creation of reporters expressed from native genomic loci for small compound phenotypic screens. From 2019 – 2021, CFG had secured KI core facility funding for precision gene editing, however, despite a large user demand and a healthy economy, this funding is currently phased out. Without an additional contribution from SciLifeLab, CFG's precision gene editing expertise cannot be sustained, which would jeopardize the platform mission. Of equal importance, SciLifeLab's Precision Medicine capability requires precision gene editing competence, for instance to establish isogenic cell line pairs by correcting/recreating pathogenic mutations or SNV's, to give just one example. Please note that any investment will not change the direction of CFG – the main focus remains on functional perturbations at scale – but will help sustain the established comprehensive service portfolio. CFG thus asks for a contribution of 500 KSEK in 2023 (300 KSEK phase-out still available from KI), and 800 KSEK in 2024 (no

more KI funding).

Chemical Proteomics. The unit is critical for the CBGE platform mission and is an integral part of all target ID and MoA studies. The unit is actively pursuing miniaturization, and adaptation of protocols to bacteria, primary cells, iPSC derived cells and organoids, aligning itself with SciLifeLab's focus areas. Compared to user demand and the challenges that come with increased throughput, intergated approaches and complexity of projects, Chemical Proteomics is understaffed. BioMS funding 2020–2024 covers nLC-MS instrumentation, but not staff. KI core facility funding was denied because the user base of Chemical Proteomics was considered too wide-spread and not local enough. A minor part (1.7 MSEK) of the funding currently comes from SciLifeLab. To provide services and meet the growing the national demand, the Chemical Proteomics unit would greatly benefit from a modest contribution from SciLifeLab of additional 500 KSEK in 2023 and 800 KSEK in 2024.

CBCS. No additional funding requested.

Requests for expanded funding 2023–2024

Unit	SciLifeLab funding 2022 (kSEK)	Requested ScilifeLab funding 2023 (kSEK)	Requested SciLifeLab funding 2024 (kSEK)
CBCS	6,000	6,000	6,000
CFG	3,200	3,700	4,000
Chemical Proteomics	1,700	2,200	2,500
CBGE TOTAL	10,900	11,900 (+ 9%)	12,500 (+5%)

Chemical Biology Consortium Sweden

Chemical Biology and Genome Engineering Platform (Web links for Unit: [Webpage](#), [Publications](#))

Basic Information

Head(s) of Unit: Anna-Lena Gustavsson, Erik Chorell (acting)
PSD(s): Erik Chorell
SciLifeLab Unit since: 2013
Host university: KI
FTEs: 11.3
FTEs financed by SciLifeLab: 6.0

Funding in 2021 (kSEK)

SciLifeLab: 6000
SciLifeLab Instrument: 1380
KI: 3000
UmU: 1850
KAW: 2000
Vinnova: 335
Total: 14565

Resource Allocation 2021

Academia (national): 80%
Academia (international): 5%
Internal tech. dev.: 10%
Industry: 5%
Healthcare: -
Other gov. agencies: -

User Fees 2021

Total (kSEK): 3400
Reagents: 23%
Instrument: 10%
Salaries: 55%
Rent: 12%
Other: -

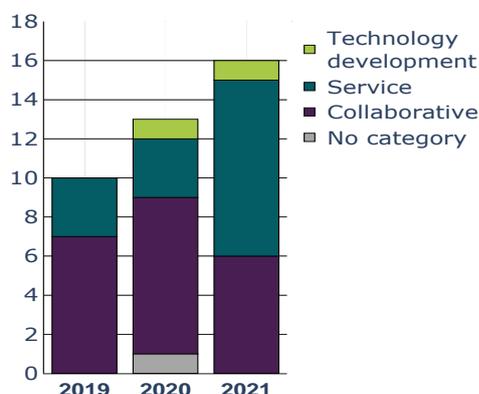
User Fees by Sector 2021

Academia (national): 80%
Academia (international): 10%
Industry: 10%
Healthcare: -
Other gov. agencies: -

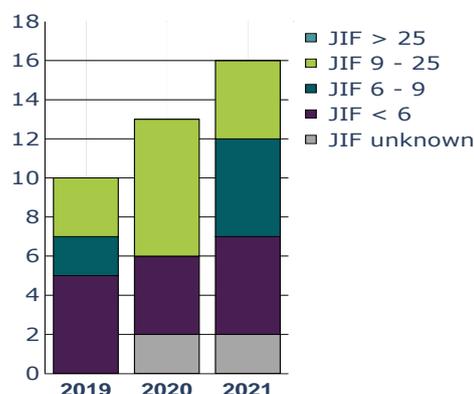
Services

- Assay development
- Biochemical, cell-based and phenotypic high-throughput screening of small-molecule screening libraries
- Computational chemistry and modelling
- High-throughput imaging technology
- Hit optimization and medicinal chemistry

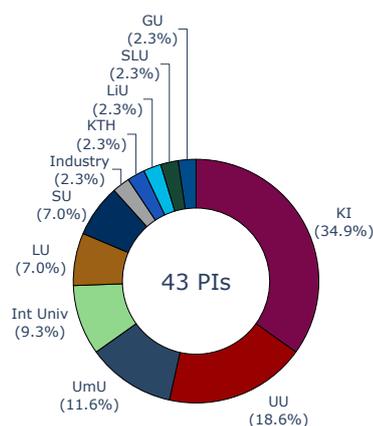
Publication by Category



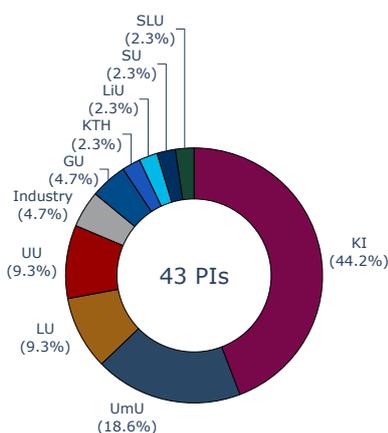
Publication by Journal Impact Factor



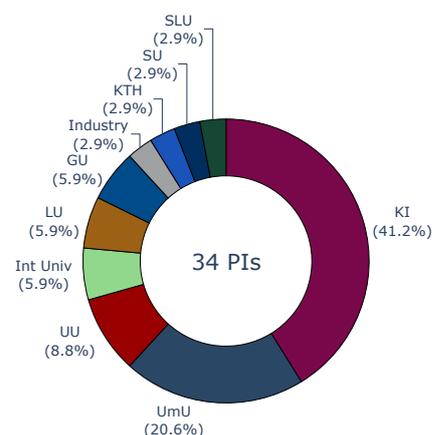
Users 2019



Users 2020



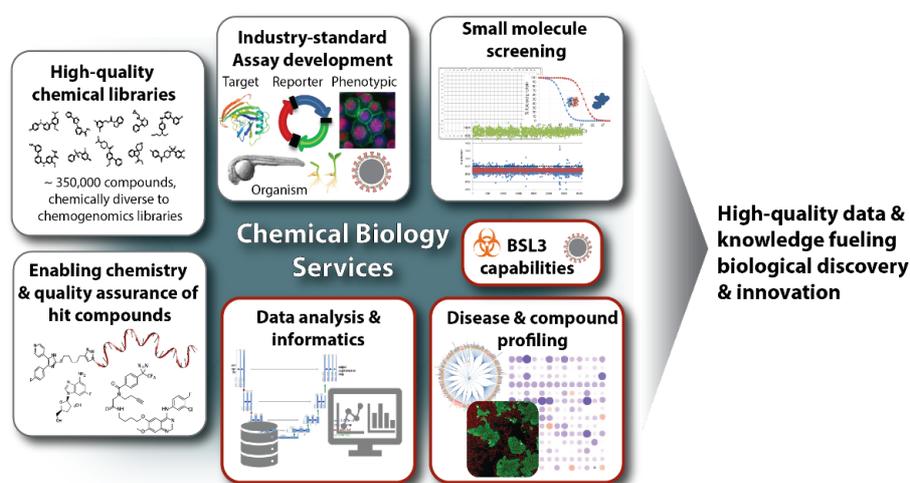
Users 2021



Unit:	CBCS
Platform:	Chemical Biology and Genome Engineering

I. Technological and scientific advances 2021–2022

Unit improvements: A successful application to SRC to the call “Research Infrastructures of national importance” in 2021 was compiled and approved. Since January 2022 CBCS is now a distributed national infrastructure with 4 new nodes at UU, LiU, GU and LU besides the main nodes at KI and UmU. During 2022 CBCS focus is to establish the new consortium and implement new services. The funding has strengthened the existing activities at the KI and UmU by creating a critical mass, as well as establishing new services highlighted in red in the figure below.



CBCS is now offering assay development and screening in BSL3 labs and is equipping these labs for HT capacity in alignment with the capability in Pandemic Preparedness. CBCS-UU is establishing services in Cell Painting, screening for compound-induced morphology changes. Alongside, CBCS-KI is establishing services for functional precision medicine to support projects monitoring patient-specific drug responses and conduct resistance profiling.

Data handling improvements: A new application for handling compound registration & logistics, connecting screening data to compounds has been developed and the plan is to implement this application across nodes.

Instruments: At both CBCS-KI and UmU new instrumentation supporting high throughput screening have been installed (fully automated screening hub (incl a FLPR quadra and the Intellicyte iQue3).

International collaborations: Sweden has now become a member of the ERIC EU-OPENSCREEN and CBCS-KI is the national node. Both CBCS-KI and UmU have applied to become partner sites.

Project support: *Large projects:* we have supported 18 projects in assay development & screening, incl hit follow up. In addition, we have supported 7 projects with synthetic chemistry. *OPEN ACCESS to our labs:* 12 research groups have used our screening labs as open access and we have housed 2 post docs from different research groups in our Medchem lab. CBCS is also supporting three projects from the call “platform pilot project” see Platform report. *Compound Center* has supported 77 different PIs with compounds and/or screening set deliveries during 2021–2022 and 24 different DDDp projects incl ENABLE2 have been supported. CBCS has invested in new targeted drug libraries. The SPECS collection for drug repurposing has been used in 17 different screens.

Several Technical Development Projects are ongoing for example: Profiling of the primary screening collection for protein degraders – “molecular glues”. Collaboration with Cristina Mayor-Ruiz IB, Spain and Improved understanding of drug mechanism-of-action by establishing a nation-wide service of morphological profiling - SLL-TDP.

Scientific achievements. CBCS has supported 21 publications during 2021–2022. First screen in 1536-format conducted. Different assays implemented to address unwanted mechanisms.

Outreach activities: CBCS has been presented at several occasions during 2022 either with a poster or talks. Together with DDDp a webinar was organized presenting our calls for project support with over 50 attendees. **Teaching:** 40 students have taken the CBCS online course "introduction to high throughput screening" 2 ECTS. Seven master students have been supervised for projects for longer period (4-6 months). CBCS and all units of CBGE platform will all contribute to the course 5541 at Karolinska Institute entitled, "Overview of Cancer Drug Discovery".

II the development plans for the unit 2023–2024 and beyond

Unit level with new nodes

During the coming years the new nodes at CBCS will be developed to enable equal and distributed access to the platform. We will work internally to harmonize protocols, standards and data-sharing practices between the nodes and develop fit-for-purpose service packages. A cross-node CBCS workshop is planned to give the basis for strategic and operational plan during the Autumn and the steering committee will provide feedback to strengthen the competitive edge.

Additionally, we plan to launch services aligning with the strategic aims of SciLifeLab and the Data Driven Life Science program. First, we are establishing routines for functional precision medicine and will align with the SciLifeLab capability in this area. Together with researcher surrounding CBCS (Evert Homan (Thomas Helleday's lab and IMI program EUBOPEN) and staff scientists at DDDp we are updating the primary screening set to better represent the full collection and secure qualitative hits. CBCS will also work to implement AI/ML in the workflows for ligand- and structure-based virtual screening to find hits and to explore analogs to validate hits. A technical development project with basis in previous performed screen at CBCS will be set up to develop the methodology and expertise on the newly installed high throughput flow cytometer instrument (Intellicyte IQue3).

Planned funding applications

CBCS is part of several funding applications in new areas spanning across platforms and infrastructures:

Application to SRC Access to infrastructures:

- FragMAX/MAXIV, supported by CBCS, DDDp and Swedish NMR Centra; the goal is to strengthen the pipeline for future fragment-based screening projects.
- Establishing a Swedish Center for Proximity Inducing Agents & Targeted Protein Degradation - with DDDp, to build on the previous TDP on protein degraders.
- National infrastructure to support molecularly-guided clinical trials with novel diagnostics development (Precision Medicine Capability) where CBCS will support with *ex vivo* functional testing and drug profiling services.

Outreach activities:

With the establishment of the new nodes CBCS is planning local outreach activities. CBCS also plans to repeat the successful outreach webinars together with DDDp.

CBCS is proud to be co-organising the 7th European Chemical Biology Symposium in Gothenburg at AZ premises in May 2023 together with EU-OPENSREEN, EU-CHEM Life Science back-to-back with the ELRIG Therapeutic Oligo meeting (Oligonova/DDDp).

Together with the Helleday and Fernandez-Capetillo research groups, the Chemical Biology Seminar series is reinitiated after the pandemic with monthly seminars inviting speakers in the chemical biology area.

International connections.

The European connection through CBCS sites as partner site in the ERIC EU-OPENSREEN will not only connect CBCS in Europe but also CFG and ChemProt as services in these areas are being piloted as well. Additionally, CBCS will strengthen its pipelines and data analysis strategies for mechanism of action investigations through the REMEDI-4ALL project. Involvement in these collaborations expand the network of expertise for CBCS personnel.

Chemical Biology Consortium Sweden

Budget 2022

Costs	2022
Personnel cost	18 539 533
Other personnel costs	423 500
Depreciation	3 357 000
Service and license costs	719 950
Other operating costs	3 055 258
Premises costs	1 708 496
Other costs	0
Sum costs (kSEK):	27 803 737

Revenues	2022
Funding from SciLifeLab	8 280 000
Funding from financier X	3 100 000
Funding from financier Y	9 100 000
KAW (predicted)	2 500 000
Funding from financier Z	840 000
User fees	4 500 000
Sum revenues (kSEK):	28 320 000

Chemical Proteomics

Chemical Biology and Genome Engineering Platform (Web links for Unit: [Webpage](#), [Publications](#))

Basic Information

Head(s) of Unit: Massimiliano Gaetani
PSD(s): Roman Zubarev
SciLifeLab Unit since: 2017
Host university: KI
FTEs: 4.85
FTEs financed by SciLifeLab: 1.65

Funding in 2021 (kSEK)

SciLifeLab: 1700
SciLifeLab Instrument: 600
KI: 1905
VR: 2568
Total: 6773

Resource Allocation 2021

Academia (national): 50%
Academia (international): 17%
Internal tech. dev.: 16%
Industry: 17%
Healthcare: -
Other gov. agencies: -

User Fees 2021

Total (kSEK): 2030
Reagents: 11%
Instrument: 62%
Salaries: 20%
Rent: 7%
Other: -

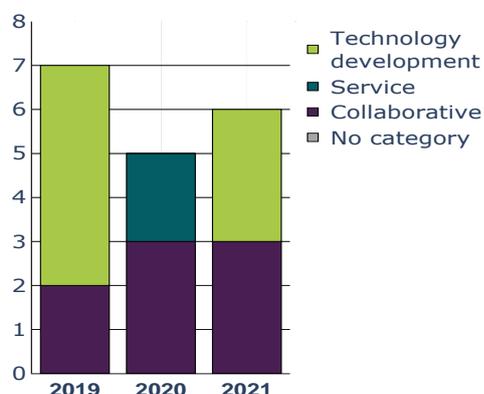
User Fees by Sector 2021

Academia (national): 35%
Academia (international): 10%
Industry: 55%
Healthcare: -
Other gov. agencies: -

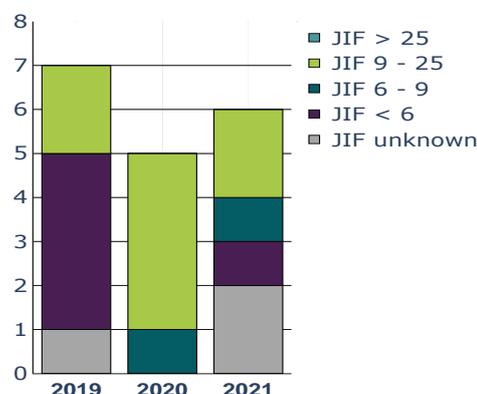
Services

- MS-based chemical proteomics for target discovery and MoA (deep, high throughput, also for low sample amount): Proteome solubility/thermal stability profiling, Expression/degradation proteomics, Interactomics, RedOx proteomics
- H/D exchange MS to map protein binding sites and conformational changes

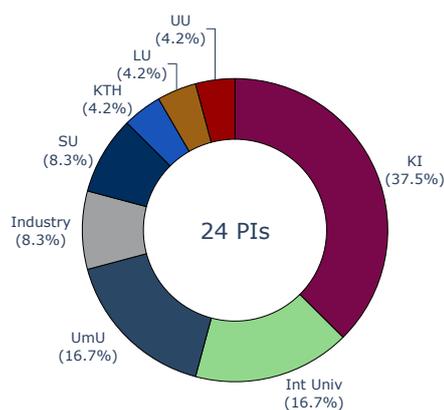
Publication by Category



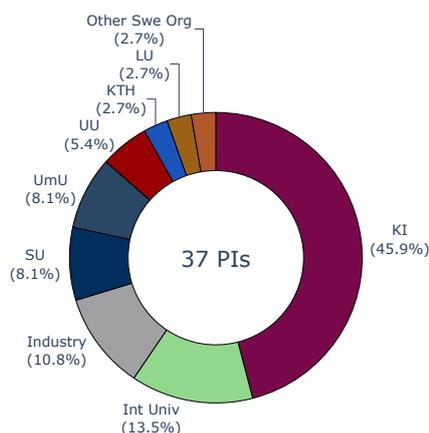
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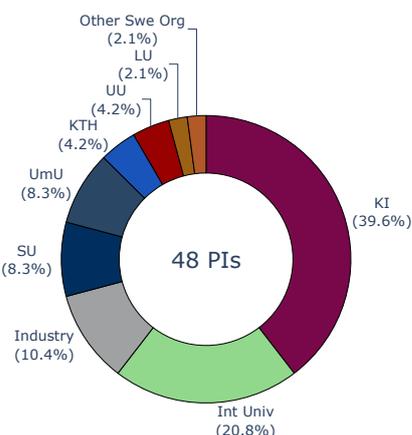
Users 2019



Users 2020



Users 2021





Unit:	Chemical Proteomics
Platform:	Chemical Biology and Genome Engineering

Development, Achievements and Plans

i) Developments and major achievements.

Our **recent method developments** are based on our invented and published method, the Proteome Integral Solubility Alteration (PISA) assay (Gaetani et al. JPR 2019) which can identify drug targets with deep and unbiased MS-based proteomics. **In 2021 and 2022 we have further optimized PISA for its proteome depth and multiplexing capacity**, using the latest technology of TMTpro 18-plex, combined to extensive high pH reversed-phase peptide fractionation prior nLC-MS. We have then developed PISA assays with up to five drugs/compounds, or different conditions (e.g. cell types, concentrations, inclusion of “mock” molecules for nonfunctional off-targets, *etc.*), with ≥ 3 biological replicates, 8000-11000 proteins identified, and highly confident identification of targets. All these aspects are highly needed for drug development and were impossible before PISA.

We also **optimized PISA reducing sample amount**, providing unprecedented target deconvolution in all types of cells, *e.g.* any cell line, primary cells, iPSC-derived cell cultures, organoids. Of relevance, we can expand our aims **towards precision medicine** and after also implementing our equipment in our cell laboratories, we successfully performed projects on human primary astrocytes and iPSCs derived astrocytes (PI: A. Herland, KTH and KI) and on human liver organoids (PI M. Ingelman-Sundberg, KI). The last was recently published (Pridgeon CS *et al.* Cells 2022).

The relevance and popularity of PISA assay- based approaches for drug target deconvolution and mechanism of action elucidation has been growing at an international level and we have been cooperating with several laboratories for its diffusion, optimization, and training, including well-established proteomics labs, such as the one of the prof. S. Gygi at Harvard University. Two version of PISA based on solvent (“Solvent-PISA”, JG Van Vranken *et al.* Elife 2021) and ions instead of temperature (CM Beusch *et al.* Anal Chem 2022) confirmed that our PISA assay is correctly focused on solubility rather than thermodynamic interpretation of protein melting, unlike previous methods. The integration of these methods by a close interaction with these laboratories is also possible for us, however now our own methods still stand as optimal. PISA assay was also modified for studying drugs in bacteria. PISA assays in plant samples are being also optimized.

One relevant development is the **integration of more orthogonal approaches in one PISA assay**. One bidimensional approach is the PISA assay integrated in one batch with expression (or global) proteomics (“PISA-Express”) after 48h exposure to the drug at its IC_{50} . In the case of anticancer drugs, the last allows to integrate previously developed tools / databases for analysis of anticancer proteome responses (“ProtTargetMiner” proteome database, A.A.Saei *et al.* Nat Commun 2019).

PISA-Express can be used also for protein solubility changes at longer time exposure, normalizing solubility changes on protein total amount change. This feature is unique and relevant for already developing drugs by pharmaceutical companies, possibly used as key to follow the target engagement by drugs in cells over time. Furthermore, we can use PISA-express for 2D proteome profiling, *e.g.* to study different cellular differentiative states (Sabatier *at al.* Nat. Commun 2021).

As service to a group in Harvard Medical School (Boston, US), we identified the target of an antibacterial drug repurposed as anticancer and such target was successfully validated (Heppler LN *et al.* J Biol Chem. 2022), showing correctness and potential of PISA also for **drug repurposing**.

The **scientific production** between our method development articles and service projects from November 2021 is of five publications, with four of them published in 2022. Four additional manuscripts are currently submitted or under revision.

A confirmation of the progressive growth of the international consideration of our services is the **increase of requests from academic groups and industry**, asking support also in experimental design and for bigger projects by means of number of molecules and conditions to be studied.

In 2022, we can count additional groups from both university and industry sectors, from KI and other universities in Sweden, as well as abroad within and outside Europe. They included: 4 more groups from KI, 3 more international industries, 5 more international universities, 3 from other Swedish universities (KTH, SLU, UmU).

We have participated in 2022 to **several outreach events** with poster and / or oral presentation including: Erlig Conference (Mölnådal at AstraZeneca conference center, 10th–12th May); PhenoTarget 2022 Conference (Sigtunahöjden, 8th–10th June); 2022 KI StratNeuro retreat, (Runö, 19–20 May); GLK Day (Stockholm, Wenner-Gren Institute, SU, 7th June); KI Science Park DAY 2022, SciLifeLab Open House (Solna, 25th Aug). In addition ChemProt was also **co-organizer and/or invited for lecture** at two events involving with top-level international scientists on MS: the [Janeiro-na-Madeira Winter Summer School 2022](#) (January 16–21, 2022) and the [4th European Fourier Transform Mass Spectrometry Workshop](#) (Lisbon, 1–14 July). ChemProt is also involved in **training activities**, *e.g.*, in the contribution to the Cancer Drug Discovery PhD course at KI, in the co-supervision of a PhD student at the University of Pisa, and in co-supervising three PhD students of the group of R. Zubarev at the Chemistry I Division, MBB, KI.

The **cross-unit activities within CBGE** have been increasing in 2022 including a project also involving CBCS (PI: M. Ankarcróna, KI), with our participation to all four finally selected Platform Pilot Projects (PIs: D. Ohlund, UmU; M. Wilhelm, KI; A. Östman, KI; S. Rudd, KI).

Activities across platforms include: the ones as part of the PhenoTarget research community program; the ones coordinated within BioMS with other SciLifeLab Units also at BioMS; coordination efforts with NBIS with a NBIS bioinformatician (S. Kapell). However, for the continuous developments, Chemical Proteomics needs a first internal analysis of data, that is project design dependent, before to possibly create a connection with NBIS.

The unit experienced **some personnel turn-over**: two persons leaving - which could also speak for the professional level of our staff- as one associated scientist (J. Astorga-Wells) was hired by Pelago Biosciences AB and a staff scientist (P. Fang) became a professor in China. Consequently, a senior postdoc scientist, expert in proteomics and HDX-MS, was hired full time.

ii) Development plans for the unit 2023–2024.

New services on newly developed methods will include: a) RedOx proteomics, *i.e.* proteome-wide analysis of the reduction-oxidation state of cysteine residues in cellular proteins, that will be the third dimension integrated with expression proteomics all-in-one in the PISA assay (“PISA REX”, manuscript in preparation); Residence Time Proteome Integral Solubility Alteration (ResT-PISA) assay which provides monitoring temporal protein solubility profiles after drug removal (“off-curve”) in cell lysate or intact cells, quantifying the lifetime of drug-target occupancy (manuscript submitted). The last will provide complementary, new type of information on drug-target interaction, with further innovation and relevance in drug development.

Due to our active method development, to the increased request of our services in number and volume, to the higher level of analysis needed by the integration of orthogonal methods, to fact that larger projects with many compounds are now possible with PISA, Chemical Proteomics **will need to hire** an additional proteomics expert with competences also in data analysis and visualization.

iii) Increased base-funding from SciLifeLab

Increased base-funding will be very important, as our unit does not receive KI core facility funding and receives from SciLifeLab a minor portion of its funding (1.7M). The need is to increase the budget to 2.2M in 2023 and to 2.5M from 2024.

Chemical Proteomics

Budget 2022

Costs	2022
Personnel cost	4 112 710
Other personnel costs	90 750
Depreciation	4 338 352
Service and license costs	484 000
Other operating costs	1 125 300
Premises costs	432 000
Other costs	48 400
Sum costs (kSEK):	10 631 513

Revenues	2022
Funding from SciLifeLab	1 700 000
VR (for BioMS)	2 568 000
KI (for BioMS)	1 905 000
User fees	2 600 000
Approved SciLifeLab Expensive Instrument application 2019	600 000
Approved SciLifeLab Expensive Instrument application 2022	300 000
Incoming Balance	855 000
Sum revenues (kSEK):	10 528 000

CRISPR Functional Genomics

Chemical Biology and Genome Engineering Platform (Web links for Unit: [Webpage](#), [Publications](#))

Basic Information

Head(s) of Unit: Bernhard Schmierer
SciLifeLab Unit since: 2017
Host university: KI
FTEs: 5.0
FTEs financed by SciLifeLab: 3.4

Funding in 2021 (kSEK)

SciLifeLab: 3400
SciLifeLab Instrument: 400
KI: 2246
Other: 1450
Total: 7496

Resource Allocation 2021

Academia (national): 60%
Academia (international): 30%
Internal tech. dev.: 10%
Industry: -
Healthcare: -
Other gov. agencies: -

User Fees 2021

Total (kSEK): 2644
Reagents: 20%
Instrument: 10%
Salaries: 60%
Rent: 10%
Other: -

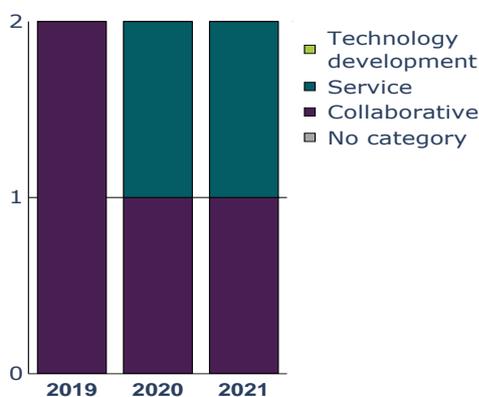
User Fees by Sector 2021

Academia (national): 66%
Academia (international): 34%
Industry: -
Healthcare: -
Other gov. agencies: -

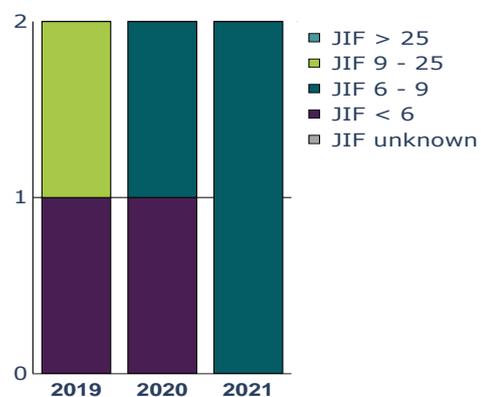
Services

- Cas9-expressing cell lines
- Genome-wide, pooled CRISPR screens
- Screens for protein coding genes, ncRNAs and non-coding elements
- CRISPR-KO, CRISPR-inhibition, CRISPR-activation
- Screen design and guide design for all types of screens
- Creation of customized guide libraries
- Small pooled CRISPR screens with single cell readout

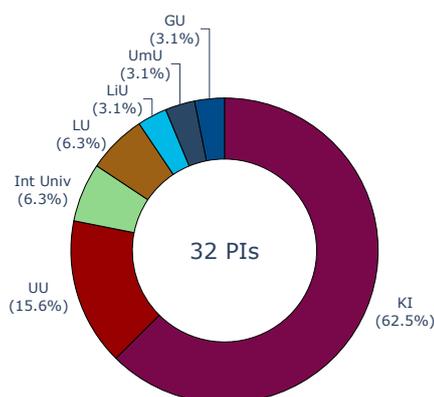
Publication by Category



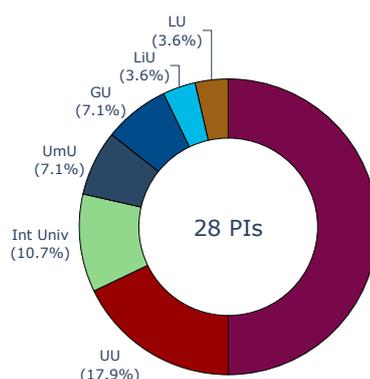
Publication by Journal Impact Factor



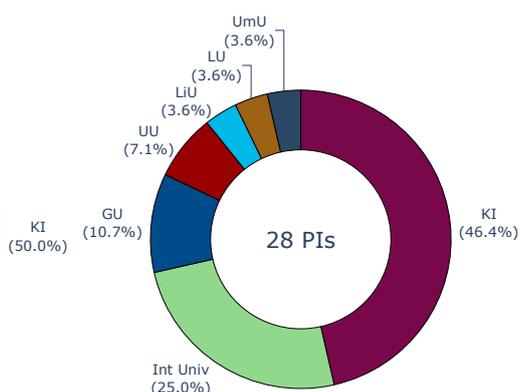
Users 2019



Users 2020



Users 2021



Unit:	CRISPR Functional Genomics
Platform:	Chemical Biology and Genome Engineering

Technological and scientific advances 2021–2022

- **Screening lncRNAs:** Transcriptional repression (CRISPR-I) and activation (CRISPR-A) screens for ~20,000 long non-coding RNAs in prostate, breast, and blood cancer (*Karina Dalsgaard Sørensen, Aarhus; Andreas Lennartsson and Sören Lehmann, KI and UU*).
- **Screening non-coding elements:** LOF screens for non-coding genetic elements (enhancers and CTCF binding sites) in pancreatic cancer cell lines (*Martin Enge, KI*) LOF screen on 120,000 open chromatin regions (*Anthony Mathelier, Oslo*)
- **RNA targeting:** Use Cas13d to identify targetable loci in the SARS-Cov2 genome (*Claudia Kutter, KI*) and lncRNAs involved in TGF- β signalling (*Peter ten Dijke, Leiden*).
- **Multiplexed screens for synthetic interactions:** We are currently performing a synthetic lethality screen using a Cas12a-based dual guide approach (*Stig Linder, LiU*)
- **Prime-editing as a screening tool:** We have implemented prime-editing for introducing precise changes in the genome and are developing this into a pooled screening method.
- **In situ CRISPR-guide sequencing:** Implementation of a method that combines pooled screens with microscopic phenotyping of large numbers of single cells (*TDP 2022–2023, with Mats Nilsson*)
- **Sequence diversification screens:** Base-editing sequence diversification screens for studying drug-target or protein-protein interactions (*TDP 2020-2021*).
- **Organoid screens:** Genome-wide screen in pancreatic organoids (*Daniel Öhlund, UmU*).

Outreach activities 2021-2022.

- PhenoTarget Conference, Sigtuna, June 2022. **Talk and Poster.**
- ELRIG Advances in Drug Discovery, AZ Gothenburg, May 2022. **Poster**
- KI SFO StratCan Retreat, Djurönäset, May 2022. **Poster**
- KI SFO StratNeuro Retreat, Åkersberga, May 2022. **Poster**
- Swedish Tumor Microenvironment Programme Webinar, March 2022, UU. **Talk**
- SciLifeLab Outreach Day, January 2022. **Talk**
- KI SFO StratRegen Retreat, Yasuragi, Oct 2022. **Poster**
- Wellcome Sanger Institute, Cambridge, UK: CRISPR conference, Sept 2022. **Poster**
- ELRIG, CRISPR in Drug Discovery, Online, March 2021. **Poster**

Grant applications as main or as co-applicant

- **SciLifeLab TDP 2022-2023.** Pooled CRISPR screens by in situ sgRNA readout. Mats Nilsson, ISS facility, Ola Spjuth, Oscar Fernandez Capetillo. **Granted, 800 KSEK.**
- **KAW 2022.** Gene knock-up at the post-transcriptional level to model and treat neurodegenerative disease. JO Andressoo and B Schmierer, KI. Prioritized by KI and submitted to KAW. **TBD.**
- **uShare SLU/UU grant.** In vitro fish bioassays via reporter gene knock-ins for environmental toxicity testing. B. Hellman, UU; S. Lungu-Mitea, SLU. **Granted, 400 KSEK for CFG.**
- **ERC advanced grant. WP2.** Drop out screens in immunocompetent mice to identify proteins necessary for MYC-driven tumorigenesis. Lars-Gunnar Larsson, KI. **TBD.**
- **Norwegian Cancer Society.** Fibroblast regulation of metastasis. A. Östman, KI. **TBD.**
- **KI Forskarstöd.** Postdoc med klinisk translationell inriktning i samarbete med SciLifeLab. Genome-wide CRISPR screen for effector functions of NK cells. Evren Alici, KI. **TBD**
- **Blood Cancer UK.** “Karonudib: A novel treatment for myeloma”, Alanna Green, Thomas Helleday, Sheffield, UK. **TBD.**

Industry interactions.

- **Countagen AB.** Bernhard Schmierer is Scientific Advisor to this start-up developing assays for detection of gene-edits. CFG will be a test bed for Countagen's assay.
- **Moligo AB.** Collaboration to test single-stranded DNA fragments synthesized by Moligo for suitability as recombination templates for precision gene editing.
- **AstraZeneca** (has recently approached CFG to explore potential interactions in gene editing (**Marcello Maresca**, AZ Gothenburg) and CRISPR screening (**Davide Gianni**, Functional Genomics, AZ Cambridge). CFG is ahead of AZ in several screening areas (non-coding elements, lncRNAs), and B Schmierer will visit the Cambridge site in Sep 2022 to further explore synergies between CFG's and AZ's CRISPR screening efforts.

Interactions within SciLifeLab and contribution to SciLifeLab capabilities.

- **Pandemic preparedness:** CFG was part of two SARS-Cov2 projects (Claudia Kutter and Oscar Fernández Capetillo)
- **Planetary Biology:** uShare SLU/UU grant: Fish cell lines for environmental toxicity testing. CFG will create fish reporter cell lines to reduce the number of animals used.
- **Precision Medicine:** CFG is involved in **REMEDI4ALL**. See CBGE platform report.
- **CBGE Platform Pilot Projects (PPP's).** For details, please see CBGE platform report.
- **TDP** "*Enabling high-content phenotyping in pooled CRISPR screens by in situ sgRNA readout*". Together with ISS unit, Mats Nilsson, SU, Jordi Carreras Puigvert, UU.
- **Pipeline with ESCG facility** for pooled CRISPR screens with scRNASeq readout.
- **CFG has tasked NBIS in a fee-for-service project** to create a data analysis- and presentation pipeline for our CRISPR screen results (Agata Smialowska, NBIS).

Teaching and international guest researchers at CFG 2021–2022

- **Guest researcher H el ene Pendeville, GIGA Institute, Li ege Universit e, Belgium.** Jan–Apr 2022. Sabbatical in preparation of setting up a gene-editing core in Li ege.
- **Guest PhD student Tom Harrijvan MD, Leiden University, The Netherlands.** Aug–Dec 2021.
- **Guest PhD student Simone Weiss, Aarhus University, DK.** Sept–Nov 2021.
- **Master project supervision, Rooma Mansoor,** Aug – Oct 2022
- **Teaching at the SciLifeLab Master programme** Lecture and project mentoring 2019–2022

Development plans for 2023–2024 and beyond

Strengthen cross-unit platform pipelines. A major goal of the CBGE platform is to build common platform pipelines for target identification and MoA studies. As is evident from current strategies in big pharma, the genetic perturbation component contributed by CFG is of great importance in this area. For details on platform pipelines, please see the platform, report. Adaptation of methodologies to smaller cell numbers and more relevant model systems such as organoids will be a focus area in the coming years.

Sustain precision gene editing services. A challenge for CFG is the loss of KI core facility funding for precision gene editing services from 2023 onwards. Funding was not extended with the argument that researchers could do their own editing. In our experience however, the community lacks expertise both in creating such edits, and in identifying, isolating, and validating correct clones. As an expert facility, we fill a major gap in Sweden in this area, which is highlighted by 10-15 active gene editing projects. Re-attracting KI funding is a major priority, and CFG will apply as one single unit with a complete service portfolio - CRISPR functional genomics, AND CRISPR precision gene editing.

Rolling out *in situ* CRISPR guide sequencing as a service. Together with Mats Nilsson's lab, we have succeeded in deconvoluting a pooled library of 48 guides directly on a microscope slide to assign a phenotype of single cells to the guide sequence. Andrew Bassett, Wellcome Sanger Institute, Cambridge, is interested in collaborating and in adopting our technology.

CRISPR symposium 2023. CFG has applied for SciLifeLab Event Support 2023. If granted, CFG will organize a two-day event in Biomedicum with high-profile international speakers. CFG's scientific advisor, John Doench, Broad Institute, one of the foremost experts in CRISPR functional genomics, has agreed to give the keynote lecture.

CRISPR Functional Genomics

Budget 2022

Costs	2022
Personnel cost	5 194 589
Other personnel costs	0
Depreciation	400 000
Service and license costs	72 600
Other operating costs	2 000 000
Premises costs	475 500
Other costs	121 000
Sum costs (kSEK):	8 263 689

Revenues	2022
Funding from SciLifeLab	3 400 000
Funding from financier X	800 000
Funding from financier Y	800 000
Funding from financier Z	725 000
User fees	2 500 000
Sum revenues (kSEK):	8 225 000

► Cellular and Molecular Imaging Platform

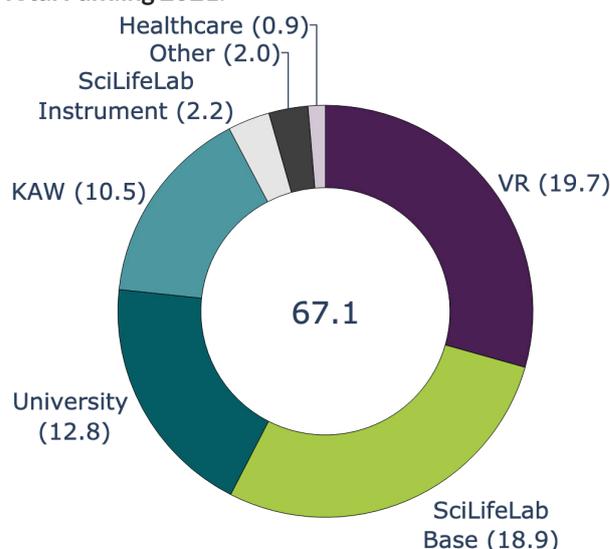
Platform Director: Marta Carroni, SU

Platform Coordination Officer: Rebecca Howard, SU (acting)

Platform and Units SciLifeLab Funding 2021:

Unit	(MSEK)
Cryo-EM	11.5
Integrated Microscopy Technologies GU	1.5
Integrated Microscopy Technologies KTH	3.5
Integrated Microscopy Technologies UU	1.5
PD, PCO, Platform Strategic Budget	0.9
Sum:	18.9

Total Funding 2021:

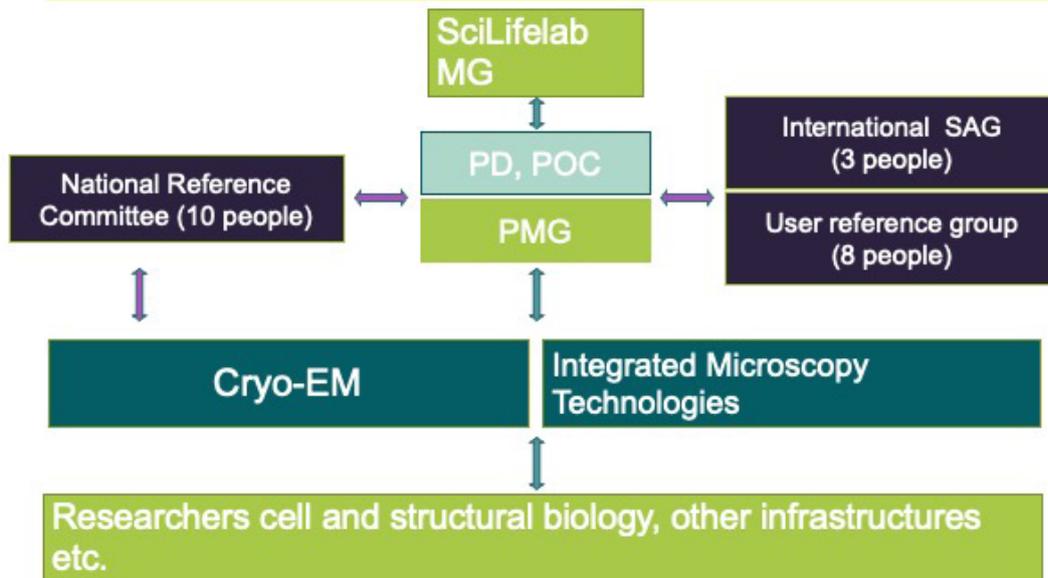


Platform Specific Terms and Conditions for Funding - Cellular and Molecular Imaging

This document concerns the terms and conditions for SciLifeLab funding of the Cellular and Molecular Imaging Platform and Units from 2021 and onwards and outlines the strategic direction MG wants the platform to take. The mid-term checkup in the middle of the 4-year funding period will focus on how well the Platform and Units have taken into account the items in this document.

- SciLifeLab funding to the Cellular and Molecular Imaging Platform and Units is meant for providing nationally unique technologies and services within advanced light and electron microscopy and cryo-EM services
- Ensure that SciLifeLab funds are used in the platform in a manner that aligns with the priorities and goals of the entire SciLifeLab organization
- Together with the SciLifeLab management suggest a clear platform governance and steering structure according to the suggested general policy for governance and steering of SciLifeLab infrastructure.
- Focus on integrating CAT and FIB-SEM technologies at GU and UmU units in the overall platform service offerings
- Launch a coordinated Cryo-EM National Grid Screening Network with personnel stationed at the universities in Lund (LU), Gothenburg (GU), Uppsala (UU), and Karolinska Institutet (KI)
- Expand services in cellular Cryo-tomography and FIB-SEM technologies to provide a bridge to structural biology and cell biology.
- Establish a network with local Imaging Core Facilities at universities across the country. Take a national responsibility to organise courses and workshops keeping Sweden nationally in the forefront of imaging technologies.
- Contribute to cross-platform capabilities, e.g. Integrated Structural Biology (particle Cryo-EM), Precision Medicine and Planetary Biology
- Enhance collaboration with the Bioinformatics platform and Data Centre to establish FAIR data sharing and links to the DDLS initiative

The organisation follows the capabilities



The CMI Platform is devoted to providing high-level technical support in the use of advanced light- and electron microscopy techniques both using photons and electrons as media for imaging. The CMI Platform strives to keep pace with the newest developments in the microscopy field as well as to develop new and robust pipelines for multidisciplinary projects.

The platform core is the Platform Management Group (PMG, Fig. 1-1), a group of 12 people representing all the CMI technologies and the SciLifeLab centers in Umeå, Gothenburg and Stockholm. The PMG meets every last Monday of the month for one and a half hour. The Platform Director (PD, Fig. 1-1) and the Platform Coordination Officer (PCO, Fig. 1-1) supervise the PMG activities and meet, report to and discuss regularly (around once a month) with the the SciLifeLab PCOs and to the SciLifeLab Management Group (MG, Fig. 1-4). On two occasions, members of the MG have been invited to attend the CMI PMG meetings (e.g. to discuss the International Advisory Board report and Key Performance Indicators).

Periodically the PMG meets with the external User Reference Group (URG, Fig. 1-6), a group of 8 expert users in the fields of both fluorescence and electron microscopy, that report on the needs of the user community. The PMG met with the URG once so far (March 2022) and the needs and possible solutions for large-data handling were discussed. We foresee that interactions with the URG will be increasingly important in defining new goals for the CMI, such as specific method development, while staying in constant contact with the real users' perspective. Another external body interacting with our platform is the National Overseeing Committee, made of 10 faculty members

appointed directly by universities all over Sweden, which is responsible for the scientific evaluation and machine-time allocation of the cryo-electron microscopy (cryo-EM) Block Allocation Group (BAG) projects.

The two units that form the CMI Platform, the Cryo-EM (Fig. 1-2) and the Integrated Microscopy Technologies Units (IMT, Fig. 1-3) work together towards the establishment of a sound cryo-EM national screening network plus focused ion beam scanning EM (FIB-SEM) and correlative array tomography (CAT) capabilities, which were our main goals under 2021–2022 (see next paragraph). Furthermore, both Units actively interact with a number of other platforms and institutions within SciLifeLab. In 2023, we initiated and hosted the Head-of-Unit Meetings, a bottom-up initiative to improve the communication between Units, Platforms and the various SciLifeLab offices (Communications, External Relations, etc.). A concern and general interest raised during the head-of-unit meetings was the development of career paths for technical personnel. We in the CMI have been quite involved in this discussion and have actively participated in the European project ARISE, a fellowship program for the training of staff scientists working in service infrastructures.

Within the SciLifeLab community, the CMI has tight interactions with **the Integrated Structural Biology (ISB) Platform**, with whom the Cryo-EM Unit has fortnightly meetings runs interdisciplinary projects; the **Drug Discovery and Development (DDD) Platform**, with whom the Cryo-EM Unit has organised a well received international webinar and has identified common research project; **National Bioinformatics Infrastructure Sweden (NBIS)**, with whom we have established a new support team

on cryo-EM data analysis; InfraLife, with whom we have worked for the realization of a national course on integrative structural biology methods; and the **Data Centre**, with whom we collaborate within the National Program on Data-

Development, Achievements and Plans

The CMI Platform in the current configuration was started in 2021 with the aim of building a strong hub for advanced imaging techniques to visualize life across different scales (from organism to compound level) using either electrons, photons, or both. Three main aims were defined in the Specific Terms and Conditions, to be achieved by the platform during the period 2021–2024: i) the establishment of a national screening network for cryo-EM, ii) the development and introduction among the user community of FIB-SEM and iii) similarly, the development of CAT. We have already established and advanced all three goals.

The National Screening Network for cryo-EM (CryoScreenNET) has been initiated according to the time schedule previously proposed. Efficient and fruitful interactions with representatives from Lund, Gothenburg and Uppsala Universities allowed us to quickly kick off the Screening Network that is now made of 4 people employed at different sites in collaboration with SciLifeLab, which supports 50% of their salary. The Network is coordinated by facility staff at the Cryo-EM Unit nodes in Stockholm and Umeå, guaranteeing an organic organization around the country. Members of CryoScreenNET take care of new cryo-EM users at each site (Lund, Gothenburg and Uppsala). They discuss new projects, often together with cryo-EM personnel in Stockholm at the Drop-In Consultation Service, and subsequently help with cryo-EM specimen preparation at their respective universities. Having a local person to refer to lowers substantially the barrier for users to undertake cryo-EM projects. When possible, initial sample screening is also done at the local universities. However, this is not always possible using the currently available instrumentation. To overcome this problem, personnel in Stockholm and Umeå have trained the cryoScreenNET members to perform screening remotely on the SciLifeLab instruments placed in Solna and Umeå. The CryoScreenNET members also participate in weekly journal clubs and group meetings held within the Cryo-EM Unit, weekly. The program has allowed CMI to start building a “we” feeling in the cryo-EM team at a national level. At the moment CryoScreenNET employees are shared with local group leaders or core facilities. In addition to the establishment this group of experts for local users’ service, faculty members at various universities have worked with the SciLifeLab Cryo-EM Unit to raise the visibility of cryo-EM community needs in the Vetenskapsrådet (VR) national needs inventory. Discussions about collaborations with the cryo-EM core facility at Karolinska Institute are ongoing.

The development and introduction among the user

Driven Life Science for the realization of pipelines for large data transfer and interactive data visualization and analysis for fluorescence microscopy data.

community of FIB-SEM has also been started and has delivered the first results. Since 2021 FIB-SEM component of the IMT Unit in Umeå has had 21 individual users where 7 has been for volume imaging, 6 material science, 7 cryo and 1 non-academic company. Among the volume imaging users 4 are local, 2 national and 1 international. Many of these are recurring users and has projects extending through several years.

FIB-SEM consists on consecutive milling (ion beam) and scanning (electron beam) to build an image and a subsequent 3D view of a given sample both biological and inorganic materials. The technique can also be combined with cryo-EM to make lamella for tomography. Each project and sample needs a specific experiment design based on the scientific question and on the unique technical challenges to be solved (e.g. staining/contrast and sample orientation). Only the area exposed on the very surface of the specimen is visible in the microscope and sometimes this area is very small and embedded which makes it difficult to localize. The unit has successfully implemented the use of CLEM (correlative light and electron microscopy) together with different software (e.g. MAPS and Icy) to target positions precisely. A method of precise targeting is the genetic introduction of the APEX2-tag which gives a dense precipitate at the site of the tag. This was successfully implemented together with the lab of Dr. Sara Sandin at NTU in Singapore and was published this year.

The development and spread among the user community of CAT has also been successfully started with first results and new exciting perspectives in terms of method development. The full CAT workflow in Gothenburg is unique in Sweden. This new imaging modality within CMI is developed by the Gothenburg Centre for Cellular Imaging (CCI), which is also involved in CryoScreenNET as described above. CAT is a technique to analyse large specimens and fields of view (tissues and cells) by making serial ultrathin sections from which images can be collected using both light and electrons. Innovative correlative imaging methods are being implemented in Gothenburg, and consultation and training are offered for the experimental design from sample preparation, image acquisition, data processing and analysis. Even though CAT has been opened to the user community only since July 2021, there are already 6 projects in the pipeline, some with international partners. In view of the large dimensions of the imaged specimens, CAT involves complex workflows which are notoriously time-consuming and require high levels of expertise. At CMI, we are currently developing new methods for sample

preparation, increased image acquisition speed in both light and electron microscopy and denoising methods for easier data analysis. The CAT component of the IMT Unit of CMI interacts already with international partners, and is part of a consortium for efficient multimodal imaging and big-data handling of human brain sections across scales (Fig. 2), with four other European partners.

Apart from the initial funding specifically dedicated to FIB-SEM and CAT development, the CMI Platform has invested strategic platform funding from 2021 and 2022 (550 sek per year) in effective communication between these two techniques and the Advanced Light Microscopy component in Stockholm (ALM). A collaboration has been initialized aimed at **facilitating sample preparation and sample exchange between the different imaging modalities and geographical sites** (Gothenburg, Stockholm and Umeå). We have a running a pilot project on kidney-tissue multimodal imaging (glomerular filtration structures resolved with EM/LM) where presently joint optimized sample protocols are being developed and tested for all three modalities.

We at the CMI are quite positive that we are working at a good pace to fully achieve our three main goals for the the next couple of years and we are working on ways to **strengthen our imaging capacity across scales, modalities and geographical locations with new longer-term plans** (see next section).

During the past year and a half, we at the CMI platform have been successful in our requests for financial support from other funding agencies. Three out of seven national Research Infrastructure Fellowships from the Swedish Foundation for Strategic Research (SSF) were granted to members of the CMI Platform, indicating the importance that the user community attributes to building national capabilities in imaging. The Cryo-EM Unit has attracted additional funding from VR and the Kempe Foundation for the upgrade of microscopes, camera and softwares to allow further development of electron diffraction techniques (micro-ED) at the Stockholm node as well as faster acquisition of single-particle cryo-EM data at the Umeå node. Further instrumentation upgrades within the platform will be

Request for additional funding 2023–2024

As presented in the previous paragraph, we plan to expand our imaging capabilities at the interface of photons and electrons, across the scales of biological specimens and with national coverage, involving all the units in our CMI Platform and fostering the development of multimodal workflows across units.

In 2021 and 2022 we used the Platform Strategic Budget to identify projects benefiting from multimodal imaging and to establish sample-preparation workflows between the nodes. For 2023–2024 we plan to follow up on this line of

available soon with the installation of SECOM, an integrated correlative light and electron microscopy platform, at the CAT component in Gothenburg, and the installation of MINFLUX, the newest nanoscopy device for fluorescence imaging of molecular and dynamic systems at the ALM node in Stockholm.

Within the CMI Platform, by each unit alone and in collaboration with other platforms, we have been particularly active in outreach and teaching activities. The Cryo-EM Unit organised in 2021 an international symposium in Umeå within CryoNET, a KAW- and Novo Nordisk-funded collaboration of Danish and Swedish cryo-EM centres. The Cryo-EM Unit node in Stockholm, together with the DDD Platform, organised a webinar on Cryo-EM in Drug Discovery and Development, that was highly subscribed with more than 250 attendees. In close collaboration with the ISB Platform and InfraLife, the Cryo-EM Unit has also organised and hosted for a week a 10-day course in Integrative Structural Biology, which was held at the end of August. The ALM component has organised two advanced workshops in superresolution and expansion microscopy techniques, with the participation of international experts. The CMI platform was presented at the outreach day organised by SciLifeLab at the National Molecular Medicine Fellows 2022 Meeting.

Based on the results obtained so far and on development in the imaging field, we plan to invest more energy in the future (2023–2025) in developing new methodologies at the interface between fluorescence and electron imaging. We will make sure that the action will be nationwide and that the results and technical pipelines will be communicated and made available to the Swedish research community. To achieve this goal we will continue strengthening and developing CAT and FIB-SEM in Gothenburg and Umeå, respectively. Additionally, we will work towards the development of correlative techniques between superresolution and cryo-electron tomography at the Stockholm node, taking advantage of the existing methodologies at the IMT and Cryo-EM Units and on the presence of expert SciLifeLab Fellows (Ilaria Testa, Erdic Sezgin).

development, increasingly involving the user community. We will work nation- and technique-wide to:

- 1) **Expand and develop our CAT capabilities and their availability to the community (Gothenburg CMI node).** This process will also be helped by the SSF grant to Rafael Camacho for the development of machine-learning techniques in image-data acquisition. For this goal the CAT component in Gothenburg should receive 500k sek extra funding per year (2023–2024).
- 2) **Expand and develop our FIB-SEM capabilities and**

their availability to the community (Umeå CMI node).

For this, we are exploring sample preparation methods, with project-specific solutions. FIB is an extremely interesting method for research in the interface between material and life science. We will work in collaboration with molecular-infection medicine researchers and EMBL partners for the combination of CLEM and FIB volume imaging of microorganisms. For this goal, the FIB-SEM facility in Umeå should receive 500k sek extra funding per year (2023–2024) to expand the services and methodology plus 500k sek in 2024 for the organisation of an international seminar series/workshop.

- 3) **Develop techniques of correlation and sequential imaging of live superresolution microscopy with cryo-electron microscopy and tomography (Stockholm CMI node).** This is a growing focus in the international imaging field; taking advantage of the proximity at SciLifeLab Campus Solna of the IMT and Cryo-EM Units, we want to develop such techniques for the Swedish research community. This process will be helped by the presence at Campus Solna of SciLifeLab research fellows

such as Ilaria Testa and Erdinc Sezgin. Some method development projects have been already identified. We will use the MINIFLUX microscope that will be installed later in 2023 to perform sequential imaging of molecular complexes first by light and then cryo-EM. For this goal, the IMT and Cryo-EM Units in Stockholm should receive 250k sek extra funding per year (2023–2024).

In order to achieve the three goals stated above in a concerted way among all the CMI components, we will organise specific workshops on the different techniques with the participation of the staff personnel from each site. Under 2023 a workshop on CAT will be held in Gothenburg with the participation of international teachers. The following year (2024) will be the turn of a workshop in FIB-SEM organised and held in Umeå. Alongside with the workshops, a retreat day for the CMI platform personnel will take place to foster community building.

This plan will guarantee the evolution of the CMI platform as a fully national and organic hub for light-and-electron-microscopy imaging.

Requests for expanded platform funding 2023–2024

Unit	SciLifeLab funding 2022 (kSEK)	Requested SciLifeLab funding 2023 (kSEK)	Requested SciLifeLab funding 2024 (kSEK)
IMT-Umeå UmU (FIB-SEM)	184k	500	500 + 500 workshop/retreat
IMT-Göteborg GU(CAT)	184k	500 + 500 workshop/retreat	500
IMT- Stockholm KTH (ALM)	184k	250	250
Cryo-EM - Stockholm SU		250	250

Budget explanation. The CMI platform will request 2MSEK extra funding per year for 2023 and 2024. Each site, Umeå, Gothenburg and Stockholm will receive 500kSEK for the development of project-specific methods and multimodal imaging between sites. Additionally, Gothenburg in 2023 and Umeå in 2024 will receive extra 500kSEK for the organization of workshops on CAT and FIB-SEM, respectively. The sum will cover costs for international invited speakers, consumable and machine time, organization and support fellowships for attending students. These SciLifeLab workshops will be opened to attendees from academia, industry and healthcare. Possibly in concomitance with the workshops, a day meeting for the platform staff will also take place.



Unit:	Cryo-EM
Platform:	Cellular and Molecular Imaging

Development, Achievements and Plans

Development, users and major achievements - During the 2021-2022 period, the Cryo-EM Unit has continued to provide extensive user training and service to the Swedish (and Nordic) scientific community. Alongside this the Unit has pursued three primary objectives: (1) the establishment of CryoScreeNET, a national screening and cryo-EM expertise network, (2) development of micro-ED and cryo-CLEM capabilities within the Unit, and (3) improved throughput and data quality for existing high-demand services (such as single-particle analysis for structural biology applications).

(1) CryoScreeNET, the national screening network for cryo-EM, was initiated and established during 2021. Efficient and fruitful interactions with representatives from host universities allowed us to quickly kick off the network, which now employs four staff members at three different sites, Lund, Gothenburg and Uppsala University, supported with 50% of their salary by SciLifeLab. The network is coordinated by experienced staff from the Cryo-EM Unit nodes in Stockholm and Umeå, guaranteeing a continuous dialog with the main nodes as well as an integrated organization around the country. CryoScreeNET staff members discuss new projects with users at the local sites, often together with cryo-EM staff in Stockholm at the Drop-In Consultation Service, and subsequently help with cryo-EM specimen preparation at their respective sites, both as a service and in the form of user training. When possible, initial sample screening is also done at the local universities. However, this is not always possible using the currently available local instrumentation, as so far only Uppsala University has invested in a local cryo-EM facility with screening capability. To overcome this problem, personnel in Stockholm and Umeå have trained the CryoScreeNET staff to perform remote screening and data collection using the SciLifeLab instruments located in Solna and Umeå. Following data collection, CryoScreeNET staff also provide substantial assistance to local users when it comes to data processing and analysis. CryoScreeNET staff are well integrated into the Cryo-EM Unit, participating actively in weekly journal clubs, group meetings and seminars. Having a local site expert in place has substantially lowered the barrier for new users to undertake cryo-EM projects, is raising the skill level of users outside Stockholm and Umeå and will lead to an increased quality of the data being collected on the high-end instruments at the main nodes.

(2) The capability to perform micro electron diffraction experiments (micro-ED) has been developed and established as a Unit service by the Stockholm node. The method has an increasing user base and investments in new hardware and software have enabled both higher capacity and quality (exemplified by Yang, T. et al, *Symmetry*, 2021; Lightowler, M. et al., *Angewandte Chemie Int.*, 2022; [Li, S. et al. *Chem. Rxiv*, 2022](#); [Yang, T. et al, *Nat Protoc*, 2022](#)), as well as technology and knowledge transfer to the Umeå node. Similarly, workflows and instrumentation for cryo correlative light and electron microscopy (cryo-CLEM) have been developed and established as a service at the Umeå node.

(3) Grants from KAW, Kempe and VR, together with financial support from SciLifeLab, Umeå University and Stockholm University, have enabled the Unit to invest in new state-of-the-art instrumentation and upgrades. Purchase of a new 200 KV cryo-TEM instrument (Glacios) in Umeå offers both improved screening availability, new user training opportunities and surprisingly fast data

aquisition. Additionally, the aquisition of new detectors for all three high-end Krios microscopes, which has taken place during 2021-2022, has effectively increased the total unit throughput for single-particle-analysis data collection by 10-fold. Besides providing improved access to more users, with shorter queing times, this also enables completely new scientific applications, including the extensive analysis of conformationally heterogenous specimens and bottom-up structural biology.

Besides the three primary developments described above, the Unit has expanded its user base to include users from the other Nordic countries as well as industrial partners (in tight collaboration with InfraLife), participated extensively in outreach activities, such as Research Friday and hosting high-school visits to national and international conferences and workshops. The Unit has also been engaged in the organization of multiple courses and events, including courses in basic and advanced cryo-EM at both the Umeå and Stockholm sites, the InfraLife course in Integrated Structural Biology (in close collaboration with the ISB platform and InfraLife), hosted annual cryo-EM user meetings, ran the SciLifeLab Head of Unit meetings and organized a symposium on Cryo-EM and Drug Discovery (in close collaboration with the DDD platform).

Alongside operational and technological developments, Unit staff are deeply engaged in research activities and collaborations, significantly contributing to high-impact research articles (exemplified by: Stsiapanava et al. 2022, *Nat. Struct. Mol. Biol.*, Iakovleva et al. 2021 *Nature Comms.*, Naschberger et al. 2021, *Nature*).

Future plans for the Unit and ongoing projects –

We plan to expand substantially towards the cellular and medical aspects of cryo-EM applications for our research community. As part of the Cellular and Molecular Imaging platform we plan to identify and facilitate more and more projects for the analysis of cellular systems using correlative light and electron microscopy (CLEM) and focused-ion-beam scanning electron microscopy (FIB-SEM). This will be possible also thanks to the SSF Research Infrastructure Fellow support to Linda Sandblad (Umeå). Additionally, we will also work towards the development of combined imaging using advanced light superresolution microscopy and cryo-EM.

Moreover, we will work on facilitating the usage and application of cryo-EM to medically relevant projects, also in this case with the help of an SSF Research Infrastructure Fellow grant to Marta Carroni (Stockholm). We will develop sound pipelines for cryo-EM Longitudinal Epitope Mapping, opening cryo-EM to the medical community in Sweden and the Nordics.

For both these two lines of expansion towards the cellular and medical aspects of cryo-EM, we will organize outreach activities and courses to involve both the research community and students across the country.

Cryo-EM

Budget 2022

Costs	2022
Personnel cost	5 654 236
Other personnel costs	0
Depreciation	12 292 561
Service and license costs	4 986 808
Other operating costs	1 021 533
Premises costs	3 105 334
Other costs	32 933
Sum costs (kSEK):	27 093 405

Revenues	2022
Funding from SciLifeLab	5 025 000
Funding from KAW 1243862	13 296 141
Funding from Erling Persson	2 678 158
Funding from SU/Rektorspengar	2 000 000
Funding from SFO/SU	960 000
Funding from VR	700 145
User fees	2 400 000
Sum revenues (kSEK):	27 059 444

Integrated Microscopy Technologies Gothenburg

Cellular and Molecular Imaging Platform (Web links for Unit: [Webpage](#), [Publications](#))

Basic Information

Head(s) of Unit: Julia Fernandez-Rodriguez
PSD(s): Julia Fernandez-Rodriguez
SciLifeLab Unit since: 2021
Host university: GU
FTEs: 7.0
FTEs financed by SciLifeLab: 1.5

Funding in 2021 (kSEK)

SciLifeLab: 1500
GU: 5500
VR: 1600
SSF: 2800
EU: 60
Nordforsk: 50
Total: 11510

Resource Allocation 2021

Academia (national): 30%
Academia (international): 40%
Internal tech. dev.: 10%
Industry: -
Healthcare: 20%
Other gov. agencies: -

User Fees 2021

Total (kSEK): 150
Reagents: 30%
Instrument: 35%
Salaries: 35%
Rent: -
Other: -

User Fees by Sector 2021

Academia (national): 20%
Academia (international): 50%
Industry: -
Healthcare: 30%
Other gov. agencies: -

Services

- Project planning & experimental design for Cellular 3D Correlative Array Tomography (CAT), & Integrated Array Tomography for 3D Correlative Light & Electron Microscopy (SECOM)
- Specimen preparation for correlative experiments (e.g. MALDI-IMS), and sample preparation for single particle Cryo-EM & screening using a Talos L120 TEM
- Provision of full image processing and analysis projects
- Access to image analysis workstations and servers

Publication by Category

No publication data available

Publication by Journal Impact Factor

No publication data available

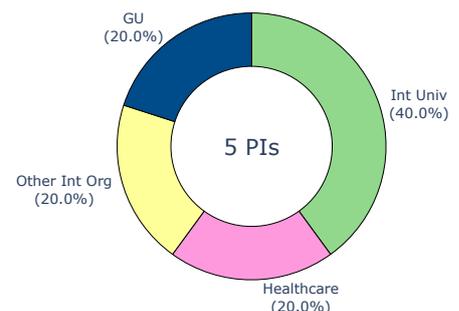
Users 2019

No user information

Users 2020

No user information

Users 2021



Unit:	Integrated Microscopy Technologies Gothenburg
Platform:	Cellular and Molecular Imaging

Development, Achievements and Plans

Development, users and major achievements – The Centre for Cellular Imaging (CCI) has been in operation since 2003 and is one of the advanced open access technology platforms at the University of Gothenburg. In July 2021 the CCI was merged with the **Correlative Array Tomography (CAT)**, into the *Integrated Microscopy Technologies SciLifeLab Unit* as part of the *Cellular and Molecular Imaging SciLifeLab platform*. The CAT encompasses a range of techniques where multiple ribbons of serial ultrathin sections of tissues or cells are collected on a solid substrate such as glass, silicon wafers, from which images can be collected using both light and electrons. Consequently, innovative correlative imaging methods are implementing at the CCI, providing researchers with consultation and training on experimental design from sample preparation to image acquisition and data processing and analysis. Although, the CAT technology has been offered to the user community since July 2021, we have already 6 projects in the pipeline. In 2021 “Instrument Call from SciLifeLab” the facility was awarded with 2 million SEK to purchase the **SECOM**, that is a unique *integrated correlative light and electron microscopy platform*, enabling us to do correlative imaging extremely fast, with the highest optical quality and overlay accuracy. The SECOM platform can easily be integrated in the existing workflow and installed as a retrofit into our scanning electron microscope, by replacing the vacuum chamber door. This update of our Unit will support research in life sciences move faster by acquiring both structural and functional information simultaneously. Our facility has also started in spring 2022 a cross-platform project for developing a *national workflow for efficient multimodal imaging across scale*: developing and implementing collaborative sample preparation methods and new trans-site workflows, to improve final results, biological broader relevancies and to save repetitive and time-consuming sample preparation steps at each site.

Future plans for the unit and ongoing projects – Many biological functions depend critically upon fine details of tissue’s molecular architecture that have resisted exploration by existing imaging techniques. Array tomography (AT) encompasses light and electron microscopy modalities that offer unparalleled opportunities to explore 3D cellular architectures of large samples in extremely fine structural and molecular detail (Fig. 1). The full CAT workflow (including, sample preparation, electron and light microscopes and management of the data) in Gothenburg is one-of-a-kind in Sweden. This new technology covers the current state-of-the-art in volume electron microscopy imaging applied to very large and complex biological samples. However, performing AT has many challenges, including sample preparation, image acquisition and data handling. This approach results in imaging complex workflows which are notoriously time-consuming and require high levels of expertise. Furthermore, in CAT the microscopes have very different fields of view, and therefore accurately overlaying the different 3D volumes is highly non-trivial and prone to bias. Thus, we are currently developing new methods for **sample preparation** and for increasing the **image acquisition speed of AT** in both light and electron microscopy. **Smart Microscopy to automate time consuming steps in AT**: Can benefit immensely from automation and

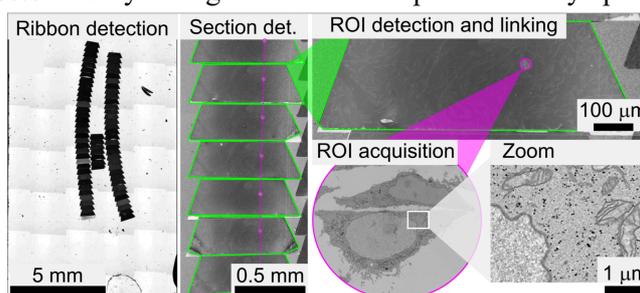


Figure 1. Array Tomography workflow: Serial sectioning of the specimen, and collection of the sections to create a ribbon; Sections in the ribbon must be identified and imaged at low resolution to find ROIs; These ROIs are later imaged at high-resolution to create a 3D view of the specimen.

image analysis at different stages, from the initial low-resolution imaging to the final acquisition of the regions of interest with very careful imaging settings (e.g., small pixel size, and large integration times, as show in Fig 1). Thus, we focus on automating tasks of object detection that must be repeated many times over, do not require human creative thinking, but are nevertheless critical for the success of the experiment. **Implementing denoising methods:** The visualisation of the specimen at low spatial resolution works as a "map" for the imaging system and is essential for finding the regions-of-interest (ROIs) that must be re-acquired with different microscope settings (e.g., high spatial resolution). Due to the large areas that must be observed, this step should be done with fast imaging settings and low spatial resolution, producing images of inherently low SNR. Therefore, we will implement denoising methods to effectively work at faster acquisition speeds. Further, we will tackle the automated detection of sections in an array, which is well suited for support by machine learning as: i) many sections are acquired for each ribbon, ii) different samples display similar image properties, and iii) human annotations for training can be generated. We are also improving the **managing of big data** (for processing and visualization) and automating some of the target identification steps that currently need human intervention. **Examples of ongonig projects:**

Renal tubular scattered cells in human Kidney tissue (Prof. Martin Johansson, Gothenburg). During kidney disease, the renal tubular cells are very vulnerable to damage due to their high metabolic activity. While the renal tubules can regenerate, there is disagreement on how this occurs. One hypothesis is: surviving tubular cells de-differentiate to initiate regeneration in the damaged area, while others propose the presence of stem or progenitor cells that induce regeneration. This project concentrates on the study of a cell population called tubular scattered cells (TSCs), which can be distinguished from proximal tubular cells based on light microscopy (LM) compatible markers for CD24, CD133 and vimentin and due to their morphological properties. LM is used to identify TSCs in large serial tissue sections (each mm in size), and direct image acquisition of the scanning electron microscopy (SEM) for detailed morphological investigation. We focus on the automated detection of TSC in both LM and SEM images to guide the acquisition of high-resolution AT datasets.

Sun damage in human skin equivalent (User: Prof. Florian Gruber, Austria) The group focuses on the interaction of skin and environment, investigating how the skin and its various cell types react to stressors and ageing, concentrating on cellular senescence. The aim of this project is to study skin equivalent models via CAT between light and electron microscopy (Figure 3). We develop tools for the automated detection of sections in an array, layers in skin samples, and cells of interest in LM. This information will then be transferred to the SEM for the high-resolution morphological investigation. For registration purposes, we are implementing machine learning assisted strategies for cell nuclei detection in both LM and SEM.

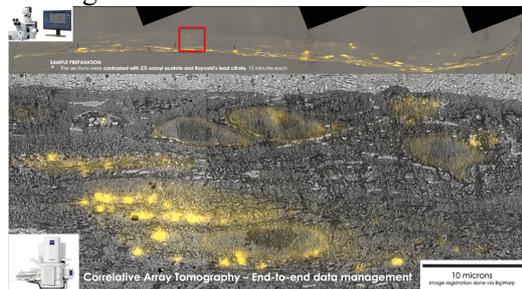


Figure 2. CAT of sun damage studies in human skin equivalents. In yellow, fluorescence overlay on the electron microscopy image, represent the positive cells treated with

In 2020 we created with 5 partnerst across Europe a consortium for efficient multimodal imaging & Big Data Handling of human brain sections across scale: **Big mUltimodal hIgh-resolution atLas Data Management, BUILD** (Fig 3). The work includes the design of polarimetric and light microscopy, x-ray, electron microscopy (single and multibeam), FIB-SEM and the implementation of image processing algorithms, as well as big data analytics utilizing high-performance computing. The combined usage of these interdisciplinary topics will finally enable the generation of unique brain atlases of different species, such as rodents, human and primates.

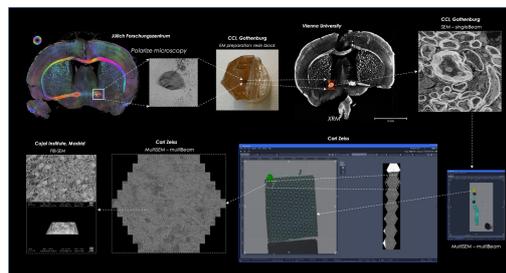


Figure 3. Big mUltimodal high-resolution atLas Data Management, BUILD, to design a proof-of-Concept study for Correlative Imaging & Big Data Handling of brain sections

Integrated Microscopy Technologies Gothenburg

Budget 2022

Costs	2022
Personnel cost	2 098 964
Other personnel costs	65 000
Depreciation	940 000
Service and license costs	0
Other operating costs	150 000
Premises costs	50 000
Other costs	0
Sum costs (kSEK):	3 303 964

Revenues	2022
Funding from SciLifeLab (CAT)	1 500 000
Funding from SciLifeLab (Cryo-EM Network)	500 000
Funding from host Universities (infrastructure support)	1 000 000
User fees	375 000
Sum revenues (kSEK):	3 375 000

Integrated Microscopy Technologies Stockholm

Cellular and Molecular Imaging Platform (Web links for Unit: [Webpage](#), [Publications](#))

Basic Information

Head(s) of Unit: Hans Blom
PSD(s): Hjalmar Brismar
SciLifeLab Unit since: 2013
Host university: KTH
FTEs: 4.2
FTEs financed by SciLifeLab: 3.0

Funding in 2021 (kSEK)

SciLifeLab: 3500
SciLifeLab Instrument: 850
VR: 1000
SSF: 1000
Total: 6350

Resource Allocation 2021

Academia (national): 85%
Academia (international): -
Internal tech. dev.: 15%
Industry: -
Healthcare: -
Other gov. agencies: -

User Fees 2021

Total (kSEK): 250
Reagents: -
Instrument: 100%
Salaries: -
Rent: -
Other: -

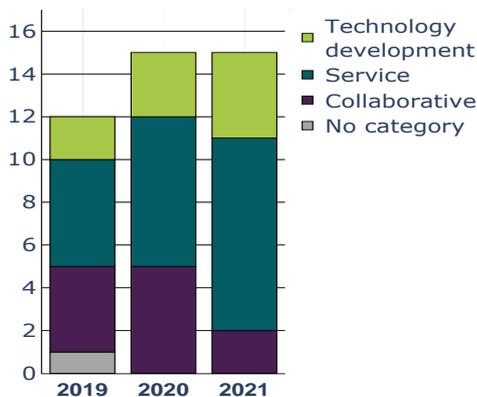
User Fees by Sector 2021

Academia (national): 100%
Academia (international): -
Industry: -
Healthcare: -
Other gov. agencies: -

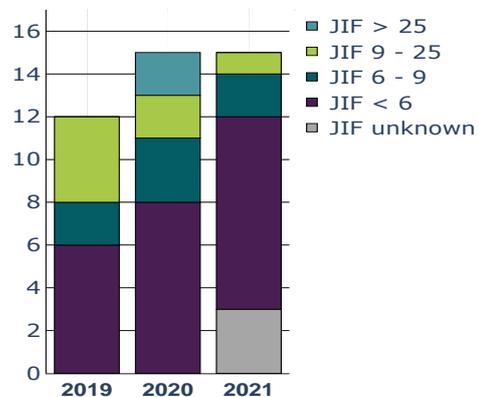
Services

- Nanoscale biological visualization with super-resolution fluorescence microscopy (SIM, STED, PALM/STORM).
- Single molecule dynamical measurement & analysis to evaluate molecular mobilities, concentrations & interactions (FCS/STED-FCS)
- Volumetric imaging of live &/or optically cleared larger samples at unprecedented speed & low phototoxicity (Light-sheet microscopy (LSFM))
- Single cell ultra-fast volumetric imaging of biological processes (Lattice LSFM)

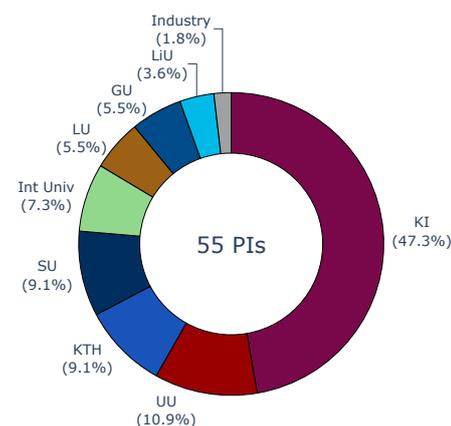
Publication by Category



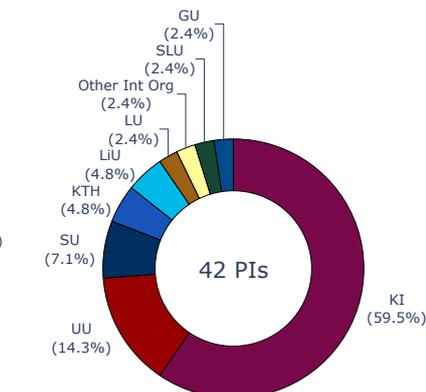
Publication by Journal Impact Factor



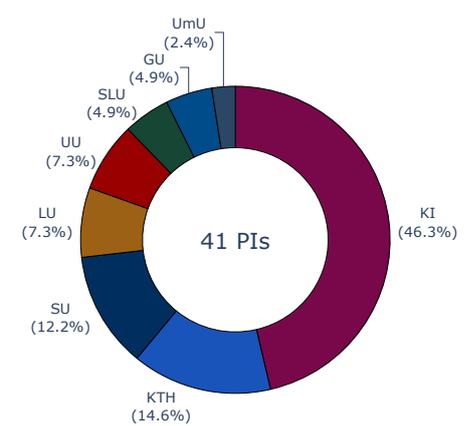
Users 2019



Users 2020



Users 2021





Unit:	Integrated Microscopy Technologies Stockholm
Platform:	Cellular and Molecular Imaging

Development, Achievements and Plans

IMT Stockholm supports three areas of light microscopy [1] – super resolution microscopy (STED, SIM, PALM/STORM etc.), single molecule dynamics studies (FCS/FCCS, FRET-FCS, STED-FCS etc.), and fast high-resolution volumetric cellular and tissue imaging (Light Sheet & Lattice Lightsheet Fluorescence Microscopy). Four staff scientists work in the facility.

Technology development – selected (21–22)

We have continued our development on giving national support with optical clearing and expansion of cellular and tissue samples. The facility today has several world-class staff scientists that develop and transfer knowledge on novel sample clearing/expansion methods to users from academia [e.g. 2–3]. Novel kidney tissue clearing/expansion knowledge and protocol [e.g. 4], has moreover been transferred to medical scientists at the university hospitals in Gothenburg, Lund and Stockholm, as well as the pharmaceutical company AstraZeneca in Mölndal.

Scientific achievements – selected (21–22)

The facility service projects from all walks of life science, where molecular medical related basic sciences frequently ask for support. Super resolution STED imaging for example helped shedding light on the Amyloidogenic Pathway involved in Alzheimer's disease [5]. Single molecule dynamical studies (use of FCCS) revealed new protein-lipid cooperative binding associated with Parkinson's disease [6]. Tissue clearing and volumetric imaging moreover allowed investigating changes in neuronal connectivity related to sleep disorder [7].

New user groups –selected (21–22)

The facility yearly support 50-60 project within the serviced microscopy areas. Example of a new field getting support from 21–22 is plant biology – plant cell differentiation processes, PI Edouard Pesquet [8], and nanocellulose wood sciences, PI Anna Svagan Hanner [9]. This added 'green' microscopy support is also in line with the new capability focusing on planetary biology at SciLifeLab (in collaboration with EMBL) – to understand from molecular to population level how microbes, plants, and animals respond to each other and to their environment.

Outreach efforts (21–22)

The facility is via its participation in national and international microscopy infrastructure networks [10–13] continuously visible to inform users of available services (during the Covid pandemic solely web based efforts). The facility with its unique expertise and light microscopy instrumentation has also been visible on 'commercially' outreach event [14]. The Advanced Light Microscopy facility is today a well-known infrastructure even on the international level (cf. EMBL's Imaging Centre or Janelia's Advanced Imaging Center [15–16]).

Training and education (21–22)

The facility staff scientists educate and train individual users during the support of their projects. Support is done to all stages of the project including (pre)planning, sample optimization, fluorescent probe selection, image acquisition, and initial post-acquisition image processing etc. For 'broader'

training and education the facility also run two yearly PhD courses, covering all three areas of supported microscopy services (#1 Super resolution; #2 FCS and LSFM etc. - both 3 ECTS). Within our national and international microscopy infrastructure networks the ALM facility also organizes several training and educational event, even in collaboration with industry, e.g. [12].

Cross-unit/cross-platform initiatives (21/22)

Within our integrated microscopy technologies (IMT) unit, the advanced light microscopy (ALM) facility in Stockholm, together with the correlative array tomography (CAT) facility in Gothenburg, and the focused ion beam scanning electron microscopy (FIB-SEM) facility in Umeå, are working on improved multimodal imaging support. The goal is to develop a national service that allows combining CAT (light/electron microscopy on thin tissue slices), as well as FIB-SEM (milling and EM imaging of ultra-thin lamellae), with advanced light microscopy analyses (STED/SIM etc.). In this initiative we have launched a pilot project on kidney-tissue multimodal imaging (glomerular filtration structures resolved with EM/LM) where presently joint optimized sample protocols are being developed and tested for all three modalities. Funding from the internal CMI platform budget is supporting this initiative.

Together with the Cryo-EM node in Stockholm, the ALM facility is moreover developing a tissue clearing preparation pipeline with cryo-sample fixation combined with light microscopy imaging (funding from the internal CMI platform budget.). This sample clearing initiative is moreover selected as a technology development project (TDP), which received national funding from SciLifeLab, with the goal of building a pipeline for clearing services.

2023–2024 development plans

The ALM facility aim to continue its services in super resolution microscopy, single molecule dynamics studies, and fast high-resolution volumetric cellular and tissue imaging. To extend services with nanoscale biological imaging and single molecule dynamical analysis, we will during 2023 install a MINFLUX microscope [17].

Together with SciLifeLab fellows and PIs Magda Bienko, Erdinc Sezgin, Ilaria Testa, and Simon Elsässer, the ALM facility will develop and support applications with fluorescence lifetime microscopy (FLIM), to enhance the possibility to reveal deeper fundamental aspects of genome architecture [18], enhance insight in cellular membrane organization and functions [19], and enable improved single molecular information from super-resolution probes [20–21] as part of a Campus Solna RED project grant.

National project support with lattice lightsheet microscopy will also be started and a national hands-on workshops in 3D tissue clearing and volumetric imaging is planned for with industry partners.

References: [1] <https://www.scilifelab.se/units/integrated-microscopy-technologies/>; [2] Jalalvand et al. *eLife* 11:e73114 (2022); [3] Pinheiro et al. *Journal of Neuroscience Methods* 348: 109002 (2021); [4] Unnersjö-Jess et al. *Kidney360* 3(3):446 (2022); [5] Yu et al. *Journal of Alzheimer's Disease* 83(2):833 (2021); [6] Makasewicz et al. *ACS Chemical Neuroscience* 12(12):2099 (2021); [7] Brodin et al. *Frontiers in Synaptic Neuroscience* 14:854160 (2022); [8] www.researchgate.net/profile/Edouard-Pesquet; [9] <https://orcid.org/0000-0002-4583-723X>; [10] www.scilifelab.se/units/integrated-microscopy-technologies/; [11] www.nmisweden.se/; [12] <https://bnmi.eu/>; [13] www.eurobioimaging.eu/; [14] www.zeiss.com/microscopy/int/cmp/lsc/21/sim-squared.html; [15] www.embl.org/about/info/imaging-centre/; [16] <https://www.janelia.org/open-science/advanced-imaging-center-aic>; [17] <https://abberior-instruments.com/products/minflux/>; [18] G. Girelli et al. *Nature Biotechnology* 38:1184 (2020); [19] Sezgin et al. *Nature Reviews Molecular Cell Biology* 18:361 (2017); [20] Matlashov et al. *Nature Communications* 11: article number 239 (2020); [21] Lafranchi et al. *Journal American Chemical Society* 142(47):20080 (2020).

Budget 2022

Integrated Microscopy Technologies Stockholm

Costs	2022
Personnel cost	4 343 958
Other personnel costs	75 000
Depreciation	6 350 000
Service and license costs	363 000
Other operating costs	250 000
Premises costs	1 044 000
Other costs	0
Sum costs (kSEK):	12 425 958

Revenues	2022
Funding from SciLifeLab	3 500 000
KTH infra - lattice	1 600 000
KTH infra - airy2	1 000 000
KTH infra - SPIM remodel	190 000
VR-RFI Elyra	3 000 000
VR-RFI MINT	250 000
VR-RFI NMI	1 600 000
Faculty funding	1 000 000
User fees	285 000
Sum revenues (kSEK):	12 425 000

Integrated Microscopy Technologies Umeå

Cellular and Molecular Imaging Platform (Web links for Unit: [Webpage](#), [Publications](#))

Basic Information

Head(s) of Unit: Sara Henriksson
PSD(s): Linda Sandblad, Richard Lundmark
SciLifeLab Unit since: 2021
Host university: UmU
FTEs: 2.25
FTEs financed by SciLifeLab: 1.0

Funding in 2021 (kSEK)

SciLifeLab: 1500
UmU: 250
Total: 1750

Resource Allocation 2021

Academia (national): 60%
Academia (international): 10%
Internal tech. dev.: 25%
Industry: 5%
Healthcare: -
Other gov. agencies: -

User Fees 2021

Total (kSEK): 62
Reagents: 80%
Instrument: 20%
Salaries: -
Rent: -
Other: -

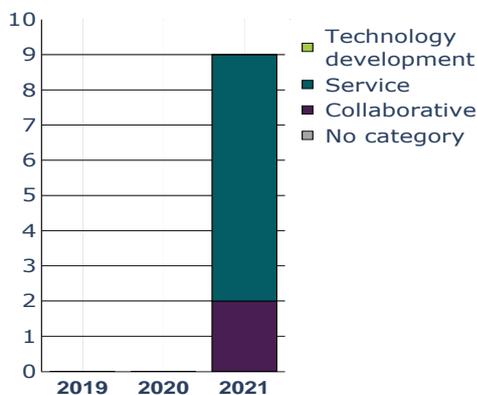
User Fees by Sector 2021

Academia (national): 100%
Academia (international): -
Industry: -
Healthcare: -
Other gov. agencies: -

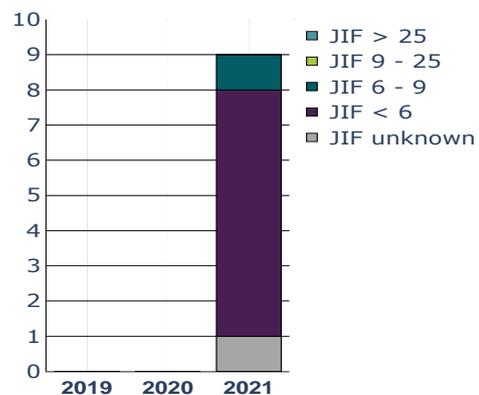
Services

- FIB-SEM volume imaging using a Thermo Fischer Scios
- Sample preparation for FIB-SEM using both conventional room temperature techniques and high pressure freezing/freeze substitution
- Correlative light and electron microscopy techniques to identify region of interest
- Sample screening on Talos L120 TEM
- Image processing and visualisation

Publication by Category



Publication by Journal Impact Factor



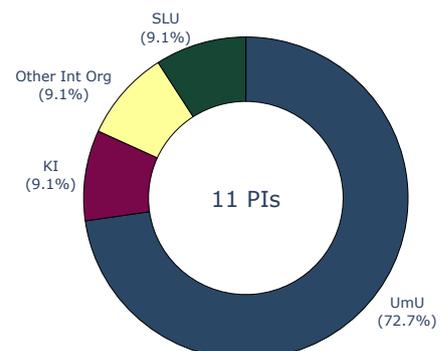
Users 2019

No user information

Users 2020

No user information

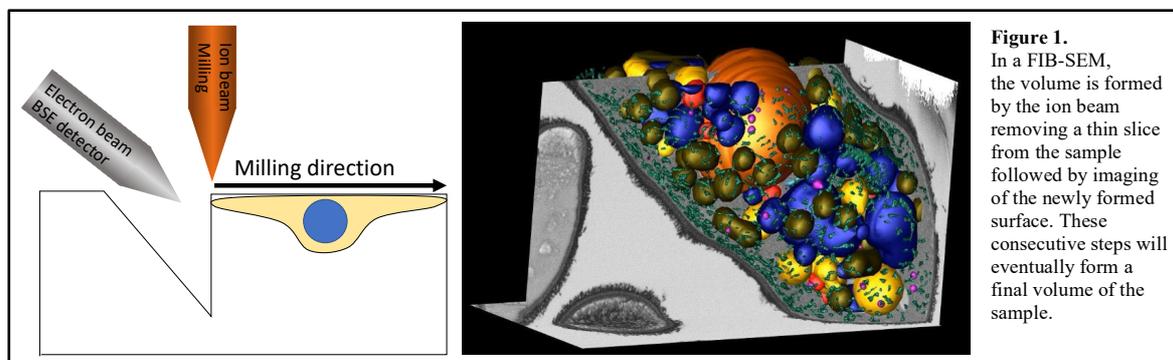
Users 2021



Unit:	Integrated Microscopy Technologies Umeå
Platform:	Cellular and Molecular Imaging

Development, Achievements and Plans

The Integrated microscopy technologies unit in Umeå is a newly established unit focused on volume electron microscopy by Focused Ion Beam SEM (FIB-SEM). This method relies on a consecutive milling (ion beam) and scanning (electron beam) to build an image and a subsequent 3D view of a given sample (Figure 1).



Major achievements

The FIB-SEM microscope (Scios DualBeam with Aquilos stage upgrade, Thermo Fischer Scientific (TFS)) in Umeå is a highly versatile instrument shared by many research groups, not only biologists but also material scientists. Since the microscope can also operate at cryo conditions it is a joint microscope together with the Cryo-EM facility that uses it to make cryo-lamellas for tomography. This internal collaboration has been a great success and enables the microscope to be heavily booked with few free slots. The collaboration has its challenges in terms of microscope setup and thus requires ongoing discussions both between the facilities but also regular meetings with the development team at TFS to improve this instrument, a fruitful development resulting in new test protocols TFS now apply worldwide.

The technology development has mainly focused on sample preparation. Each project/sample needs a specific experiment design based on the scientific question but also because it has unique technical challenges to be solved e.g. staining/contrast and sample orientation. Only the area exposed on the very surface of the sample is visible in the microscope and sometimes this area is very small and embedded in the sample which makes it difficult to localize perfectly. We have successfully implemented the use of CLEM (correlative light and electron microscopy) together with different software (MAPS – by TFS and Icy – by academic community) to target positions precisely. One successful example of this is in collaboration with the lab of Dr. Barbara Sixt at the Department of molecular biology, Umeå University (Figure 2).

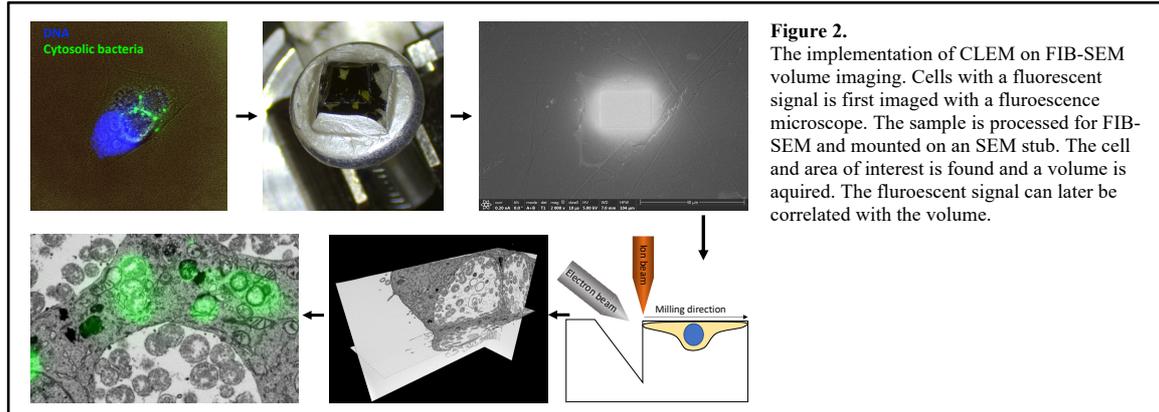


Figure 2. The implementation of CLEM on FIB-SEM volume imaging. Cells with a fluorescent signal is first imaged with a fluorescence microscope. The sample is processed for FIB-SEM and mounted on an SEM stub. The cell and area of interest is found and a volume is acquired. The fluorescent signal can later be correlated with the volume.

Another method of precise targeting is genetic introduction of the APEX2-tag which gives a dense precipitate at the site of the tag. This was successfully implemented together with the lab of Dr. Sara Sandin at NTU in Singapore and was published this year¹.

Since 2021 the microscope has had 21 individual users where 7 has been for volume imaging, 6 material science, 7 cryo and 1 non-academic company. Among the volume imaging users 4 are local, 2 national and 1 international. Many of these are recurring users and has projects extending through several years.

During the last years our unit has participated in the following doctoral/postdoc courses and outreach activities:

- Online lecture for the basic electron microscopy course 22–23 March, 2021
- Online lecture for the basic electron microscopy course 14–16 September, 2021
- Online lecture for the NMI-course Advanced microscopy for life sciences 22–24 September, 2021
- Lecture and demonstration of the FIB-SEM for the TEM II practical course in TEM sample preparation 14–18 November, 2021
- Lecture for the basic electron microscopy course 22–24 February, 2022
- Visit from Balderskolan in Skellefteå, 8 April, 2022

In addition to these lectures our unit always offer individual training on both sample preparation, microscopy and image processing based on the researchers request.

Future plans

In the future we aim to more frequently offer our users sample preparation by high pressure freezing (HPF) and freeze substitution (FS). This is a superior technique for preservation of ultrastructure and would give a more reliable result. However, the protocol is sample dependent and therefore needs more extensive testing of the contrast enhancement needed for FIB-SEM imaging. We are planning a new lab specifically for HPF and FS. This lab will also have possibilities for cell culture together with an adjacent fluorescence microscope to quickly transfer the cells for freezing/fixation at the time point of interest.

A long-term future plan is to invest in further FIB-SEM instruments (currently only one) to have dedicated microscopes for room temperature and cryo-EM techniques. This would enable a better microscope, stage and detection system configuration for the unique purposes and also a more flexible booking schedule.

1.Hübner, B. *et al.* Ultrastructure and nuclear architecture of telomeric chromatin revealed by correlative light and electron microscopy. *Nucleic Acids Res* **50**, 5047–5063 (2022).

Budget 2022

Integrated Microscopy Technologies Umeå

Costs	2022
Personnel cost	986 926
Other personnel costs	0
Depreciation	300 000
Service and license costs	394 200
Other operating costs	197 100
Premises costs	100 000
Other costs	0
Sum costs (kSEK):	1 978 226

Revenues	2022
Funding from SciLifeLab	1 000 000
Funding from VR	80 000
Funding from Umeå University	250 000
User fees	250 000
Sum revenues (kSEK):	1 580 000

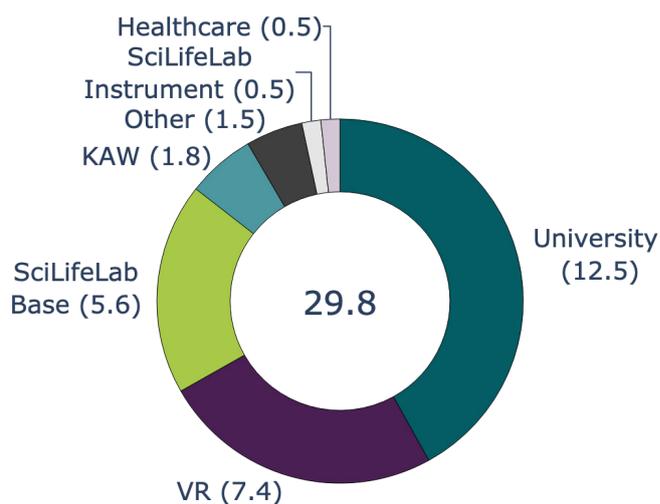
► Integrated Structural Biology Platform

Platform Director: Göran Karlsson, GU

Platform Coordination Officer: Cecilia Persson, GU

Platform and Units SciLifeLab Funding 2021:

Unit	(MSEK)
Swedish NMR Centre	3.5
Structural Proteomics	1.5
PD, PCO, Platform Strategic Budget	0.6
Sum:	5.6

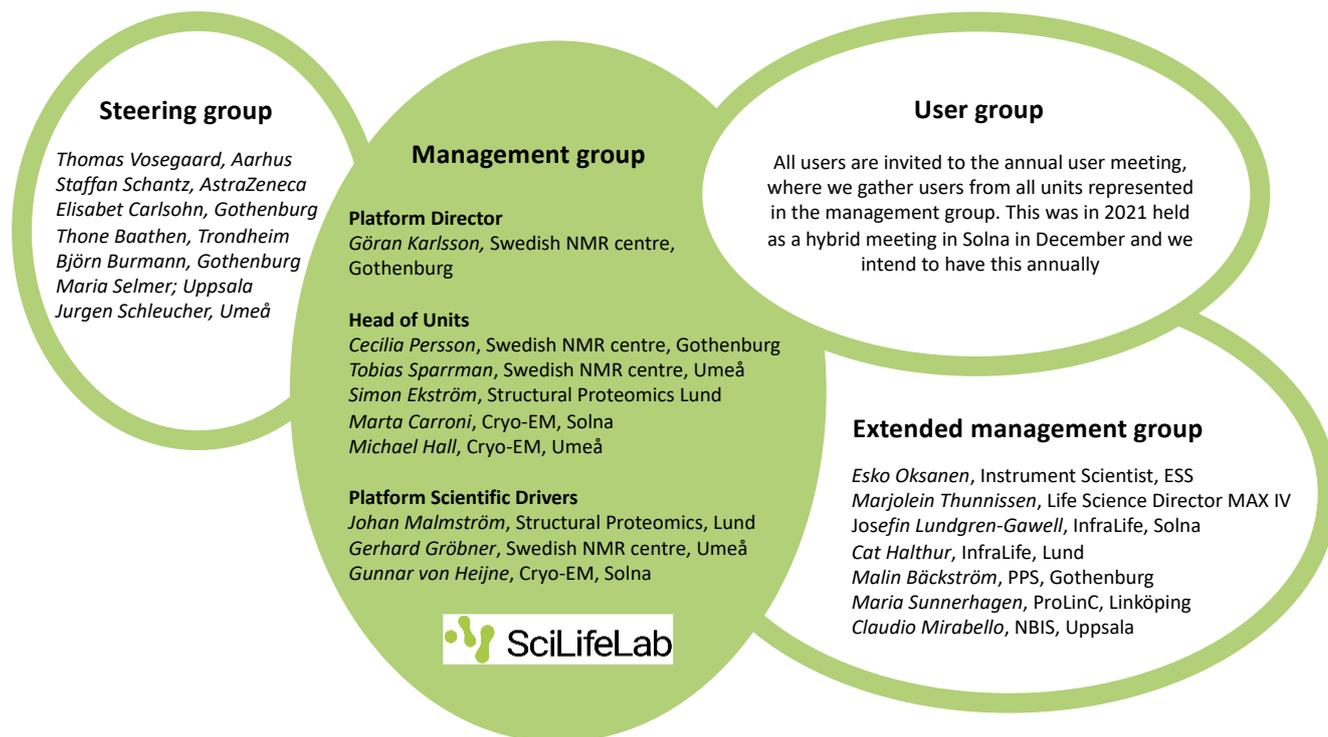


Platform Specific Terms and Conditions for Funding - Integrated Structural Biology

This document concerns the terms and conditions for SciLifeLab funding of the Integrated Structural Biology Platform and Units from 2021 and onwards and outlines the strategic direction MG wants the platform to take. The mid-term checkup in the middle of the 4-year funding period will focus on how well the Platform and Units have taken into account the items in this document.

- SciLifeLab funding to the Integrated Structural Biology Platform and Units is meant for providing nationally unique technologies and services within structural biology
- Ensure that SciLifeLab funds are used in the platform in a manner that aligns with the priorities and goals of the entire SciLifeLab organization
- Provide resources to engage in the SciLifeLab capabilities including Precision Medicine and Planetary Biology, integrating data and know-how from several different platforms
- Together with the SciLifeLab management define an organization, governance and steering for the platform, with representation also from MAX IV and ESS, according to the suggested general policy for governance and steering of SciLifeLab infrastructure
- Coordinate the service area Integrated Structural Biology in collaboration with Cryo-EM, MAX IV, ESS, the national protein production network, and other relevant stakeholders.
- Form a single/central entry point for structural biology questions, especially addressing non-expert users and contribute to the construction of the new SciLifeLab infrastructure web page for guiding users
- Collaborate with the InfraLife initiative at the External Relations Offices at SciLifeLab and MAX IV/ESS and contribute in outreach activities towards industry and health care users
- Enhance collaboration with the Bioinformatics platform and Data Centre to establish FAIR data sharing and links to the DDLS initiative

Organization and Management



The ISB platform is organized according to the above scheme and comprises the Swedish NMR centre (nodes at GU & UmU), and Structural Proteomics (LU). The cryo-EM unit (nodes at SU & UmU) is virtually associated with the ISB platform. The ISB platform is interacting with external stakeholders on a national level, i.e. MaxIV, ESS, PPS, ProLinC and relevant functions within SciLifeLab, specifically InfraLife and NBIS. Discussion with LINXS are progressing.

Platform discussions are conducted in two fora. In the platform management group (PMG) meetings, the platform director, the heads of units and the platform scientific drivers discuss operative and strategic questions, e.g. separate and joint activities, interactions with other units and platforms, visibility home page and budget. Applications for expensive equipment and technology development projects are also discussed in the PMG meeting. Since April 2021 PMG met every second week and since June 2022 each third week.

The extended management group (EMG) comprises the PMG

Development, Achievements and Plans

Platform development 2021–now

The ISB platform was established in 2021, and has made good progress towards the platform mission, e.g. through establishment of web-based entry point, harmonization of support landscape, frequent exchange on a unit level, enhancement of SciLifeLab capabilities and more.

members and representatives from other stakeholders. The EMG initially had meetings on a monthly basis (April 2021–) and since June 2022 each sixth week to discuss strategies and routes for the implementation of national support for integrated structure biology, development at each node, joint activities etc.

The current meeting frequency will be kept for the PMG and the EMG, respectively. The agenda is published in NextCloud (preferably at least two days before the meeting). Notes are taken and are available to all participants via the NextCloud folder.

In parallel, there is interactions with units other than SciLifeLab, e.g. the research infrastructure (RI) consortia funded by the research council. The Structural Proteomics unit is part of the BioMS RI, the Swedish NMR Centre is part of the CBCS RI, and the Protein Production Sweden R I , and is coordinating the SwedNMR RI.

The platform comprised the two nodes of the Swedish NMR Centre (GU and UMU), and the nodes of the virtually associated cryo-EM unit. The Structural Proteomics unit joined the ISB platform in July 2021. Platform operations have been affected by the Corona pandemics. Visits from

external users as well as direct meetings between the different nodes were affected, particularly since both the Swedish NMR Centre and the Structural Proteomics are geographically distributed over Sweden. However, the PMG comprises a fairly small group of people which has enabled an informal, positive and open discussion climate via zoom. Despite starting during Corona, PMG members (Head of units (HU)) have now met several times in real life, e.g. through HU physical visits at other nodes (Solna, Lund), but also at national meetings, e.g. the ISB users meeting (Dec.2021) and the SweProt meeting (June 2022). Visits at Umeå and Gothenburg nodes are planned late 2022 or early 2023.

Decisions by the ISB MG regarding strategic platform budget

- organizing the ISB users meeting
- supporting the SweProt meeting
- initiating a flagship users project
- fund staff scientist rotation program
- ISB platform retreat
- plans for inviting an ISB lecturer was postponed due to the Corona pandemic

Specific ISB platform actions and achievements (in accordance with platform mission):

- The ISB platform has been operational since start (January 2021) and has since then provided access to PIs from all major Swedish universities to its expertise within structural biology and unique instrumentation, e.g. first Scandinavian DNP-NMR system, first world-wide cryo-MAS NMR equipment, first Swedish certified IVDR metabolomics system, etc.
- Through its website, the ISB platform has created biology (<https://www.scilifelab.se/services/integrated-structural-biology/>). The entry point is available also to users outside the SciLifeLab.
- The ISB platform has extensively interacted with the surrounding society, including SMEs (e.g. AstraZeneca, Saromics), governmental agencies and regional health care providers.
- Enhanced SciLifeLab capabilities, by providing access to advanced and unique metabolomics expertise and instrumentation. Operations together with e.g. the Swedish Biobank RIs, concern sample pre-analytical handling and QC of biobanked samples, with a clear focus towards precision medicine, and in climate change research, NMR quantifies the magnitude of “CO₂ fertilization” of photosynthesis, a key uncertainty for modeling the global C cycle and future crop productivity.

- The ISB platform has established an extended platform management group which includes representative from relevant stakeholders, i.e. MAX IV, ESS, PPS, ProLinC, InfraLife and NBIS. The steering group for the Swedish NMR centre (appointed by the GU vice chancellor) will be suggested as steering group also for the SciLifeLab ISB platform.

- The regular EMG meetings is, through its direct contact with national RIs and user communities a forum for the strategic development of integrated structure biology on a national level. The ISB MG and EMG continuously identifies and invites relevant national stakeholders to this discussion. The EMG meetings constitute an arena for coordinated activities, e.g. a national PhD course for integrated structural biology (vide infra).

- Platform interactions were established, involving the ISB platform or units within the platform:
 - the TDP project on AlphaFold 2, “BeyondFold, main applicant Björn Nystedt, Bioinformatics platform, Swedish NMR Centre and the Cryo-EM units were both co-applicants).

- interaction on the unit level (the Swedish NMR Centre) include joint applications to the research council (Main applicant: HU Otto Savolainen, the Metabolomics platform) and utilization of NMR resources in drug development (main applicant: Tobias Kröger, MAX IV).

- the ISB platform has initiated a “flagship” project, where a user project relevant for all capabilities (NMR, MS, Cryo-EM) within the ISB platform was selected for support (vide infra).

- Platform technology development

The ISB platform nominated applications for expensive instruments. In the last two years, the Swedish NMR centre applications for a world unique 3.2 mm cryoMAS probe (Umeå) and the upgrade of a console and cryoprobe for an existing NMR system (Gothenburg) were approved.

- Outreach, training, courses, etc.

Users meeting: The first ISB users meeting was organized in Solna, December 13, 2021 (Integrated with the cryo-EM users meeting). The meeting was organized as a hybrid meeting.

The second ISB users meeting is scheduled for December 12, 2022.

PhD course: During the last year, the ISB platform, including the EMG, has planned and organized the “Integrative Structural Biology” course (Aug 22-Sept 2, 2022, Lund, Gothenburg, Stockholm) with more than 25 participants from Sweden and other Nordic countries. The course comprised lectures and hands-on tutoring from experts associated with all EMG stakeholders and was carried out

on-site at the relevant national RIs.

Web-page: The first SciLifeLab service area page (entry point) has been established for the ISB platform. The ISB entry point will present a short introduction to the field and contact details to all stakeholders in EMG, with the aim of gathering information for the whole Structural Biology pipeline available in Sweden, and serve as a direct contact point for users support.

Reach out: The ISB platform was presented at several local and national meetings, notably

- presentation at the NMMP day, Ystad, May 4, 2022
- panel discussion at the third LINXS symposium, Lund, May 5, 2022
- presentation at the SweProt meeting, Tällberg, June 18, 2022

Development plans for the period 2023-2024 and beyond

- We envisage a continued consolidation between units. Despite that all units are part of the structural biology field, the underlying physical observables are totally different, and the methodology in merging results from different techniques is constantly developing.
- We aim to develop the service areas, as further described

During the fall of 2022, hybrid drop-in sessions will be organized to further spark the integrative aspects of structural biology. The drop-in sessions will be organized together with local SciLifeLab nodes at the different universities.

Joint scientific project across units: Part of the strategic funding for the ISB was earmarked for (an external users) flagship scientific project, where contribution from the different ISB units (MS, NMR, Cryo-EM) is required.

Reach In: A platform retreat is planned for the fall 2022. The first occasion when the major part of all staff scientists meet will be the facility forum in Djurönäset in October. However, the facility forum will gather all SciLifeLab staff, and a dedicated ISB platform retreat was deemed required.

in the budget document.

- In the EMG, we will investigate the possibilities to associate Sweden to the INSTRUCT ERIC.
- Finally, and foremost, continue to reach the missions goals for the platform.

Request for additional funding 2023–2024

The ISB platform was recently established but the participating units are well established research infrastructures and have for several years provided extensive service and support to the scientific community. However, despite the concise and comprehensive name “Integrated Structural Biology”, (and unlike several other SciLifeLab platforms), the underlying technologies at the participating units are based on vastly different physical principles. In order to fully explore the potential and capabilities of the participating units, additional funding is requested for 2023-2024.

For the Structural Proteomics Unit in Lund: The covid pandemic has sparked the interest in analysis of antibodies and their epitopes. To meet this demand, we intend to establish a dedicated pipeline for analysis of antibody binding based on the knowledge gained the past year. The service will be directed towards in-depth mass-spectrometry structural characterization of antibodies, epitopes and the interaction between monoclonal/polyclonal antibody mixtures and epitopes. The equivalent of a 50% staff scientist is required for 2023, which will be extended to a full-time position from 2024.

The development of ultra-fast MAS NMR represents a change of paradigm in the field. Size limitations are

completely eliminated, while maintaining full access to protein dynamics. In the next years, the method will develop and completely change advanced NMR-based structural biology. In this process, particularly the high costs for the required, special rotors may be discouraging for user. For the methodological development, including costs for 0.6–0.7 mm rotors, 300 kSEK/yr for 2023 and 2024 is requested.

The NMR methodology is one of two (the other being MS) which is used to address metabolomics. The Swedish NMR Centre has for several years provided this as a service, but the capability has not reached its full potential within SciLifeLab. We now ask for funding for a dedicated metabolomics staff scientist position for 2023–2024. The position will focus on the application of metabolomics in precision medicine, and on the integration of NMR and MS metabolomics data in analysis. The position will be placed at the Swedish NMR Centre in Gothenburg, and from there interact with other relevant units and nodes within SciLifeLab, and with the expressed goal to enhance cross-platform capabilities.

The ISB PhD course will be updated and repeated in 2024. The SciLifeLab contribution, 100 kSEK (InfraLife) and 20 kSEK (SciLifeLab) is requested in 2023 & 2024 in the strategic platform budget.

Request for additional funding 2023–2024

Specify all costs in kSEK

Unit	SciLifeLab funding 2022 (kSEK)	Requested SciLifeLab funding 2023 (kSEK)	Requested SciLifeLab funding 2024 (kSEK)
Structural Proteomics	2000	2500	3000
Swedish NMR Centre	3500	4800	4800
Strategic Platform Budget	250	300	400

Swedish NMR Centre

Integrated Structural Biology Platform (Web links for Unit: [Webpage](#), [Publications](#))

Basic Information

Head(s) of Unit: Cecilia Persson, Tobias Sparrman
PSD(s): Göran Karlsson (PD), Gerhard Gröbner
SciLifeLab Unit since: 2016
Host university: GU, UmU
FTEs: 10.7
FTEs financed by SciLifeLab: 3.7

Funding in 2021 (kSEK)

SciLifeLab: 3500
SciLifeLab Instrument: 320
GU: 6500
UmU: 2350
VR: 200
KAW: 1200
Total: 14070

Resource Allocation 2021

Academia (national): 65%
Academia (international): 5%
Internal tech. dev.: 15%
Industry: 13%
Healthcare: 1%
Other gov. agencies: 1%

User Fees 2021

Total (kSEK): 3700
Reagents: 10%
Instrument: 40%
Salaries: 35%
Rent: 15%
Other: -

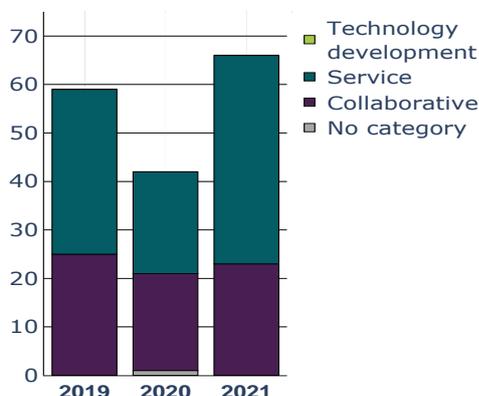
User Fees by Sector 2021

Academia (national): 60%
Academia (international): 8%
Industry: 30%
Healthcare: 2%
Other gov. agencies: -

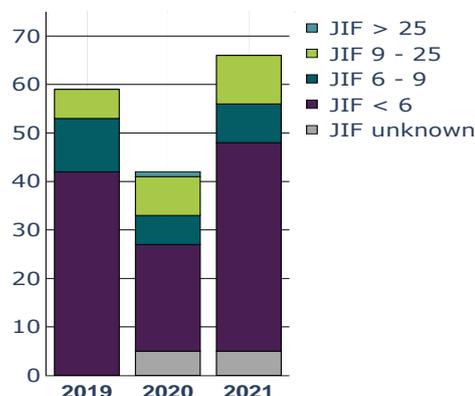
Services

- Structural biology
- Metabolomics
- Chemical biology and small molecule NMR
- Diffusion, microimaging and MAS NMR

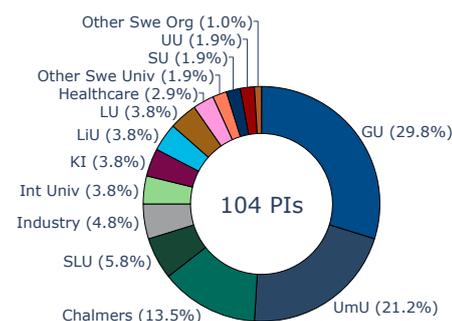
Publication by Category



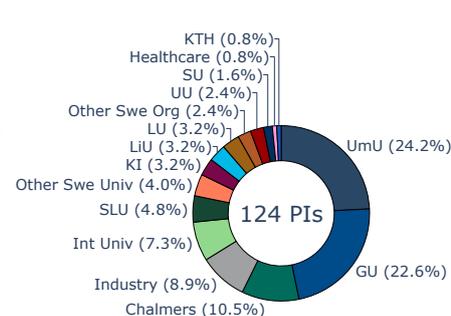
Publication by Journal Impact Factor



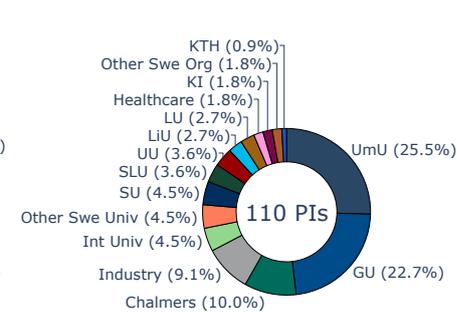
Users 2019



Users 2020



Users 2021



Unit:	Swedish NMR centre
Platform:	Integrated Structural Biology
Development, Achievements and Plans	
<p>The Swedish NMR Centre (SNC) is located at two nodes, one in Gothenburg and one in Umeå. NMR is a fundamental method that provides information on the atomic level about distance, dynamics and interactions on a wide time scale. Hence, the methodology has wide-spread use, <i>e.g.</i> in the study of small molecules, fragment based screen, materials science, metabolomics and structural biology (SB). Since the observables are complementary to those of other SB techniques (X-ray, cryo-EM, structural mass-spectrometry), NMR confers added capabilities to Integrated Structural Biology (ISB). Within SciLifeLab, the SNC provides three major capabilities, in ISB, and <i>cross-platform</i> in chemical biology and in metabolomics.</p> <p>i) Technology Development 2021–2022:</p> <p>The unit has seen a strong development in the last two years. At the Gothenburg site, the re-installation of the 900 MHz magnet was completed in December 2020. The world’s first 3mm 900 MHz cryoprobe was installed in April 2021, providing unsurpassed sensitivity. In parallel, installation of the first Scandinavian DNP-NMR system, was completed in late 2020 and taken in full use in 2021. The DNP-NMR system addresses new user groups, <i>e.g.</i> pharmaceutical industry where “NMR crystallography” is a game changer in the study of the active pharmaceutical ingredient. The DNP-NMR system is a joint project together with AstraZeneca and served to propel the SNC into the H2020 research infrastructure (RI) consortium PANACEA (<i>vide infra</i>). At the Umeå site, the first Ultra-Fast Magic Angle Spinning (UF-MAS) 0.7 mm HXY probe was installed at the 850 MHz magnet in late 2021. UF-MAS is probably the most interesting development in NMR-based structural biology in recent years, since it allows the study of macromolecules irrespective of size, while retaining the unique dynamical information, one of the hall marks of NMR. Currently, also in Umeå, the world’s first cryo-MAS probe is being installed on a 600 MHz system, providing a 3–4 fold increase in sensitivity for solid state biosamples and intact specimen while observing them at biologically relevant temperatures. The cryoMAS together with the UF-MAS system opens completely new avenues in structural biology and life science.</p> <p>Research consortia and human expertise</p> <p>The SNC was successful in the 2021 VR-RFI call for RIs, and is since 2022 coordinating the national RI SwedNMR, comprising 10 major Swedish Universities. Furthermore, the Gothenburg node is also partner in the chemical biology RI consortium CBCS (also part of SciLifeLab), and in the Protein Production Sweden (PPS) RI. Two first research engineers were recruited, starting in March and May 2022, respectively. This development will strengthen the SB part of the unit by bringing the protein production part of the SB pipeline closer and contribute to the optimization of the cell-free protein production node of PPS. The CBCS node in Gothenburg provides an excellent opportunity to widen the SciLifeLab activities nationally and at the same time address new user groups from academia, health service and pharmaceutical industry.</p> <p>On the international arena, the SNC in Gothenburg is partner in two EU H2020 RI consortia; PANACEA, 2021–2025, focusing on solid state NMR applications and R-NMR, 2022–2025, where best practice and remote access are in focus.</p> <p>Science and User groups</p> <p>The scientific output from the SNC remains on a high level with several publication in <i>e.g.</i> JACS, Science Advances, Nature communication. A new methodology approach is the unambiguous</p>	

tracking of protein phosphorylation by fast high-resolution FOSY NMR developed within the unit and published in *Angewandte Chemistry* 2021. The unit is already firmly established with the NMR user community and the SB user community. The technology development will provide new opportunities within these groups, but we foresee an increased use in NMR based metabolomics, especially from regional biobanks and university hospitals.

Outreach, training and education

The SNC is closely interacting with the newly established SciLifeLab *nodes* in Gothenburg and Umeå, respectively. In Gothenburg, the SciLifeLab Site office will serve as a physical meeting point for user drop in where co-workers from all Gothenburg platforms units will help increasing SciLifeLab visibility. In this context, it should be mentioned that the HU of the SNC in Gothenburg contributed to nationally increased visibility as co-organizer of the SciLifeLab reach-out day in January 2022 and since spring 2022 is the organizer of the HU meetings, currently being planned for the autumn 2022.

In addition, the ISB platform (including the unit) was presented in national meetings, *e.g.* NMMP Ystad, May 4, 2022, at the LINXS meeting, Lund, May 5 2022, at the SweProt meeting in Tällberg June 18 and at ISB users meetings (Solna, December 2021 and 2022). The SNC co-organised the ISB course (Lund, Gothenburg, Stockholm, August 22–September 2, 2022) and will organize an international PhD course in Gothenburg on Sept 26–30, 2022 on “Biomolecular NMR: Advanced Tools, Machine Learning”. On October 4–6, 2022, the unit will organize the Swedish NMR meeting 2022 in Gothenburg.

Contribution to cross-platform capabilities

The future participation in the CBCS RI and the PPS RI was already mentioned. In 2021, the Swedish NMR Center completed the screening of the SPECS library, provided by the CBCS compound library, against Covid19 Nsp5 major protease. In 2021–2022, the unit is part of the TDP project “BeyondFold” (main applicant: Björn Nyqvist, NBIS). The project will investigate how ISB experimental observations (*e.g.* NMR and cryo-EM) can contribute to AlphaFold 2.0 technology. The unit is also co-applicant in the 2022 research council call for RIs (main applicant: Otto Savolainen, Metabolomics platform) in a project investigating the possibility of home sampling of bioliquids. One first research engineer at the Gothenburg is co-funded from NBIS and provides expertise in multivariate analysis of metabolomics data

ii) Development plans for the Swedish NMR Centre

During the fall of 2022, several technology installation projects will be completed, and need further development to benefit the user community. The ultra-fast MAS probe in Umeå has already been applied in projects with users from both academia and industry. Future plans include optimization of rotor use, which currently is the largest economic bottle neck. The Cryo-MAS (installation planned in October–November) will enable measurements on very small tissue samples and from 2023–24 adapted for implementation in user projects. The In-sight cell system from Bruker, enabling to record NMR data of proteins or drugs inside a living cell, will be installed at the SNC in Gothenburg during fall 2022, and become available to users from both academia and industry during 2023–24.

The SNC provides access to advanced and unique metabolomics expertise and instrumentation. Operations together with *e.g.* the Swedish Biobank RIs, focus on sample pre-analytical handling and QC of biobanked samples. We also offer access to IVD_r, a tool where metabolomics samples (urine and/or serum) are measured in a highly standardized manner, thereafter compared and analysed against a worldwide data base, providing a unique resource in precision medicine. We envisage a closer interaction with the Metabolomics platform from 2023 and onwards.

iii) The university of Gothenburg carried out an international evaluation of SNC in the fall of 2021. The report is available at www.gu.se/en/nmr/about-us.

Budget 2022

Swedish NMR Centre

Costs	2022
Personnel cost	9 624 214
Other personnel costs	400 000
Depreciation	2 839 333
Service and license costs	1 310 000
Other operating costs	3 400 000
Premises costs	2 362 000
Other costs	0
Sum costs (kSEK):	19 935 547

Revenues	2022
Funding from SciLifeLab	4 600 000
Funding from VR-RFI	1 800 000
Funding from GU	6 900 000
Funding from UmU	2 345 000
Funding from KAW	1 400 000
Funding from EU	400 000
User fees	2 500 000
Sum revenues (kSEK):	19 945 000

Structural Proteomics

Integrated Structural Biology Platform (Web links for Unit: [Webpage](#), [Publications](#))

Basic Information

Head(s) of Unit: Simon Ekström
PSD(s): Johan Malmström
SciLifeLab Unit since: 2021
Host university: LU
FTEs: 2.1
FTEs financed by SciLifeLab: 1.0

Funding in 2021 (kSEK)

SciLifeLab: 1500
LU: 1330
VR: 1340
Total: 4170

Resource Allocation 2021

Academia (national): 70%
Academia (international): -
Internal tech. dev.: 15%
Industry: 10%
Healthcare: -
Other gov. agencies: 5%

User Fees 2021

Total (kSEK): 200
Reagents: 50%
Instrument: -
Salaries: -
Rent: 50%
Other: -

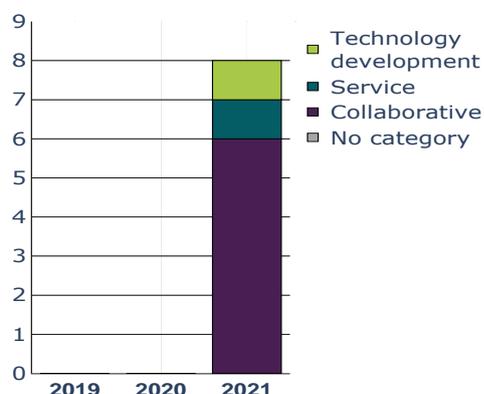
User Fees by Sector 2021

Academia (national): 80%
Academia (international): -
Industry: 20%
Healthcare: -
Other gov. agencies: -

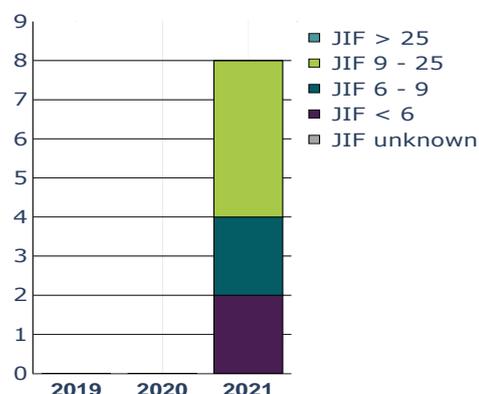
Services

- Hydrogen Deuterium Exchange Mass Spectrometry (HDX-MS)
- Cross linking Mass Spectrometry (XL-MS)
- Affinity purification Mass Spectrometry
- Mass Spectrometry based QA and validation of proteins used in structural biology studies

Publication by Category



Publication by Journal Impact Factor



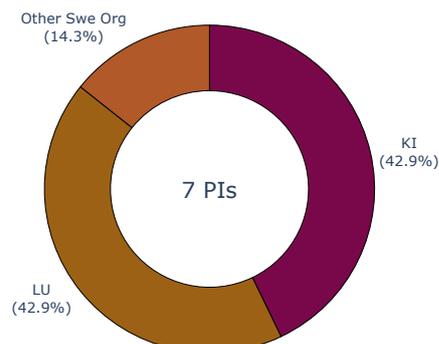
Users 2019

No user information

Users 2020

No user information

Users 2021



Unit:	Structural Proteomics
Platform:	Integrated Structural Biology
Development, Achievements and Plans	
<p>i) The Structural Proteomics Unit became a part of SciLifeLab and organisation wise placed in the Integrated Structural Biology platform in Jun/Jul 2021. This has been a major milestone for our unit and the open and dynamic interactions with all different stakeholders involved in the ISB platform has very beneficial, both for us as a unit and our users.</p> <p><i>Technology development:</i> We have installed two new MS instruments (funded by VR/BioMS grants) enabling analysis with improved sensitivity, speed and depth, these instruments will allow for the development of several advanced or even entirely new services. Although, due to a recent large increase in service request, we are a bit behind with our technology development.</p> <p><i>Scientific achievements:</i> During 2021–2022 we could see an overall improvement in the quality of publications from our users, 13 user publications total and 50% of these in journals with IF>10. Since the start of the covid pandemic we have done a lot of antibody epitope mapping with HDX-MS which has resulted in significant improvements in through-put and quality for our epitope mapping pipeline.</p> <p>The unit has also been heavily involved in the Integrated Structural Biology course (Aug 22–Sept 2, 2022), where we hosted more than 25 students for one day of lectures and practical exercises on site in Lund. Thanks to the broad reach of the ISB platform network and active participation in <i>outreach activities</i> and scientific meetings we have seen an increase in <i>new user groups</i>, and a better geographical spread of users.</p> <ul style="list-style-type: none"> • CryoEM/ISB user meeting in Solna, dec. 2021 • Visualising life at the molecular level, SciLifeLab Infrastructure outreach week, 2022, jan • NMMP days, Ystad, May 2022 • SweProt, Tällberg, June 2022 <p>ii) <i>Development plans 2023–2024</i></p> <ul style="list-style-type: none"> • Development and implementation of XL-MS workflows with new enrichable crosslinkers. • Development and implementation of MS methods taking advantage of the ion mobility feature of our new TIMS-TOF instrumentation for improved analysis of crosslinked peptides. • The establishment of a dedicated pipeline for analysis of antibodies based on the knowledge gained the past year. The service will be directed towards in-depth mass-spectrometry structural characterization of antibodies, epitopes and the interaction between monoclonal/polyclonal antibody mixtures and epitopes. Here several of our MS techniques will need to be combined, also additional MS methods and software needs to be implemented. High potential for cross-platform interactions with CMI (CryoEM), NGS and DDD. • To continue and expand the outreach activities within the ISB platform, to reach new users at universities with low or no current representation. 	

iii) Here we would like to point out that Structural Proteomics is a very small and streamlined unit (2.1 FTE), with that in mind we are very happy and proud of what we have achieved during the period. The most difficult challenge during 2023–2024 will be to ensure that we have sufficient time for development work, while maintaining the current service level. Becoming part of the ISB platform (family) has already been a success story for our unit and we hope to build further on this in the coming years.

Budget 2022

Structural Proteomics

Costs	2022
Personnel cost	2 195 831
Other personnel costs	24 200
Depreciation	1 341 334
Service and license costs	65 703
Other operating costs	266 200
Premises costs	245 100
Other costs	36 300
Sum costs (kSEK):	4 174 667

Revenues	2022
Funding from SciLifeLab	1 100 000
Funding from VR	1 341 334
Funding from Lund University	1 333 333
	0
User fees	400 000
Sum revenues (kSEK):	4 174 667

Summary Requested Additional SciLifeLab Funding 2023 and 2024

Platform	Unit	Funding 2022 (kSEK)	Requested Funding 2023 (kSEK)	Requested Funding 2024 (kSEK)
Bioinformatics	Support, Infrastructure and Training	18 000	19 500	19 500
	AIDA Data Hub	2 000	4 000	4 000
	Requested additional funding		3 500	3 500
Genomicss	NGI Uppsala (SNP&SEQ)	13 900	14 342	14 350
	MSCG /SCG Uppsala	2 000	2 000	2 000
	NGI Stockholm	21 900	22 700	22 716
	NGI Uppsala (UGC)	8 700	8 880	8 885
	Ancient DNA	2 000	2 470	2 470
	Joint platform funding	1 200	1 850	3 800
	Requested additional funding		2 542	4 521
Clinical Genomics	NGI Uppsala (SNP&SEQ)	14 800	15 727	16 437
	Joint platform funding		927	1 637
Clinical Proteomics and Immunology	Affinity Proteomics Stockholm	2 560	3 000	3 800
	Affinity Proteomics Uppsala	2 500	3 000	3 800
	Autoimmunity and Serology Profiling	2 400	3 000	3 800
	Cellular Immunomonitoring	4 000	3 800	3 800
	Global Proteomics and Proteogenomics	3 000	3 000	3 800
	Glycoproteomics	2 000	2 600	3 800
	Requested additional funding		1 940	6 340
Metabolomics	Exposomics	1 800	2 550	2 550
	SMC (Chalmers)	600	1 350	2 100
	Joint platform funding		1 500	2 250

Platform	Unit	Funding 2022 (kSEK)	Requested Funding 2023 (kSEK)	Requested Funding 2024 (kSEK)
Spatial and Single Cell Biology	Spatial Proteomics	3 000	3 700	4 700
	Spatial Mass spectrometry	2 000	3 500	4 500
	In situ sequencing	1 900	3 900	4 700
	Advanced FISH pilot	1 500	1 500	1 500
	ESCG	5 000	6 000	6 000
	ST	-	1 000	1 000
	Requested additional funding			6 200
Cellular and Molecular Imaging	Strategic Platform Budget	550	1 550	1 550
	Requested additional funding		1 000	1 000
Integrated Structural Biology	Structural Proteomics	2 000	2 500	3 000
	Swedish NMR Centre	3 500	4 800	4 800
	Strategic Platform Budget	250	300	400
	Requested additional funding		1 850	2 450
Chemical Biology and Genome Engineering	CFG	3 200	3 700	4 000
	Chemical Proteomics	1 700	2 200	3 000
	Requested additional funding		1 000	2 100
Drug Discovery and Development	Requested additional funding		?	?
SUM Requested additional funding			20 459	32 798

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