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New international consortium set to advance AI and multimodal data integration in personalised cardiovascular medicine



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Editor: Magdalena Lindén Layout: Edna Fagerstedt



New international consortium set to advance AI and multimodal data integration in personalised cardiovascular medicine

The CMM groups of Ljubica Matic and Ulf Hedin (Vascular Surgery Group at MMK, Karolinska Institutet) have teamed up with 20 clinical research centres, universities, professional associations, SMEs and non-profit representative organisations of civil society in a new EU Horizon Europe project NextGen, aiming to develop the next generation tools for genome-centric multimodal data integration in personalised cardiovascular medicine.

The EU Horizon "NextGen" project, under the European Health and Digital Agency (HADEA), is run through a large international collaboration coordinated by Utrecht University Medical Center (NL). The project has been funded for 4 years with 7.6 MEUR totally, and at Vascular Surgery KI the team is led by Ljubica Matic (Principal Invstigator, PI) and Ulf Hedin (co-PI), who are also group leaders at CMM.

Personalized medicine is emerging as a crucial strategy for improving treatment of cardiovascular diseases (CVD), involving tailored, cost-effective approaches for prevention, diagnosis, monitoring and treatment. To this end, it is imperative to integrate large amounts of CVD healthcare and genomic data available, by support from artificial intelligence (AI), specifically machine learning (ML) algorithms. However, there are major challenges to privacy and governance when it comes to integrating multi-modal data, in addition to diverse standards, distinct data formats, complexity and volume of data.

NextGen aims to make the most of the AI/ML advancements by bringing various stakeholders together in developing ways to process large amounts of individual



CVD data, complying with GDPR rules about how data is handled, stored and used across collaborators. The project adopts a privacy-by-design, integrated data governance and federated learning models to solve this issue and guarantee secure access to multi-modal data across multiple jurisdictions, in alignment with similar initiatives such as the "1+ Million Genomes", UK Biobank and the European Health Data Space: "Several real-world, use-case studies will showcase the efficacy of NextGen tools and will be incorporated into the NextGen Pathfinder framework, comprising five collaborating clinical sites. For example, we will jointly work on refined risk stratification in CVD, prediction of future adverse events, response to drugs, etc. NextGen, funded as a flagship EU project, will serve as a self-contained data ecosystem and a comprehensive proof of concept for the implementation of AL/ML technologies in personalised CVD medicine" says the Karolinska Institutet PI for this project, associate professor and CMM group leader Ljubica Matic.

The large NextGen consortium includes also the Earlham Institute (UK), Wellspan Health (USA), Queen Mary University of London (UK), Scuola Universitaria Professionale della Svizzera Italiana (CH), EURECOM (FR), Göthe Universitat Frankfurt (DE), HUS (FI), University of Virginia (USA), Technical University Münich (DE), European Society of Cardiology (FR), Human Colossus



Ljubica Matic and Ulf Hedin. Photo: Private

Foundation (CH), HL7 International Foundation (BE), HIRO Microdatacenters B.V. (NL), Drug Information Association (CH), MyData Global (FI), DPO Associate Sarl (CH), DataPower Srl (IT), LiKE Healthcare Research Gmbh (DE), NEBS (BE).

More information on the NextGen project can be found on the forthcoming website: www.nextgentools.eu and European Society of Cardiology (ESC) news platform https://www.escardio.org/The-ESC/Press-Office/ Press-releases/heart-patients-set-to-receive-treatmenttailored-to-their-genetic-and-health-inf



New CMMers



Daphne Chen is a master student from the Biomedical Sciences program at Leiden University in the Netherlands, and she has started her internship in Helena Harris' research group. She will be working on investigating the juvenile idiopathic arthritis associated neuroinflammation under the supervision of PhD student Xingzhao Wen.



Merel Sijbranda has started a PhD in Karine Chemin's Team. She will work on "Tissue-resident memory T cells biology in rheumatic diseases". Merel performed her master thesis at CMM.



Dr. Henrique Hadad is a new postdoc in the Team of prof. Ola Nilsson. Dr. Hadad graduated in Dentistry and pursued a PhD in Oral & Maxillofacial Surgery São Paulo State University, Brazil. Henrique 's expertise lies in the study of osteonecrosis of the jaw and therapeutic interventions to prevent it. Recently, he completed a Research Fellowship at the Massachusetts General Hospital in Boston, USA, where he delved into tissue engineering and cartilage repair, expanding his horizons in the field. His primary areas of interest encompass bone and cartilage remodeling, biomaterials, bone grafts, and bone and cartilage biology.





New groups moving in

This summer, five new research groups with the focus on lung medicine, are moving to CMM, floor 02 in the L8 building. The new CMM Group Leaders are Apostolos Bossios, Anders Lindén, Magnus Sköld, Craig Wheelock and Åsa Wheelock. Their research groups will be presented in upcoming issues of CMM News.











Apostolos Bossios.

Mag

Magnus Sköld

Craig Wheelock

Åsa Wheelock

Appointments

Anders Lindén

New CMM Group Leader



Volker Lauschke has been appointed new CMM Group Leader as of April 19th 2024.

Volker Lauschke. Photo: Stefan Zimmerman

New CMM Team Leader



Maurice Michel. Photo: Stefan Zimmerman

Maurice Michel has been appointed CMM Team Leader within Michael Sundström's Group as of May 23rd 2024.



Funding and Grants

Miranda Stiernborg receives a postdoc grant from the Swedish Research Council



Miranda Stiernborg defended her PhD thesis in March this year, with CMM Group Leader Catharina Lavebratt as main supervisor. She has now received a postdoc grant from the Swedish Research council (Vetenskapsrådet) consisting of SEK 1,300,000 per year for three years. During her postdoc she will work on a project titled "Recurrent urinary tract infections in women despite antibiotic treatments: Novel tools uncovering microbial-host dynamics."



Funding and Grants

CMM researcher Harald Lund is one of the awardees of this year's StratNeuro Startup Grant which is intended to support outstanding Neuroscience researchers at the beginning of their careers. Each funded project will receive SEK 500,000/year for a period of two years.

Harald Lund, who belongs to the Department of Physiology and Pharmacology, received the start-up grant for a project titled "Macrophages regulating homeostasis and breakdown of the blood-nerve barrier".

In an article published on the Karolinska Institutet website, by communications officer Charlotte Brandt, Harald Lund described his research as follows:

"Sensory neurons are some of the longest cells in the body. They have peripheral axons extending into skin, muscle or bone and central axons innervating the spinal cord. Their neuronal cell bodies, however, are collected in dorsal root ganglia (DRG). DRG are peculiar in that they lack a conventional blood-nerve barrier. They are highly vascularized, their blood vessels are permeable to blood proteins and the vasculature is guarded by an active immune cell network.

I am interested in understanding how the vascular, immune and neuronal cells interact in the DRG to maintain homeostasis. I am also interested in understanding whether manipulating the blood-DRG barrier can be a strategy to treat disorders where sensory neurons are damaged or destroyed. One such example is chemotherapy-induced peripheral neuropathy.

This grant comes at a critical time point as I am building up my own research group. It will help me employ a PhD student that can work on the project. The grant also means being part of the StratNeuro network which I am excited about."







Grants from Reumatikerförbundet

Reumatikerförbundet allocates over 15 million kronor for research on rheumatic diseases in 2024. Out of a total of 98 approved projects, 34 are located at the Karolinska Institutet, of which 16 are at CMM.

Here is a list of the awardees from CMM and their awarded projects (Swedish titles):

Begum Horuluoglu

Karolinska Institutet, Department of Medicine, Solna, Division of Rheuma-tology.

- Cellulär mekanism av autoimmun muskelinflammation och utvecklingen av en musmodell

Bence Rethi

Karolinska Institutet, Department of Medicine, Solna, Division of Rheuma-tology.

 Autoantikroppar och utveckling av reumatoid artrit - molekylära mekanismer och nya behandlingsmöjligheter

Caroline Grönwall

Karolinska Institutet, Department of Medicine, Solna, Division of Rheuma-tology.

- B-celler och autoantikroppar vid reumatisk sjukdom – kartläggning av komplexa interaktioner

Dionysis Nikolopoulos

Karolinska Institutet, Department of Medicine, Solna, Division of Rheuma-tology.

- Precisionsmedicin vid neuropsykiatrisk systemisk lupus erythematosus (PreNeuroLup)

Helena Erlandsson Harris

Karolinska Institutet, Department of Medicine, Solna, Division of Rheuma-tology.

- Att förstå orsakerna till ledgångsreumatism hos barn

Ingrid Lundberg

Karolinska Institutet, Department of Medicine, Solna, Division of Rheuma-tology.

- Sjukdomsmekanismer och behandlingseffekter vid kronisk reumatisk muskelinflammation, myosit

Ioannis Parodis

Karolinska Institutet, Department of Medicine, Solna, Division of Rheuma-tology.

- Studier för att optimera användningen av biologisk terapi samt monitorering, behandlingsutfall och långtidsprognos vid systemisk lupus erythematosus och lupusnefrit

Jon Lampa

Karolinska Institutet, Department of Medicine, Solna, Division of Rheuma-tology.

 - Kvarstående smärta och trötthet trots anti reumatisk behandling, en epidemiologisk och mekanistisk kartläggning vid tidig RA

Karin Lodin

Karolinska Institutet, Department of Medicine, Solna, Division of Rheuma-tology.

- Biomarkörer och prognostiskt verktyg för prediktion av klinisk förbättring av myosit

Karin Lundberg

Karolinska Institutet, Department of Medicine, Solna, Division of Rheuma-tology.

 Om uppkomst och funktion av autoantikroppar i reumatoid artrit – studier av en möjlig koppling till mikrober

Karine Chemin

Karolinska Institutet, Department of Medicine, Solna, Division of Rheuma-tology.

- Hur överlever T-celler vid inflammation? - Metabolisk kartläggning av vävnadsinfiltrerande T-celler i reumatiska sjukdomar



Lina Marcela Diaz Gallo Norlén

Karolinska Institutet, Department of Medicine, Solna, Division of Rheumatology.

- Ett nytt perspektiv att undergruppera systemisk lupus erythematosus genom att integrera genetik och klinisk information

Marie Wahren-Herlenius

Karolinska Institutet, Department of Medicine, Solna, Division of Rheuma-tology.

 Sjögrens syndrom - kliniska och immunologiska studier

Per-Johan Jakobsson

Karolinska Institutet, Department of Medicine, Solna, Division of Rheumatology.

 Tidig diagnostik och tidig behandling vid reumatisk sjukdom

Vivianne Malmström

Karolinska Institutet, Department of Medicine, Solna, Division of Rheumatology.

- Lymfocyters betydelse vid inflammatorisk reumatisk sjukdom

Lars Alfredsson

Karolinska Institutet, Institute of Environmental Medicine/ Department of Clinical Neuroscience.

- Betydelsen av påverkbara levnadsvanor/arbetsmiljöfaktorer för insjuknande och förlopp av reumatoid artrit - en studie av levnadsvanors/ arbetsmiljöfaktorers påverkan på behandlingsresultat i vården.



CMMer Daniel Johansson and CEO Maria Knudsen holding the Abbvie Scandinavian Golden Ticket award.

Abbvie Scandinavian Golden Ticket award to CMM research spin-off AAX Biotech AB

AWARDS

AAX Biotech AB, a spin-off from academic research work by Daniel Johansson and Mats Persson at CMM:01, recently won the Abbvie Scandinavian Golden Ticket award in Lund. AAX Biotech AB develops proprietary technologies that solve unmet needs in the development of next-generation antibody therapeutics. Currently, they offer the Seqitope[™] technology, which is used to resolve in detail epitope-binding properties at an early stage, as well as Opti-mAb[™], which is a molecular stabilization strategy for scFv antibodies.

Antibodies have followed CMM Team Leader Mats Persson throughout his research career. During these years he has had the opportunity to experience the development of different techniques for studying them.

"We have worked with cloning and characterizing human monoclonal

antibodies in our lab at CMM for many years, and in one project we had considerable trouble with epitope mapping by HDX-MS of antibodies to a bacterial toxin. This mass-spectrometry based method requires protein in a high concentration, which for certain proteins can be a huge challenge for researchers to obtain. So, Daniel designed a new method based on mutational scanning and phage display, which worked surprisingly well and solved the problems we had had with the epitope mapping. AAX Biotech now provides this analysis, Seqitope, as a fee for service, mainly to biopharma companies," says Mats Persson

"Similarly, we and many others have experienced much grief when working with so called single-chain-Fv antibodies, a mini-format of the antibody molecule, since they often aggregate, are hard to express and sometimes are unstable. Here we could also find an invention that has general application to scFvs regardless of clone or species, resulting in increased expression, higher stability and that their tendency to aggregate is abolished. In 2020 we formed AAX Biotech around these two inventions, "Segitope" and "Opti-mAb", here at CMM. We hope that winning the Abbvie Scandinavian Golden Ticket will give additional traction in promoting our services and know-how, and lead to new interactions with the antibody research community in general," Mats Persson concludes.

The AbbVie Scandinavia Golden Ticket is awarded to one early-stage company developing novel, transformational therapies for immunology, oncology, neuroscience, eye care or aesthetics.



Publications

CMMers IN BOLD

Aouad K, de Wit M, Elhai M, Benavent D, Bertheussen H, Zabalan C, Primdahl J, **Studenic P**, Gossec L. Patient research partner involvement in rheumatology research: a systematic literature review informing the 2023 updated EULAR recommendations for the involvement of patient research partners. *Ann Rheum Dis.* 2024 May 8 doi:10.1136/ard-2024-225567.

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Microneedle patch can detect early signs of skin cancer

PUBLICATION

Researchers at CMM and Karolinska Institutet have developed a new method for detecting malignant melanoma. A new type of patch equipped with microneedles can identify the biomarker tyrosinase directly in the skin, according to a study published in Advanced Materials.

The patch is equipped with microneedles that can detect tyrosinase, an enzyme that is an important biomarker for malignant melanoma. By measuring the enzyme's levels directly in the skin, researchers can quickly identify changes linked to the disease.

"We used human tissue from healthy individuals. By applying tyrosinase directly to the skin, we were able to mimic skin cancer," explains the study's last author Onur Parlak, CMM Team Leader and Associate Professor at the Department of Medicine, Solna, Karolinska Institutet, and continues:

"This is an important advance to improve skin health monitoring and can also be used to screen other biomarkers through a simple change in design."

Malignant melanoma is the most serious form of skin cancer and the fastest growing cancer. The study shows that the new patch could be an alternative to current diagnostic methods, leading to earlier detection and treatment of malignant melanoma. The researchers hope their work will help reduce the number of procedures and improve patients' quality of life.

PUBLICATION: Poursharifi N, Hassanpouramiri M, Zink A, Ucuncu M, Parlak O. Transdermal sensing of enzyme biomarker enabled by chemo-responsive probe-modified epidermal microneedle patch in human skin tissue. *Advanced Material*, online May 11, 2024, doi: 10.1002/ adma.202403758



Onur Parlak. Photo: Magdalena Lindén

"Our method is less invasive and has the potential to provide faster and more reliable results compared to traditional biopsies," says Onur Parlak:

"Our goal is to continue developing and improving this technique to offer more accurate and painless diagnostics", concludes Onur Parlak.

See the study for how it was funded and possible conflicts of interest.



CMM Events and Outreach

Andy Feinberg speaks about non-Mendelian inheritance of DNA methylation patterns

CMM Seminar Series



Dr. Andy Feinberg. Photo: Michael Sundström.

On June 14th, CMM arranged the first event within the new CMM Seminar Series format.

The invited speaker, Andrew (Andy) Feinberg, Bloomberg Distinguished Professor at Johns Hopkins University, is a pioneer in the field of epigenetics in general, and he is considered the founder of the field of cancer epigenetics, having discovered altered DNA methylation in cancer. His seminar at CMM, titled ' Widespread non-Mendelian inheritance of DNA methylation patterns', attracted a broad variety of researchers from CMM, different departments at Karolinska Institutet, as well as SciLifeLab.

After the seminar, the participants were given the opportunity to continue scientific discussions, mingle and network during a reception with some drinks and light bites outside the CMM Lecture Hall.



Would you like to nominate a speaker for the CMM Seminar Series?

You are very much welcome to nominate excellent Swedish and/or international scientists that could be of broader scientific interest to the CMM community.

The nominations should include a brief description of the speaker's scientific profile and relevance to the CMM scientific community (not to exceed more than one page).

Please send your nominations to CMM Communication communication@cmm.se (no specific deadline). Selection of speakers will be made by the CMM Steering Group.

CMM will (together with the nominator) arrange a scientific programme for the invited speaker, hosting the seminar as well as providing the opportunity for networking reception after the talk, with some drinks and light bites. For a selected number of guests/speakers CMM can also contribute towards travel and accommodation costs if required.



CMM Events and Outreach

The 3rd ESVS Translational Spring Meeting 2024

On June 3rd and 4th, international vascular surgeons, scientists and trainees gathered in the Sune Bergström Auditorium to present and discuss translational vascular research.

This was the third time the Vascular Surgery group at the Department of Molecular and Medicine, Karolinska Institutet, including Ulf Hedin's and Ljubica Matic's CMM Groups, hosted the meeting, in 2020 in a virtual format, in 2022 and this year in the welcoming venue of Bioclinicum. The initiative by the European Society for Vascular Surgery (ESVS) to start up this bi-annual event in 2020 was inspired by a series of similar meetings, 'Bringing Basic Science into Clinical Practice', arranged by the Vascular Surgery group 20 years ago, in an attempt to strengthen basic and translational science within the society, and bridge the gap between basic and clinical researchers.

This years' program was dedicated to 'Frontiers in Precision Medicine for Peripheral Vascular Disease'. The meeting started with two interactive workshops, highlighting the concept of translational research with an image processing workshop and a biobanking workshop in collaboration with the KI Biobank Core Facility. The meeting then continued with five separate scientific sessions focusing on the essential components of the concept of personalized medicine, including pathophysiology of atherosclerosis and aneurysm disease, genetics in disease prediction, plasma and imaging biomarkers, computational medicine, and clinical



Poster session at the 3rd ESVS Translational Spring Meeting in the Sune Bergström Auditorium, Bioclinicum.



Invited speakers and abstract presenters at the 3rd ESVS Translational Spring Meeting in the Sune Bergström Auditorium, Bioclinicum.

implementation. Each one included lectures by keynote speakers, followed by oral presentations of selected abstracts to complement the theme of the session.

Additionally, three separate poster sessions were arranged, which incited numerous scientific discussions on novel translational research projects that carried over into coffee and lunch breaks. At the end of the meeting, awards were presented to the best abstract (Julie Csoré, USA), best poster (Melody Chemaly, Sweden) and best oral presentation (Ravindhran Bharadhway, UK). The meeting attracted approximately 100 scientists from around the world, including delegates and presenters from South America and South Korea. The participants got to enjoy a lively atmosphere of discussions and scientific networking, accompanied by sunny Stockholm weather.



Melody Chemaly, Karolinska Institutet, was awarded for best poster.



Upcoming Events

Cardiovascular Research Retreat

from molecule to medicine

November 28 - 29, 2024

The program includes international speakers and short talks selected from submitted abstracts

Preliminary program and abstract deadlines to be communicated soon!





We wish you a great summer!

Next deadline for sending in contributions to CMM News: 27th of August

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