

CMM News



Page 2-4

More than 25 years of translational research at CMM - A dream that became a reality thanks to donations



Page 7-8

EU funding for prediction of risk and severity of immune diseases using AI




Page 15-16

Publication: Immune cells in the liver can eat up 'bad cholesterol'



Download this
newsletter here

Editor: Magdalena Lindén
Layout: Edna Fagerstedt



More than 25 years of translational research at the Center for Molecular Medicine

- A dream that became a reality thanks to donations

CMM EVENT

On February 22nd CMM hosted an event for donors and other stakeholders, show-casing the center's translational research and unique scientific environment – a result of more than 25 years of fruitful collaborations between basic researchers, clinicians and patients at Karolinska Institutet and the Karolinska University Hospital and elsewhere. The program ended with an enjoyable networking dinner and a beautiful view over Stockholm at the Svarta Råfven restaurant in Aula Medica.

In 1994 the Stockholm County Council instituted the Center of Molecular Medicine Foundation with the aim of building a translational research center which was finished in 1997. The research at CMM is driven by a close partnership between the Karolinska University Hospital and Karolinska Institutet and combines trans-

lational and basic science by providing a meeting place for university and hospital-based researchers. Donations from foundations, companies and patient organizations formed the basis for the establishment of the CMM foundation, the purpose-built research building and associated research infrastructures.

By organising a half-day event with presentations, a tour and a networking dinner, the CMM Foundation wished to thank the donors, and show them, as well as other stakeholders, some examples of what CMM has achieved so far and where the research center is heading.

Among the guests, were representatives from Swedish public and private funding agencies, several large pharma companies, policy-makers and patient organisations. A specially invited guest speaker was Siv Andersson, professor at Uppsala University and Head of Basic Research at the Knut and Alice Wallenberg's Foundation (KAW), who held a much-appreciated presentation about Knut and Alice Wallenberg Foundation's initiatives in life science.



Top: Mingling with the guests and CMM researchers outside the lecture hall during the coffee break. Bottom: Peder Olofsson, Siv Andersson and Maja Jagodic presenting during the CMM 25+ years event.

The event started off with an introduction by Liselotte Jansson, chair of the CMM Foundation, where she guided the listeners through the vision, mission and history of CMM. Michael Sundström, the director of CMM, then presented where the research center is at today and the way forward.

Siv Andersson, provided the listeners with insights into the current strategic initiatives of KAW, one of the largest private funders of research in Europe. The scientific highlights consisted of talks from the CMM faculty: Maja Jagodic, Peder Olofsson and Ingrid Lundberg, who talked about MS genetics, neural regulation of inflammation, and patient benefit of myositis research, respectively.

One of Ingrid Lundberg's patients, Gunilla Billing, was invited to take part in the presentation. For several years she had suffered from a treatment-resistant form of myositis and could now share with the audience how



Gunilla Billing receives flowers from Michael Sundström, thanking her for sharing her story during the CMM event. Also on the photo: Gunilla's doctor, Ingrid Lundberg.

myositis research at CMM had led to the finding that she belonged to a subgroup of patients characterized by a specific type of antibodies. This permitted the testing of a treatment that she would finally respond to and that has led to a significant reduction of the myositis-related symptoms and disabilities.



The tour of CMM included visits to the major core facilities, viewing of the freezer hotel that harbors millions of biobank samples, as well as a presentation of the works of art decorating the CMM building.



Moments from the buffet dinner that concluded the CMM 25+ years event.

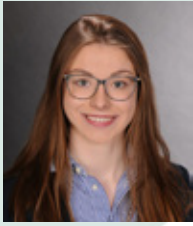
After a tour of CMM consisting of four 'stations' where former CMM Directors together with scientific experts were hosts, the event participants crossed the Solna Road (Solnavägen) to Aula Medica and Restaurant Svarta Räfven where the evening was concluded with buzzing scientific and non-scientific conversations, while enjoying a buffet dinner and a beautiful night view of Stockholm from the 7th floor.

One more time, the CMM Foundation wishes to thank all the donors for enabling more than 25 years of constructing a flourishing translational research environment. CMM is an example of a success story built through collaboration. We hope that we can continue working together towards an even brighter future of patient benefits based on cutting-edge translational research.

Text: Magdalena Lindén
 Photos: Petter Stahre, Birdy Communications

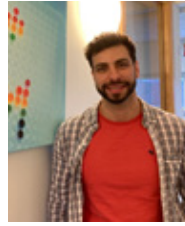
New CMMers

MAGDALENA PAOLINO'S TEAM



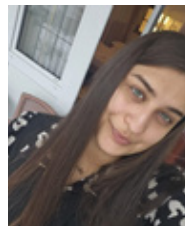
Sandra Künstle is a new PhD student in the Team of Magdalena Paolino. Her project aims to decipher the role of atypical ubiquitin chains in T cells. She completed her Master's degree in Biochemistry at the Technical University of Munich (TUM) but performed her master's thesis abroad at Karolinska Institutet. In her thesis, she explored the role of deubiquitinases in regulating cancer metabolism and cancer cell growth. She is now motivated to further explore the interesting field of ubiquitination, an essential post-translational modification, in the context of T cells and T-cell-dependent pathologies during her PhD.

SVEN-CHRISTIAN PAWELZIK'S TEAM



Miguel is a new postdoc in the Team of Sven-Christian Pawelzik. Miguel graduated with a PhD from the University of Geneva, Switzerland, on the phenotypic plasticity of smooth muscle cells in atherosclerosis, which may be exploited to stabilize atherosclerotic lesions. As postdoc, he is going to explore how smooth muscle cells respond to different lipid mediators during the resolution phase of cardiovascular inflammation.

AISHA AHMED'S TEAM



Melisa Faydaver, is a visiting PhD student from Romania, currently conducting research on tissue regeneration, with a specialization in tendon tissue, while working in Italy. She will be at CMM in Aisha Ahmed's Team until July for an exchange program.

ROBERT HARRIS' GROUP



Stefan Bencina is a new PhD student in Bob Harris' Group. After his Master's degree in Biomedicine at the University of Milan, he came to Karolinska Institutet as an Erasmus Student for a one-year traineeship where he started working with placenta stem cells. Now he is joining Bob Harris' group and will focus on evaluating the therapeutic potential of amniotic epithelial cells (AECs) in mouse models of ALS.

PEDER S. OLOFSSON'S GROUP



Anne-Sophie Haller is a new masterstudent from Switzerland in Peder S. Olofsson's Group. She completed her Bachelor's in Pharmaceutical Sciences at ETH Zurich. Her master thesis project is focused on neuroimmune interactions with hepatic stellate cells.

New CMM Group Leaders



Christopher Sundling is appointed CMM Group Leader as of 24 January 2024.



Carmen Gerlach is appointed CMM Group Leader as of 6 March 2024.



Volker Lauschke is appointed CMM Group Leader as of 19 April 2024.

Appointments

Göran K. Hansson is appointed honorary member of the American Society of Clinical Investigation

The American Society of Clinical Investigation, ASCI, has appointed Göran K. Hansson as an honorary member at the society's annual conference in Chicago on April 5-6.

Founded in 1908, ASCI is one of America's oldest and most respected medical research organizations. Its mission is to support and provide a forum for medical, and above all, clinical research. It publishes the *Journal of Clinical Investigation*, JCI, and a series of prizes for medical research efforts.

Honorary members of ASCI are individuals who have made important contributions to the society's goal, to increase knowledge of diseases

and develop new treatment options through research. Göran K. Hansson was nominated in particular for his discovery of the role of inflammation in atherosclerosis and his efforts to identify new therapeutic options in cardiovascular disease.

CMMer Göran K. Hansson, is professor of cardiovascular research at the Department of Medicine Solna, Karolinska Institutet, member of the Swedish Royal Academy of Sciences and the Academia Europaea. He has previously been permanent secretary of the Swedish Academy of Sciences and chairman of the Nobel Committee for Physiology or Medicine.




Göran K. Hansson. Photo: Stefan Zimmerman.

New docent in physiology



Zhichao Zhou was appointed associate professor (docent) in physiology at the Department of Medicine Solna on February 13th 2024.

Zhichao Zhou. Photo: Private.



EU funding for prediction of risk and severity of chronic immune-mediated diseases using AI

FUNDING

Around 10% of the European population has some form of chronic inflammatory disease. Researchers from CMM are coordinating the WISDOM project which intends to apply AI models to better predict and manage chronic immune-mediated diseases, mainly multiple sclerosis. The project was granted approximately €10 million from Horizon Europe's Pillar II, of which the Karolinska Institutet-based part has received €2.3 million.

The WISDOM project has been designed to enable integration of medical and research data, secure data sharing, and leverage responsible state-of-the-art artificial intelligence (AI)-mediated models with the aim of mitigating the impact of chronic immune-mediated diseases (CIMDs), mainly multiple sclerosis, but also rheumatoid arthritis and myasthenia gravis.

- 'Using AI, we will transform complex biological information from existing data sources into clinically applicable models. If we can identify and treat patients with

chronic inflammatory diseases at an earlier stage, there is a good chance of slowing the progression of the disease and reducing symptoms and relapses,' says CMM Group Leader Ingrid Kockum, Professor of Genetic Epidemiology at the Department of Clinical Neuroscience at Karolinska Institutet and principal investigator of the WISDOM project.

WISDOM received €10 million (of which €2.3 million was granted to Karolinska Institutet) within the framework of Horizon Europe's Pillar II - Global Challenges and European Industrial Competitiveness. To be granted funding, the research projects must also be conducted in partnerships involving not only academia, but also industry, authorities, patient organizations and other important stakeholders.

Karolinska Institutet is the coordinator of WISDOM and a total of three departments are involved in the project, which is carried out with partners from nine countries, including universities, companies, patient organizations and legal experts. A majority of the project partners from the Department of Clinical Neuroscience at Karolinska Institutet, are also CMM researchers, such as Ingrid Kockum and her research group, as well as Narsis Kiani, Maja Jagodic, Fredrik Phiel and Susanna Brauner.

EU funding for prediction of risk and severity of chronic immune-mediated diseases using AI

The project started on December 1, 2023 and will run for five years. Building these AI models requires an extensive amount of personal data, which needs to be managed in accordance with the GDPR. Therefore, the project will also identify solutions that can contribute to increased and secure data sharing, not only within an organization but also across national borders.

- 'In the next phase, we will use the models in a study involving first-degree relatives of people with multiple sclerosis, in order to predict the risk of relatives being affected. One hope is that the models can be applied to other diseases in the future,' says Ingrid Kockum.

The project partners foresee that the success of WIS-DOM will have far-reaching implications for chronic disease management and the use of health data for research and innovation, benefiting patients, healthcare providers, and society.



Ingrid Kockum. Photo: Creo Media Group.

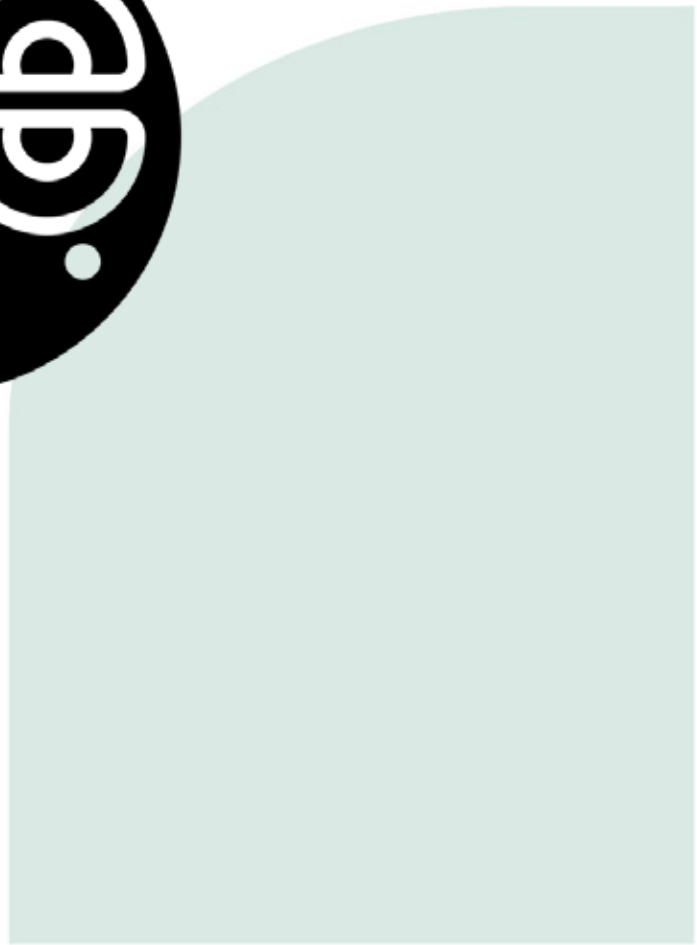
Grant for reparative medicine

FUNDING



Eduardo Villablanca. Photo: Magnus Begström, Knut och Alice Wallenbergs Stiftelse.

CMM Group Leader Eduardo Villablanca received a Ming Wai Lau center for Reparative Medicine seed grant (2024-2026), of SEK 3,000,000 for the project 'Progenitor Cell Location as Determinant of Fate and Regeneration' in which he will collaborate with Maria Genander from the Department of Cell and Molecular Biology, Karolinska Institutet. The 2023 Ming Wai Lau Centre for Reparative Medicine (MWLC) Seed Grant Programme was established for researchers from Karolinska Institutet to fund and promote new research collaborations within stem cell differentiation, reprogramming and biomanufacturing toward translational application.



The Dark Immunome Project receives a donation from the af Jochnick Foundation

FUNDING

The immunome is the set of genes that code for proteins which constitute the immune system. Many genes that are associated with inflammatory and immune-related diseases have been identified but finding linkages between gene variants and diseases is only the start of a long process. We need to understand the biological consequences of the function of the gene variants, which proteins of the immunome are affected, what their role is in the disease and whether it possible to target them in order to treat or understand disease.

The majority of disease-linked gene variants have not been thoroughly studied, both because of the lack of high-quality research tools and because of the prevailing tendency to focus research on better-studied areas. Which potential therapeutic targets can be found within the yet unknown 'Dark Immunome'?

This question will be addressed within a research project that has been initiated at CMM where many research groups and teams harbor extensive resources for studies of inflammatory and immune-related diseases in terms of broad, as well as deep-going knowledge, patient material, and technologies.

In the pilot phase of the Dark Immunome project, six target proteins, identified from work by CMM scientists, and linked to diseases within their areas of interest (including MS, IBD, cardiovascular/inflammatory diseases, RA and neuroinflamma-



tion) has been selected in order to seed the first proof of concept studies. For each of the proteins a 'Functional Target Enabling Package' will be developed. It consists of a relevant subset of research tools needed to test therapeutic hypotheses: What would be the consequences of modulating the

target protein in cells, tissues and organisms?

One of the first donors that supported research positions at CMM during its first years of existence as a translational research center is the af Jochnick Foundation. Now the foundation has granted a donation

'We are extremely pleased that the af Jochnick Foundation agreed with our view on the future value of targeting the truly understudied.'

Michael Sundström, CMM Director

The Dark Immunome Project receives a donation from the af Jochnick Foundation

of SEK 2,500,000 to support the pilot phase of the Dark Immunome project which is planned to run for up to 30 months.

The project is coordinated by CMM and headed up by Team Leader Opher Gileadi in Michael Sundström's Group. Current collaborators from CMM include Maja Jagodic and Eduardo Villablanca Groups. There are also other partners at Karolinska Institutet, such as the Carl

Sellgren group, as well as research groups from the University of Oxford.

In subsequent phases the collaborations will be broadened to include companies and more universities in the Dark Immunome Project.

- 'We are extremely pleased that the af Jochnick Foundation agreed with our view on the future value of targeting the truly understudied drug targets. In general, getting support

for the obvious, that is to focus your efforts where much remains to be discovered, is unfortunately very difficult to obtain from conventional academic funding sources. The contributions from the af Jochnick Foundation will hopefully help triggering many additional donations and contributions for the project in the nearest years to follow!', says Michael Sundström, Director of CMM.

'The contributions from the af Jochnick Foundation will hopefully help triggering many additional donations and contributions for the project in the nearest years to follow!'



Translational Seed Funding Grant to Fredrik Wermeling and Richard Rosenquist Brandell

Fredrik Wemeling received a Translational Seed Funding Grant from Cancer Research KI together with Richard Rosenquist Brandell. The grant consists of SEK 1,500,000 for two years (plus 25% coverage of indirect costs for support activities at university and department levels).

The project titled 'CRISPR-based identification of combinatorial vulnerabilities and drug targets in chronic lymphoid leukemia' is described as follows by Fredrik Wermeling:

"Chronic lymphoid leukemia (CLL), a very heterogenous cancer diagnosis characterized by numerous genetically defined subpopulations. Together with Richard Rosenquist Brandell (MMK), a world-leading expert on CLL, we are going to try to identify drug targets that affect the response to currently used drugs (BTK inhibitors and BCL2 inhibitors), and if differences between the subpopulations of patients can be seen. The aim is to identify effective drug combinations and genetic diagnostic tests to stratify patients to the different treatments."



Fredrik Wermeling. Photo: Erik Holmgren

Characterization of immune cells in myositis

Begum Horuluoglu was granted SEK 400,000 from Åke Wiberg's Stiftelse for her project 'Characterization of antigen specific T cells in patients with myositis'. Together with post-doc Yue-Bei Luo as co-applicant, Begum also received SEK 250,000 from the KI Rheumatology Grant for their project 'Spatial characterization of infiltrating immune cells in muscle tissue of patients with idiopathic inflammatory myopathy'.



Publications

CMMers IN BOLD

Adams C, **Manouchehrinia A**, Quach HL, Quach DL, **Olsson T**, **Kockum I**, Schaefer C, Ponting CP, **Alfredsson L**, Barcellos LF. Evidence supports a causal association between allele-specific vitamin D receptor binding and multiple sclerosis among Europeans. *Proc Natl Acad Sci U S A*. 2024 Feb 20;121(8):e2302259121. doi: 10.1073/pnas.2302259121. Epub 2024 Feb 12.

Bansal R, **Torres M**, **Hunt M**, **Wang N**, **Chatzopoulou M**, **Manchanda M**, **Taddeo EP**, **Shu C**, **Shirihai OS**, **Bachar-Wikstrom E**, **Wikstrom JD**. Role of the mitochondrial protein cyclophilin D in skin wound healing and collagen. *JCI Insight*. 2024 Apr 2:e169213. doi: 10.1172/jci.insight.169213. Epub ahead of print.

Di Nunzio G, **Hellberg S**, **Zhang Y**, **Ahmed O**, **Wang J**, **Zhang X**, **Björck HM**, **Chizh V**, **Schipper R**, **Aulin H**, **Francis R**, **Fagerberg L**, **Gisterå A**, **Metso J**, **Manfé V**, **Franco-Cereceda A**, **Eriksson P**, **Jauhiainen M**, **Hagberg CE**, **Olofsson PS & Malin SG**. Kupffer cells dictate hepatic responses to the atherogenic dyslipidemic insult. *Nat Cardiovasc Res*, online 11 mars 2024, doi: 10.1038/s44161-024-00448-6.

Huang J, **Kockum I**, **Stridh P**. Recovering Misidentified Samples Through Genetic Discordance Clustering. *Curr Protoc*. 2024 Jan;4(1):e972. doi: 10.1002/cpz1.972.

Huang J, Tengvall K, Bomfim Lima I, Hedström AK, Butt J, Brenner N, **Gyllenberg A**, **Stridh P**, **Khademi M**, **Ernberg I**, **Al Nimer F**, **Manouchehrinia A**, **Hillert J**, **Alfredsson L**, **Andersen O**, **Sundström P**, **Waterboer T**, **Olsson T**, **Kockum I**. Genetics of immune response to Epstein-Barr virus: prospects for multiple sclerosis pathogenesis *In press Brain* **Johansson E**, **Alfredsson L**, **Strid P**, **Kockum I**, **Olsson T**, **Hedström AK**. Head trauma results in manyfold increased risk of multiple sclerosis in genetically susceptible individuals. *J Neurol Neurosurg Psychiatry*. 2024 Jan 11:jnnp-2023-332643. doi: 10.1136/jnnp-2023-332643. Online ahead of print.

Kmezic I, **Gustafsson R**, **Fink K**, **Svenningsson A**, **Samuelsson K**, **Ingre C**, **Olsson T**, **Hansson M**, **Kockum I**, **Adzemovic MZ**, **Press R**. Validation of elevated levels of interleukin-8 in the cerebrospinal fluid, and discovery of new biomarkers in patients with GBS and CIDP using a proximity extension assay. *Front Immunol*. 2023 Nov 23;14:1241199. doi:10.3389/fimmu.2023.1241199. eCollection 2023.

Kukanja P, **Langseth CM**, **Rodríguez-Kirby LAR**, **Agirre E**, **Zheng C**, **Raman A**, **Yokota C**, **Avenel C**, **Tiklová K**, **Guerreiro-Cacais AO**, **Olsson T**, **Hilscher MM**, **Nilsson M**, **Castelo-Branco G**. Cellular architecture of evolving neuroinflammatory lesions and multiple sclerosis pathology. *Cell*, March 20, 2024. DOI: <https://doi.org/10.1016/j.cell.2024.02.030>.

Kvedaraite E, **Lourda M**, **Mouratidou N**, **Düking T**, **Padhi A**, **Moll K**, **Czarnewski P**, **Sinha I**, **Xagoraris I**, **Kokkinou E**, **Damdimopoulos A**, **Weigel W**, **Hartwig O**, **Santos TE**, **Soini T**, **Van Acker A**, **Rahkonen N**, **Flodström Tullberg M**, **Ringqvist E**, **Buggert M**, **Jorns C**, **Lindfors U**, **Nordenvall C**, **Stamper CT**, **Unnersjö-Jess D**, **Akber M**, **Nadisauskaite R**, **Jansson J**, **Vandamme N**, **Sorini C**, **Grundeken ME**, **Rolandsdotter H**, **Rassidakis G**, **Villablanca EJ**, **Ideström M**, **Eulitz S**, **Arnell H**, **Mjösberg J**, **Henter JI**, **Svensson M**. Intestinal stroma guides monocyte differentiation to macrophages through GM-CSF. *Nat Commun* 2024 Feb 26

Lidströmer N, **Davids J**, **El Sharkawy M**, **Ashrafi H**, **Herlenius E**. Systematic review and meta-analysis for a Global Patient co-Owned Cloud (GPOC). *Nat Commun* 15, 2186 (2024). <https://doi.org/10.1038/s41467-024-46503-5>.

Monasterio G, **Morales RA**, **Bejarano DA**, **Abalo XM**, **Fransson J**, **Larsson L**, **Schlitzer A**, **Lundeberg J**, **Das S**, **Villablanca EJ**. A versatile tissue rolling technique for spatial-omics analyses of the entire murine gastrointestinal tract. *Nat Protocols*. In press.

Publications

CMMers IN BOLD

Neidhart S, Vlad B, Hilty M, **Asplund Högelin K**, Ziegler M, Berenjeno-Correa E, Reichen I, **Stridh P**, Jelcic I, **Khademi M**, **Kockum I**, Sospedra M, **Al Nimer F**, Martin R, Jelcic HLA associations of Intrathecal IgG Production Against Specific Viruses in Multiple Sclerosis *In press Ann Neurology*

Parodis I, **Lindblom J**, Barturen G, Ortega-Castro R, Cervera R, Pers JO, Genre F, Hiepe F, Gerosa M, Kovács L, De Langhe E, Piantoni S, Stummvoll G, Vasconcelos C, Vigone B, Witte T; PRECISESADS Clinical Consortium; Alarcón-Riquelme ME, Beretta L. Molecular characterisation of lupus low disease activity state (LLDAS) and DORIS remission by whole-blood transcriptome-based pathways in a pan-European systemic lupus erythematosus cohort. *Ann Rheum Dis*. 2024 Feb 19;ard-2023-224795. doi: 10.1136/ard-2023-224795.

Schäfer P, Dimitrov D, **Villablanca EJ**, Saez-Rodriguez J. Integrating single-cell multi-omics and prior biological knowledge for a functional characterization of the immune system. *Nat Immunol*. 2024, Mar 25

Sorini C, **Cardoso RF**, **Tripathi KP**, Mold JE, **Diaz OE**, Holender Y, Kern BC, Czarnewski P, Gagliani N, Villablanca EJ. Intestinal damage is required for the pro-inflammatory differentiation of commensal CBir1-specific T cells. *Mucosal Immunol*. 2024 Feb;17(1):81-93. doi: 10.1016/j.mucimm.2023.11.001. Epub 2023 Nov 10.

Spildrejorde M, **Samara A**, Sharma A, et al. Multi-omics approach reveals dysregulated genes during hESCs neuronal differentiation exposure to paracetamol. *iScience*. Oct 20 2023;26(10):107755. doi:10.1016/j.isci.2023.107755

Stiernborg M, Prast-Nielsen S, Melas PA, **Skott M**, Millischer V, Boulund F, Forsell Y, **Lavebratt C**. Differences in the gut microbiome of young adults with schizophrenia spectrum disorder: using machine learning to distinguish cases from controls. *Brain Behav Immun*. 2024 Mar;117:298-309.

Next deadline for sending in
contributions to CMM News:
30th of April 2024

Immune cells in the liver can eat up ‘bad cholesterol’



Hanna Aulin, Giada di Nunzio, Stephen Malin, Veronika Chizh, Xueming Zhang, Alina Li. Photo: Stefan Zimmerman.

PUBLICATION

A new publication from Stephen Malin’s lab at CMM and Karolinska Institutet, shows that Kupffer cells in the liver react to high cholesterol levels and eat up excess cholesterol. High LDL cholesterol causes damage to arteries and initiates atherosclerotic cardiovascular disease. The findings, published in Nature Cardiovascular Research, could potentially indicate new ways of preventing and treating cardiovascular and liver diseases.

Some of our organs, such as the beating heart or pumping muscles, have a high demand for energy. Fats, in the form of triglycerides, can be burned by these organs to provide fuel. These fats are produced in the liver, or absorbed from the intestines after a meal, and enter the blood as small particles together with cholesterol. The problem is that you can have too much of a good thing

and this cholesterol can build-up in places where they shouldn’t, and your arteries can start to become furry. This marks the onset of atherosclerotic cardiovascular disease, the primary underlying cause of heart attacks, strokes, and the leading cause of death worldwide.

What we didn’t know was how tissues respond over time. Does this bad cholesterol first start building plaques in your arteries, or does it begin causing damage throughout the body everywhere all at once? This is important, because we have traditionally seen atherosclerosis as disease that is focused on blood vessels. If many organs are being affected, then we need to consider the disease in a more holistic perspective.

To test this, we wanted to make a system where we could rapidly increase the bad cholesterol in the blood of mice. Essentially, we wanted to detonate a cholesterol-bomb and see what happened next. What we found is that the liver almost immediately responded to what we have termed the ‘dyslipidemic insult’. However, what surprised us was the type of cells that respond-



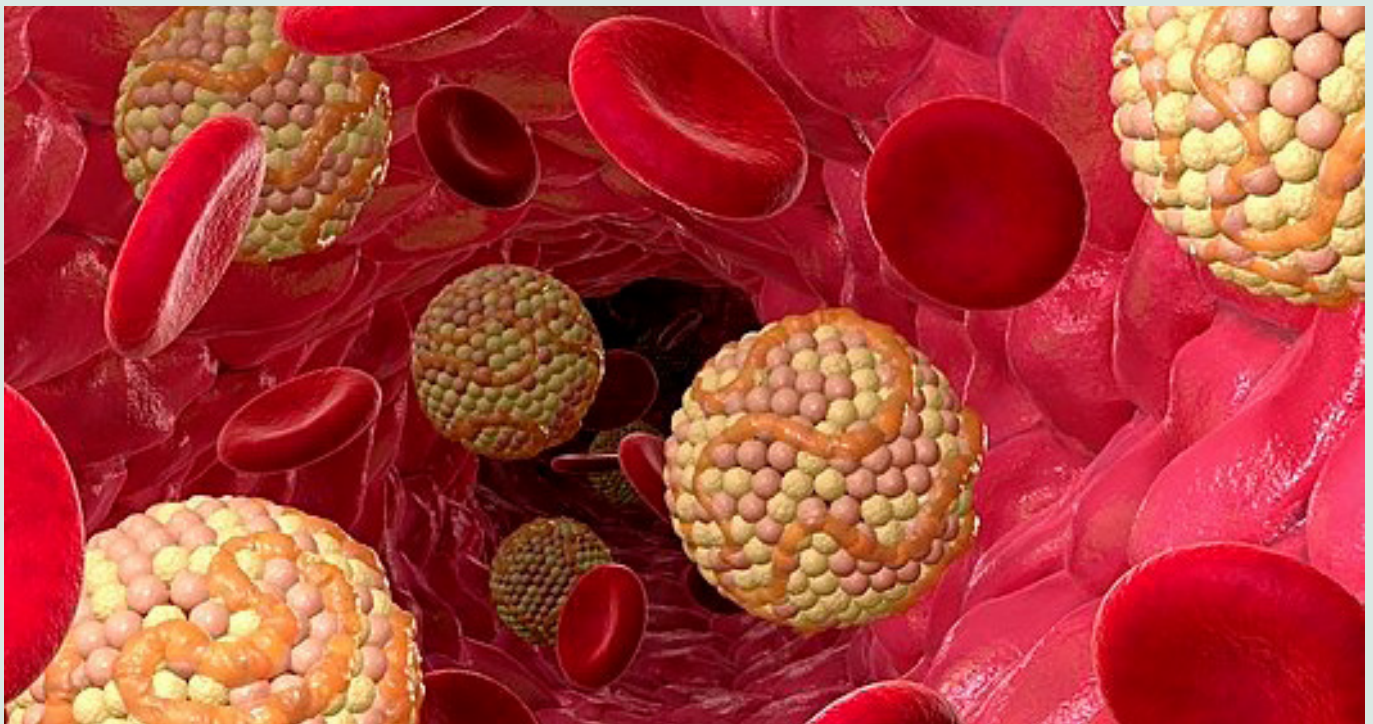
Immune cells in the liver can eat up ‘bad cholesterol’

ed. Instead of it being the classical liver cells, known as hepatocytes, it was a type of immune cell known as Kupffer cells. Kupffer cells are macrophages, an immune cell known for being an expert at recognising something as bad or dangerous and eating it up.

What our experiments are hinting at is that when we have too much of this bad cholesterol, it is not just your blood vessels that will get damaged but also your liver

will be affected at the same time. As with all scientific investigations though is that where you shine a light is where you make a discovery. Our next steps are to look at all the other organs and see if they are responding too. We hope that once we know this, we can try to figure out how the cells and tissues are talking to each other after being insulted, and then find out what this conversation means for cardiovascular and liver diseases.

PUBLICATION: Giada Di Nunzio, Sanna Hellberg, Yuyang Zhang, Osman Ahmed, Jiawen Wang, Xueming Zhang, Hanna M. Björck, Veronika Chizh, Ruby Schipper, Hanna Aulin, Roy Francis, Linn Fagerberg, Anton Gisterå, Jari Metso, Valentina Manfé, Anders Franco-Cereceda, Per Eriksson, Matti Jauhiainen, Carolina E. Hagberg, Peder S. Olofsson & Stephen G. Malin. Kupffer cells dictate hepatic responses to the atherogenic dyslipidemic insult. *Nat Cardiovasc Res*, online 11 mars 2024, doi: 10.1038/s44161-024-00448-6.



A Global Patient co-Owned Cloud



Image: Niklas Lidströmer (copyright).

PUBLICATION

In a recent article in *Nature Communications*, researchers from CMM introduce the concept of a Global Patient co-Owned Cloud (GPOC). Dr. Niklas Lidströmer and co-authors investigate the technical and security aspects of the GPOC, emphasizing its patient co-ownership model, cloud-based infrastructure, encryption, and blockchain protection. The vision of the authors is to promote the implementation of GPOC on a global level which they believe holds significant promise for the development and dissemination of artificial intelligence in medical science and healthcare.

Since 2010, Dr Niklas Lidströmer has been driving the vision of a cloud-based, blockchain-protected, encrypted, patient co-owned personal health record (PHR) platform. Initially known as GlobeDoc. For the past five years it has been known as the Global Patient co-Owned Cloud (GPOC). This initiative is promising for the devel-

opment and dissemination of artificial intelligence in medical science and healthcare. Dr Lidströmer is in Eric Herlenius' Group at CMM.

The recently published article investigates the technical and security conditions for a GPOC, emphasizing its patient co-ownership, cloud-based nature, encryption, and blockchain protection.

Cloud-based personal health records are on the rise globally. This article series introduces the concept of a GPOC of PHRs, consisting of five parts, with the current article focusing on systematic review and meta-analysis. It scrutinizes technical, computer scientific, and security-based prerequisites, analyzing twelve factors including data security, efficiency, cost, integrity, cryptography, and access. The study reveals a lack of prior publication on patient co-ownership of health data or PHRs, and an absence of a global standard in this area.

It also underscores the importance of patient co-ownership of health data. It presents a patient centric global PHR with co-ownership, facilitating patient insight, access, and active participation in healthcare. Additionally, the series suggests that patient co-ownership of health data could represent a new human rights entity. Technical and cryptological conditions are thoroughly examined, with a meta-analysis that highlights the

A Global Patient co-Owned Cloud

potential of a globally distributed, homomorphically encrypted, and blockchain-protected PHR where patients are co-owners.

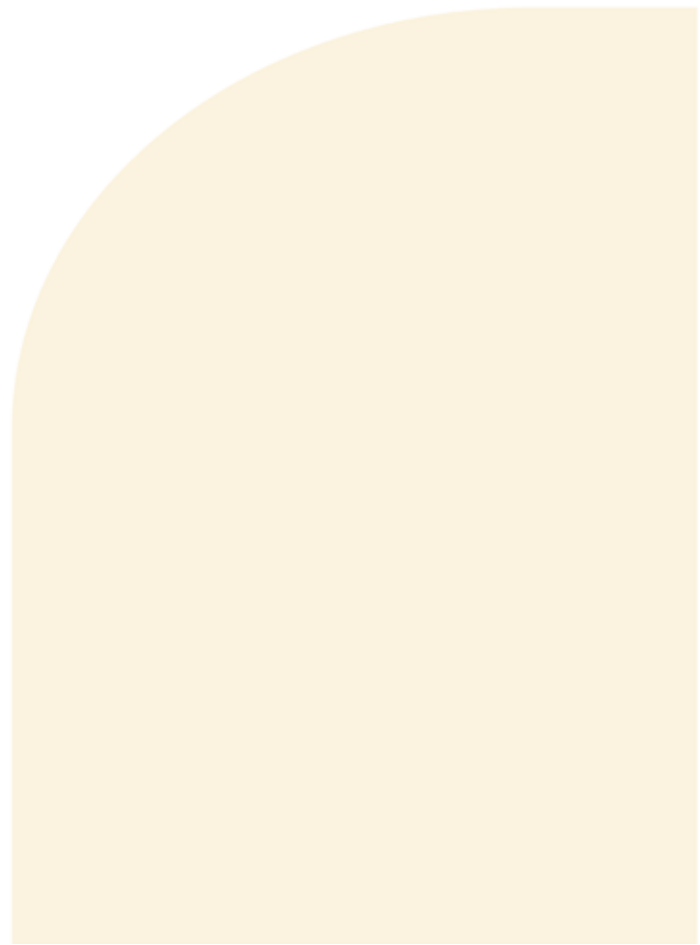
Conducted at the Karolinska Institutet University Library, the study involved a comprehensive review of 16,000 articles, followed by a meta-analysis—the first of its kind in this domain. Comparisons were made on encryption, cost (gas), performance, effectiveness, blockchain, data transfer, and other vital parameters impacting network function, stability, and security.

The GPOC series comprises four additional forthcoming articles. It begins with a global GPOC Survey among all the world's health ministries and major organizations, followed by a review of relevant ethics, policies, and regulations. Subsequently a Delphi Summit convened delegates worldwide to discuss the GPOC concept. Finally, a technical GPOC Sandbox is presented, built upon insights from the entire series and shared as open source for global experimentation, development, and realization of GPOC.

PUBLICATION: Lidströmer, N., Davids, J., ElSharkawy, M., Ashrafian, H., Herlenius, E. Systematic review and meta-analysis for a Global Patient co-Owned Cloud (GPOC). *Nat Commun* 15, 2186 (2024). <https://doi.org/10.1038/s41467-024-46503-5>.



Niklas Lidströmer. Photo: Private.



Upcoming events

RESEARCH LECTURE

16 May, 13:00

Research lecture on the glymphatic system

Nobel Forum, Nobels väg 1

Speaker: Maiken Nedergaard, M.D., D.M.Sc. professor at the Center for Translational Neuromedicine, University of Copenhagen

Topic: The Glymphatic System

Host: Eric Herlenius

After the lecture refreshments will be served in the Gallery, Nobel Forum

The speaker describes the research topic that she will present as follows:

We have recently described a macroscopic pathway in the central nervous system – the glymphatic system that facilitates the clearance of interstitial waste products from neuronal metabolism. Glymphatic clearance of macromolecules is driven by cerebrospinal fluid (CSF) that flows in along para-arterial spaces and through the brain parenchyma via support from astroglial aquaporin-4 water channels. The glymphatic circulation constitutes a complete anatomical pathway; para-arterial CSF exchanges with the interstitial fluid, solutes collect along para-venous spaces, then drain into the vessels of the lymphatic system for ultimate excretion from the kidney or degradation in the liver. The glymphatic system is only active during sleep. As such, this circulation represents a novel and unexplored pathway for understanding the biological necessity for sleep.

DISSERTATIONS

19 April, 9:00

Dissertation of Rika Kojima: Translational studies of glucocerebrosidase in Parkinson's disease

J3:14 Kerstin Hagenfeldt, Bioclinicum, Karolinska University Hospital Solna - and online

Opponent:

Agnete Kirkeby, Associate Professor, Department of Neuroscience, University of Copenhagen.

Principal supervisor:

Xiaoqun Zhang, Researcher, Department of Clinical Neuroscience, Karolinska Institutet

Co-supervisors:

Per Svenningsson, Professor, Department of Clinical Neuroscience, Karolinska Institutet

Ernest Arenas, Professor, Department of Medical Biochemistry and Biophysics, Karolinska Institutet

Examination Board:

Per Nilsson, Docent, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet

Sophia Schedin Weiss, Docent, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet

John Löfblom, Professor, Department of Protein Science, KTH



Upcoming events

DISSERTATIONS

26 April, 13:00

Dissertation of Philip Sarajlic: Physiological and lifestyle-related cardiovascular risk factors for vessels, ventricle, and valve

CMM Lecture Hall, Visionsgatan 18, L8:00, Karolinska University Hospital, Solna

Opponent:
Professor Christian Jung
University of Düsseldorf, Department of Cardiology,
Pneumology and Angiology.

Principal supervisor:
Professor Magnus Bäck, Karolinska Institutet, Depart-
ment of Medicine, Solna

Co-supervisors:
Associate Professor Susanna Larsson, Uppsala Univer-
sity, Department of Surgical Sciences.
Associate Professor Camilla Hage
Karolinska Institutet, Department of Medicine, Solna.

Examination Board:
Associate Professor Krister Lindmark, Karolinska Insti-
tutet, Department of Clinical Science.

Docent Bruna Gigante, Karolinska Institutet, Depart-
ment of Medicine, Solna.

Docent Andreas Martinsson, Sahlgrenska University,
Department of Cardiology.





Next deadline for sending in
contributions to CMM News:
30th of April 2024