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First molecule identified that promotes gut healing while inhibiting tumour progression



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**Editor:** Magdalena Lindén **Layout:** Edna Fagerstedt



## **18 CMMers receive Swedish Research Council Grants 2025**

The funds will finance projects, research constellations and positions within a wide range of basic medical and clinical research.



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## Project Grants in Medicine and Health



Lars Alfredsson is awarded a total of 3,000,000 SEK for the project "The role of environment and lifestyle factors in the onset and course of multiple sclerosis".



Ingrid Lundberg is awarded a total of 3,000,000 SEK for the project "Mechanisms of disease and treatment effects in rheumatic myositis".



Carolina Hagberg is awarded a total of 5,600,000 SEK for the project "Mapping the metabolic cooperation between adipocytes and endothelial cells to prevent obesity-associated disease".



Ida Nilsson is awarded a total of 5,600,000 SEK for the project "Anorexia nervosa - a developmental perspective involving hypothalamic appetite regulation and microglia dysfunction".



Ingrid Kockum is awarded a total of 5,600,000 SEK for the project "Improving multiple sclerosis prediction and prognosis; algorithmic approaches and biomarkers".



Peder Olofsson is awarded a total of 6,100,000 SEK for the project "Cellular and molecular mechanisms of neural control of inflammation and metabolism in cardiovascular disease".



Jon Lampa is awarded a total of 5,600,000 SEK for the project "Residual pain in rheumatoid arthritis - Treatment outcome after biological therapy and clinical significance of a newly discovered causal signaling pathway".



Volker Lauschke is awarded a total of 2,142,857 SEK for the project "Use of a novel 3D human liver system for prediction and understanding of liver toxicity of biologics".



John Pernow is awarded a total of 6,100,000 SEK for the project "The importance of erythrocytes as a mediator and treatment target in cardiovascular disease".



Richard Rosenquist Brandell is awarded a total of 5,600,000 SEK for the project "Mapping the complex molecular landscape of chronic lymphocytic leukemia: the road to precision medicine".



### **Project Grants in Medicine and Health**



Per Svenningsson is awarded a total of 5,600,000 SEK for the project "Receptor-mediated mechanisms in Parkinson's disease and depression".



Åsa Wheelock is awarded a total of 5,600,000 SEK for the project "Sub-phenotypes of CAL: A systems biology framework to map phenotypic and mechanistic subgroups of patients with chronic airway obstruction in never-smokers".



Fredrik Wermeling is awarded a total of 3,000,000 SEK for the project "Studies of neutrophil granulocytes in autoimmune joint inflammation".



Ning Xu Landén is awarded a total of 5,600,000 SEK for the project "Decoding the RNA regulome for human skin healing - towards a future in wound treatment".

### **Establishment Grants in Medicine and Health**



Harald Lund is awarded a total of 6,000,000 SEK for the project "Cellular and molecular mapping of the blood-nerve barrier in health and disease".



Gustavo Monasterio is awarded a total of 6,000,000 SEK for the project "Mapping the oral-gut connection in bowel disorders".



Kyla McKay is awarded a total of 6,000,000 SEK for the project "From predictors to precision medicine: Using regional health information for the study of multiple sclerosis".

### **Clinical Treatment Research**



Anna Färnert is awarded a total of 1,200,000 SEK for the project "Treatment of malaria in travelers in an era of increasing drug resistance".



### **New CMMers**



Paula Gigerl is a second-year biomedicine master student at Karolinska Institutet. She joined Maja Jagodic's group for a short project in November and will stay for the master's thesis until May 2025. She will work on epigenome targeting of smoking-associated genes in the context of Multiple Sclerosis together with Chandana Rao Prakash and Majid Pahlevan Kakhki under the supervision of Lara Kular. In her free time, she likes bouldering and running.

Annelien Hooijsma has started as a PhD student in the group of Vivianne Malmström. In the upcoming years she will be focusing on autoreactive T and B cells at onset of Rheumatoid Arthritis.

Rosalie van Hulst started her doctoral studies in the Carmen Gerlach group. She will be looking at CD8+ T cells during infections in both mice and humans. She studied in Groningen, the Netherlands previously for her Master's in Biomedical Sciences, but did her Master's internship at Biomedicum in the group of Gunilla Karlsson Hedestam.

Emmy Erskine recently joined the CMM as a new PhD student in the Translational Psychiatry lab, supervised by Dr. Ida Nilsson. Emmy obtained her Master's at Queen's University Belfast in Biochemistry before working as a research assistant at the University of Cambridge and is now thrilled to be joining the CMM at Karolinska Institutet for her PhD studies. Over the next 4 years she will be researching the neurobiology of anorexia nervosa with a particular focus on hypothalamic cell interactions, and aims to defend her thesis in the autumn of 2028.









## **New CMMers**



Mario Codemo recently joined the group of Carmen Gerlach as Research Assistant. Mario completed his PhD in microbiology and host-pathogen interactions at Karolinska Institutet in the group of Birgitta Henriques-Normark, where he characterized membrane vesicles from Streptococcus pneumoniae and investigated their potential use as vaccine candidates. Mario will help other members of the Gerlach group in different research projects dealing with CD8+ T cell responses to infection and cancer, as well as with laboratory management tasks.

Marina Galesic is a PhD student in Begum Horuluoglu's Team at CMM, studying myositits.





Tianxu Feng is a second-year master's student in Nutrition Science at KI. She started her master's thesis with Ida Nilsson's team in September. The main topic of her thesis is explicating the function of stem cell derived hypothalamic appetite regulating neurons in anorexia nervosa.



## **New CMM Team Leader**

APPOINTMENTS



Begum Horuluogu's research team. From the left: Yue-Bei Luo, Begum Horuluoglu, Martina Galesic and Andrea Kemp.Photo: Lina Marcela Diaz-Gallo.

Begum Horuluoglu has been appointed CMM Team Leader as of November 14th 2024.

Begum is an Assistant Professor at the Division of Rheumatology, Department of Medicine Solna, and is a part of Ingrid Lundberg's CMM Group.

Andrea Kemp (research assistant), Yue-Bei Luo (postdoc) and Marina Galesic (PhD student) are members in Begum Horuluoglu's CMM Team.



### Research on peripheral vascular disease receives SEK 22.5 million from MedTechLabs

#### FUNDING AND GRANTS

Ulf Hedin, CMM Group Leader and Professor of Vascular Surgery at Karolinska Institutet, and Christian Gasser, Professor of Biomechanics at KTH, are jointly leading a new research project focusing on technology to enable individual treatment of fatal forms of stroke and carotid artery disease. The project is now being granted research funding of SEK 4.5 million per year for five years by MedTechLabs.

The research project "Improving health care in peripheral vascular disease: from population-based to individualized decision-making" aim to improve diagnostics in important disease areas: peripheral vascular disease and epilepsy. In addition to a clear link to clinical application, the projects have great potential to contribute to better treatment of broad patient groups both in Sweden and internationally.

Stroke disease from carotid atherosclerosis, aortic aneurysm rupture and aortic rupture account for a significant proportion of cardiovascular disease mortality with major consequences for both individuals and society. Today, these diseases are managed with strategies based on population studies where the choice of treatment is based on algorithms that optimize treatment outcomes for many, but far from all, patients. New technologies for molecular, morphological, biomechanical and imaging analyses make it possible to profile patients to individualize their risk assessment and treatment.

The new project is based on a translational research platform in collaboration between the Vascular Surgery Department at Karolinska University Hospital, Karolinska Institutet, SciLifeLab and the Department of Materials



and Structural Mechanics, KTH Royal Institute of Technology. Initially, the researchers will develop molecular markers in blood, biomarkers, through advanced protein analysis for patients at high risk in each disease. In the next step, high-resolution imaging will be implemented to characterize in detail molecular, morphological and biomechanical features for risk assessment of disease expression. With this approach, patients with established clinical risk factors for unfavorable disease progression can be stepwise risk assessed and efficiently selected for appropriate treatment. This optimizes both individual survival and the use of health care resources.

"Our research project is based on an already well established collaboration between researchers at Karolinska Institutet, Karolinska University Hospital, SciLifeLab and KTH, which gives us stability and thanks to the large research grant we get a unique opportunity to develop precision medicine for patients with peripheral vascular disease", says Ulf Hedin, CMM Group Leader, senior physician and vascular surgeon at Karolinska University Hospital, Professor and research group leader of the Vascular Surgery group at the Department of Molecular Medicine and Surgery.



## Carmen Gerlach receives the Wallenberg Academy Fellows prolongation grant

#### FUNDING AND GRANTS

CMM Group Leader Carmen Gerlach was chosen as a Wallenberg Academy Fellow five years ago and now she has received a Wallenberg Academy Fellows prolongation grant for another five years. In her research, Carmen searches for better vaccines and cancer therapies inspired by the body's immune system.

CMM Group Leader Carmen is exploring the workings of our immune system. If we can learn from nature's own mechanisms, it may be possible to develop better vaccines and more effective immune therapies for cancer and various autoimmune diseases.

"What I wonder is how this system can respond so effectively to so many different kinds of attack – from virus infections to a tumor, parasite or bacterium." Therefore, Carmen Gerlach has decided to focus her research field of interest on the fundamental principles and mechanisms of T-cell immune reaction, with particular emphasis on CD8-T-cells.

Part of the research is now focusing on identifying and analyzing the behavior of the various cells in detail. Among other things, Gerlach wants to understand how important the absence or presence of certain groups of cells is to the immune system.





Carmen Gerlach's research group is using a number of techniques to map the origin and identity of the cells. These include flow cytometry and single-cell RNA sequencing. Much remains unknown about how cells acquire their different characteristics, but greater knowledge may even enable scientists to induce specific, desirable cells.

"The result may be better vaccines or therapies for autoimmune diseases, as well as more effective cancer therapies. But what drives me is not the idea of curing a given disease – I want to do as much as possible to understand the underlying biology in the hope that this will lead to major medical breakthroughs in the future." This text is based on a press release from the Knut and Alice Wallenberg Foundation.

Wallenberg Academy Fellows is a long-term program that addresses young researchers. In the end of the first five-year period the Wallenberg Academy Fellows can be nominated for another five years of funding. During 2024 were 15 researchers admitted a Wallenberg Academy Fellows prolongation grant.



## **Funding and Grants**

### The Heart-Lung foundation

#### **Project Grants**

Gunnar Nilsson is awarded a total of SEK 2,400,000 for the project "Deciphering phenotypical and functional human lung mast cell heterogeneity and its impact in asthma".

Stephen George Malin is awarded a total of SEK 2,400,000 for the project "How are atherosclerosis plaques formed and can they be reversed?".

Marianne van Hage is awarded a total of SEK 1,600,000 for the project "Clinical iImplications of IgE sensitization to the carbohydrate  $\alpha$ -Gal for respiratory and coronary artery disease".

Magnus Bäck is awarded a total of SEK 4,500,000 for the project "Stimulating resolution of inflammation for an optimized cardiovascular prevention".

#### **Research Position or Research Months**

Stephen George Malin is awarded a total of SEK 3,312,000 for the project "How are atherosclerosis plaques formed and can they be reversed?".

#### **Research Months for PhD Students**

Rebecka Hultgren is awarded a total of SEK 1,560,000 for the project "Hereditära aspekter av abdominellt aortaaneurysm".

Åsa Wheelock is awarded a total of SEK 800,000 for the project "CAL sub-phenotypes: A systems medicine framework for investigating molecularly & mechanistically distinct groups with chronic airflow limitations (CAL) in never-smokers".

Peder Olofsson is awarded a total of SEK 4 ,500,000 for the project "Neurophysiological regulation of immunometabolic niches in cardiovascular inflammation – The NERVICI initiative".

Marie Wahren-Herlenius is awarded a total of SEK 5,100, 000 for the project "Clinical and molecular pathogenesis of Kawasaki disease".

Begum Horuluoglu is awarded a total of SEK 552,000 for the project "Pathogenic role of autoantibodies in myositis associated interstitial lung disease: Mechanisms and functional implications".



## **Funding and Grants**

### Cancerfonden

Anna Lindstrand is awarded a total of SEK 1,200,000 for the project "Resolving structural variant complexity in hematological malignancies".

Ann Nordgren is awarded a total of SEK 3,000,000 for the project "Constitutional genetic aberrations behind childhood cancer predisposition".

### Barncancerfonden

Ann Nordgren is awarded a total of SEK 6,000,000 for three years for the project "Improved precision diagnosis of childhood cancer predisposition".

### The Swedish Cancer and Allergy Fund

Docent Hans Grönlund, Department of Clinical Neuroscience, Project: "Personalized immunotherapy against cancer".

Professor Marianne van Hage, Department of Medicine, Solna, Project: "Clinical implications of sensitization to the carbohydrate  $\alpha$ -Gal".

Carmen Gerlach is awarded a total of SEK 2,400,000 for the project "Improving cancer immunotherapy through the concept of T cell diversification axes".

Taras Kreslavskiy is awarded a total of SEK 3,750,000 for the project "Antigen recognition by tumor-infiltrating gamma delta T lymphocytes in neuroblastoma".



Professor Susanne Gabrielsson, Department of Medicine, Solna, Project: "Extracellulära vesiklar som biomarkörer och mål för terapi i urinblåsecancer" (Extracellular vesicles as biomarkers and targets for therapy in bladder cancer)

### **Other grants**

Matthew Hunt, postdoc in Jakob Wikströms Group received a grant from Åke Wibergs Foundation of SEK 450,000 for his project titled "Deciphering the role of mitophagy in wound healing pathophysiology". Kittikorn Wangriatisak, postdoc in Vivianne Malmström's Group, received a grant, approximately SEK 160,000, from Karolinska Institutet Research Foundation Grants 2024-2025 for 2 years. The grant title is "Immune profiling of DNA-autoreactive B-cells in systemic lupus erythematosus and lupus nephritis: Association with clinical parameters points toward candidate biomarker".



## **Publications**

#### CMMers IN BOLD

**Collado A, Jiao T, Kontidou E**, Carvalho LRRA, **Chernogubova E, Yang J,** Zaccagnini G, Zhao A, **Tengbom J,** Zheng X, Rethi B, Alvarsson M, Catrina SB, **Mahdi A**, Carlström M, Martelli F, **Pernow J, Zhou Z**. miR-210 as a therapeutic target in diabetes-associated endothelial dysfunction. *Br J Pharmacol.* 2024 Oct 14. doi: 10.1111/bph.17329. Online ahead of print.

Hunt M, Torres M, Bachar-Wikstrom E, Wikstrom JD (2024) - Cellular and molecular roles of reactive oxygen species in wound healing. *Communications Biology* 7, 1534.

Kontidou E, Humoud R, Chernogubova E, Alvarsson M, Maegdefessel L, Collado A, Pernow J, Zhou Z. Red blood cells as potential materials for microRNA biomarker study: overcoming heparin-related challenges. *Am J Physiol Heart Circ Physiol.* 2024 Oct 18. doi: 10.1152/ ajpheart.00609.2024. Online ahead of print. PMID: 39422364

**Oasa S**, Sezgin E, Ma Y, Horne DA, Radmilović MD, Jovanović-Talisman T, Martin-Fardon R, **Vukojević V\*, Terenius L.\*** Naltrexone blocks alcohol-induced effects on kappa-opioid receptors in the plasma membrane. *Translational Psychiatry* 2024 14:477. https://doi.org/10.1038/ s41398-024-03172-8

**Pernow J, Yang J**. Red blood cells: a new target to prevent cardiovascular disease? *Eur Heart J*. 2024 Sep 11:ehae454. doi: 10.1093/eurheartj/ ehae454. Online ahead of print. Sánchez-Ceinos J, Hussain S, Khan AW, Zhang L, Almahmeed W, Pernow J, Cosentino F. Repressive H3K27me3 drives hyperglycemia-induced oxidative and inflammatory transcriptional programs in human endothelium. *Cardiovasc Diabetol.* 2024 Apr 5;23(1):122. doi: 10.1186/s12933-024-02196-0.

**Tengbom J, Humoud R, Kontidou E, Jiao T, Yang J, Hedin U, Zhou Z,** Jurga J, **Collado A, Mahdi A, Pernow J.** Red blood cells from patients with ST-elevation myocardial infarction and elevated C-reactive protein levels induce endothelial dysfunction. *Am J Physiol Heart Circ Physiol.* 2024 Oct 11. doi: 10.1152/ajpheart.00443.2024. Online ahead of print.

**Tengbom J, Kontidou E, Collado A, Yang J**, Alvarsson M, Brinck J, Rössner S, **Zhou Z, Pernow J, Mahdi A.** Differences in endothelial function between patients with Type 1 and Type 2 diabetes: effects of red blood cells and arginase. *Clin Sci* (Lond). 2024 Aug 7;138(15):975-985. doi: 10.1042/ CS20240447.

Turcinov S, Sharma RK, De Vries C, Cîrciumaru A, Gerstner C, Mathsson-Alm L, Raposo B, Dubnovitsky A, Rönnblom L, Kwok WW, Chemin K, Malmström V, Hensvold A. Arthritis progressors have a decreased frequency of circulating autoreactive T cells during the at-risk phase of rheumatoid arthritis. *RMD Open.* 2024 Nov 18;10(4):e004510. doi: 10.1136/ rmdopen-2024-004510. Wang Q, **Niu G, Liu Z**, Toma MA, **Geara J, Bian X**, Zhang L, Piipponen M, Li D, Wang A, Sommar P, **Landén NX**. Circular RNA circASH1L(4,5) protects microRNA-129-5p from target-directed microRNA degradation in human skin wound healing. *Br J Dermatol*-. 2024 Oct 18:ljae405. doi: 10.1093/bjd/ljae405.

Wangriatisak K, de Vries C, Sharma RK, Huang W, Grönwall C, Pisitkun P, Gunnarsson I, Malmström V, Chootong P, Faustini F. Association between peripheral activated naive and double negative 2 B-cell subsets and clinical parameters in lupus nephritis patients. *Scand J Immunol.* 2024 Nov 26:e13427. doi: 10.1111/sji.13427.

**Wodaje T, Mahdi A**, Venkateshvaran A, Häbel H, Zenlander R, Gaylard B, Angelin B, **Pernow J**, Brinck J. Higher prevalence of coronary microvascular dysfunction in asymptomatic individuals with high levels of lipoprotein(a) with and without heterozygous familial hypercholesterolaemia. *Atherosclerosis*. 2024 Feb;389:117439. doi: 10.1016/j. atherosclerosis.2023.117439.

## First molecule identified that promotes gut healing while inhibiting tumour progression

#### PUBLICATION

In a recent publication in the journal *Na-ture*, researchers from CMM show that the molecule called Liver X receptor (LXR) can both help the intestines to heal after damage and suppress tumour growth in colorectal cancer. The discovery could lead to new treatments for inflammatory bowel disease (IBD) and cancer.

Many patients with inflammatory bowel disease (IBD) such as Crohn's disease or ulcerative colitis do not respond to available treatments, highlighting the need to identify novel therapeutic strategies. In a new study published in *Nature*, researchers propose that promoting mucosal healing through tissue regeneration could be a valid alternative to immunosuppressive drugs.

"However, it's virtually impossible to promote tissue regeneration without the risk of inducing tumour growth, as cancer cells can hijack the body's natural healing processes and start to grow uncontrollably," says lead author Srustidhar Das, research specialist in Eduardo Villablanca's CMM Group and at the Department of Medicine, Solna, Karolinska Institutet. "We've now identified a molecule that can help the intestines to heal after damage while suppressing tumour growth in colorectal cancer."

#### New drug candidates

This molecule is a protein called the Liver X receptor (LXR) and it was found among the handful of molecules with drug-candidate potential for treatment of IBD, identified by the research team. The strength of LXR as a IBD drug candidate lies in its capacity to both promote regeneration and suppress tumour growth in colorectal cancer.

"The discovery of both these functions was astonishing," says CMM Group Leader Eduardo J. Villablanca, docent at Karolinska Institutet. "We now need to study how LXR controls tumour formation more closely."



Srustidhar Das. Photo: Ulf Sirborn

"We've now identified a molecule that can help the intestines to heal after damage while suppressing tumour growth in colorectal cancer."



Eduardo J. Villablanca Photo: Jann Lipka, Cancerfonden

"The discovery of both these functions was astonishing. We now need to study how LXR controls tumour formation more closely."





Liver X receptor is a protein that has been found to promote gut healing as well as inhibit tumour progression. Illustration: Chiara Zagami.

The researchers used a collection of advanced technologies to conduct their study, which included mapping the transcriptome of intestinal cells. They also cultivated what are known as 3D organoids: small, three-dimensional cell structures that mimic the function and structure of the body's own organs, albeit in miniature format.

They then used spatial transcriptomics to map the gene expression in the different tissues, a technique that has been developed at SciLifeLab by scientists from the Royal Institute of Technology (KTH) and Karolinska Institutet in Sweden.

#### Third most common cancer

Every year, over 7,000 people in Sweden develop bowel or rectal cancer, making it the third most common form of cancer in Sweden. Patients are often treated with chemotherapy and radiotherapy, but this can cause irritation and swelling of the bowel mucosa with subsequent chronic intestinal inflammation.

"Thus, this new therapeutic molecule has the potential to treat not only IBD patients but also cancer patients to prevent chronic bowel disorders after radiotherapy and/ or chemotherapy," says Eduardo J. Villablanca. The study was conducted with grants from several bodies, including the Swedish Research Council, Formas (The Swedish Research Council for Environment, Agricultural Sciences and Spatial Planning), the Silicon Valley Community Foundation, Novo Nordisk, the Swedish Cancer Society, the Knut and Alice Wallenberg Foundation and the Åke Wiberg Foundation.

Two of the authors have reported potential conflicts of interest: Eduardo J. Villablanca has received research funding from the pharmaceutical company F. Hoffmann-La Roche and Srustidhar Das works as a consultant for Cellphi Biotechnology AB.

PUBLICATION: "Liver X receptor unlinks intestinal regeneration and tumorigenesis", Srustidhar Das, S. Martina. Parigi, Xinxin Luo, Jennifer Fransson, Bianca Carola Kern, Ali Okhovat, Oscar E. Diaz, Chiara Sorini, Paulo Czarnewski, Anna T. Webb, Rodrigo A. Morales, Sacha Lebon, Gustavo Monasterio, Francisca Castillo, Kumar P. Tripathi, Ning He, Penelope Pelczar, Nicola Schaltenberg, Marjorie De la Fuente, Francisco López-Köstner, Susanne Nylén, Hjalte List Larsen, Raoul Kuiper, Per Antonson, Marcela A. Hermoso, Samuel Huber, Moshe Biton, Sandra Scharaw, Jan-Åke Gustafsson, Pekka Katajisto, Eduardo J. Villablanca, *Nature*, online November 20 2024, doi: 10.1038/s41586-024-08247-6.



## Blocking THBS1 with antibodies may heal radiotherapy induced skin injury

**PUBLICATION:** Epigenetic memory of radiotherapy in dermal fibroblasts impairs wound repair capacity in cancer survivors. Bian X, Piipponen M, Liu Z, Luo L, Geara J, Chen Y, Sangsuwan T, Maselli M, Diaz C, Bain CA, Eenjes E, Genander M, Crichton M, Cash JL, Archambault L, Haghdoost S, Fradette J, Sommar P, Halle M, Xu Landén N. *Nat Commun* 2024 Oct;15(1):9286.

Image: iStock

In a study, published in *Nature Communications* in October, researchers at Karolinska Institutet and Karolinska University Hospital show that radiotherapy (RT) creates an "epigenetic memory" in skin fibroblasts which impairs skin healing in cancer survivors. By targeting this memory with antibodies, they found that the damage could be reversed.

Radiotherapy (RT) can cause not only short-term skin damage but also long-lasting effects like chronic ulcers and fibrosis, which may appear years after treatment and severely affect cancer survivors' quality of life.

The researchers studied 46 breast cancer survivors who had radiotherapy, collecting skin biopsies from irradiated and non-irradiated areas during reconstructive surgeries. They investigated fibroblast activity and chromatin changes using ATAC-seq, RNA-seq, single-cell RNA-seq, and single-cell multiome ATAC+RNA-seq. They also tested a topical treatment on human ex vivo wound models, targeting THBS1 to enhance healing.

"This study explores the long-term effects of radiotherapy on dermal fibroblasts, uncovering a persistent epigenetic memory that compromises wound healing. By identifying THBS1 as a key player in this maladaptive radiation memory, we demonstrate how targeting this gene can mitigate radiotherapy-induced skin toxicity and improve tissue repair. These findings not only enhance our understanding of epigenetic memory but also open new avenues for therapeutic interventions to address late-onset adverse effects of radiotherapy in cancer patients.', explains Xiaowei Bian, PhD student in Ning Xu Landén's CMM Group and first author of the publication in *Nature Communications*.

The next step is to further investigate the therapeutic potential of anti-THBS1 antibodies and inhibitors of CD47 - a receptor of THBS1 in clinical settings, to evaluate their effectiveness in preventing and treating late-onset skin complications of radiotherapy in cancer survivors. The researchers will also explore the broader implications of epigenetic memory in other tissues and diseases, aiming to better understand how this process can be leveraged to prevent or treat diseases.



Xiaowei Bian and Ning Xu Landén. Photos: Private



## Mapping of atherosclerotic plaque cells may predict future risk of stroke or heart attack

Image: Wikimedia Commons

In a study published in the European Heart Journal in November, researchers affiliated with CMM found that genetic traits influence the cellular makeup of atherosclerotic plaques, over time affecting risk of stroke and heart attack caused by the leasions. This discovery could enhance future risk assessments and treatments for atherosclerosis patients.

It is well known that atherosclerosis causes cardiovascular diseases such as stroke and heart attack. Atherosclerotic plaques are abnormal accumulations of cells, lipids and fibrous connective tissue innermost layer of the arterial vessel wall. The exact composition of the plaque can vary from patient to patient. With time the plaques become unstable and rupture. Blood clots are then formed and can completely block the vessel or be carried by the bloodstream to other organs such as the brain. In either case, there is a lack of oxygen in the tissues as the blood does not reach them, which can cause a heart attack or a stroke. Despite better preventtion and treatments, these conditions are still the leading causes of death in Sweden.

Researchers at Karolinska Institutet, and at CMM, together with colleagues at the universities of Stanford and Virginia in the USA, have now succeeded in mapping the association between genetic factors and the composition of different cell types in atherosclerotic plaques. The research was based on analyses of tissue samples from patients with atherosclerosis stored in the so called Biobank of Karolinska Endarterectomies, (BiKE).

Previous studies have shown that the genetic setup or heredity is important for the levels of cholesterol, other lipids and circulating immune cells in the blood, but now we see that heredity also affects the composition of smooth muscle cells in the blood vessels of atherosclerotic patients," says Ljubica Matic, CMM Group Leader nd docent at the Department of Molecular Medicine and Surgery at Karolinska Institutet who led the study. "This can affect the development of atherosclerotic plaques, but also the tendency for the plaques to become unstable and cause a stroke."

#### Three different groups of patients

Using this data on heredity, the researchers have been able to categorise patients into three different groups. "The first group are those with the most severe profile and in our material they have usually already had a stroke," says Ljubica Matic. "For patients at lower risk, the vessels have formed plaques but without causing a stroke. The third group of patients is somewhere in between these two and often have kidney disease in combination with atherosclerosis. We also have preliminary evidence that the same concept may be valid in heart attacks."





From left to right: Ljubica Matic, Sofija Vuckovic, Sampath Narayanan and Ulf Hedin. Photo: Antti Siika

The new knowledge about genetic influence on plaque cells can be used together with modern diagnostic imaging and AI to make better assessments of future risk of stroke or heart attack, or prediction of response to different drugs. "We have done similar integrative studies for smaller cohorts of patients in other previously published papers to prove that it works, but of course the concept needs to be tested on a larger scale before it can be introduced into clinical practice," says Professor Ulf Hedin at the same department at Karolinska Institutet. "We will be working intensively on these modern, so called multi-modal studies in the future, through our new EU Horizon 2020 NextGen and MedTechLabs funded projects".

The research was funded by, among others, the Swedish Research Council, the Swedish Heart-Lung Foundation and Karolinska Institutet. Clint L. Miller has received support from Astra Zeneca for an unrelated project. The other authors declare no conflicts of interest.

**PUBLICATION:** "Atheroma transcriptomics identifies ARNTL as a smooth muscle cell regulator and with clinical and genetic data improves risk stratification", Sampath Narayanan, Sofija Vuckovic, Otto Bergman, Robert Wirka, Jose Verdezoto Mosquera, Mariette Lengquist, Clint L. Miller, Thomas Quertermous, Ulf Hedin, Ljubica Matic. *European Heart Journal*, online 18 November 2024, doi: 10.1093/eurheartj/ehae768.

## CMM researchers lead IMI-funded projects with the highest publication output

#### 6.5 IMI funded publication output by project

BTCure continues to be the most productive IMI funded project with 749 publications between 2010 and 2023. EUbCPEN and U-BICPRED moved into the top 10 projects in 2023 based on publication volume, with CANCER-ID and RTCure not featuring in the top 10 for 2023 (Figure 6.5.1). The top 10 projects account for almost one-third (32.9%) of the total publications.



Figure 6.5.1 Top ten IMI funded projects with the highest number of publications 2010-2023\*

The Innovative Medicines Initiative (IMI) is a European initiative to improve the competitive situation of the European Union in the field of pharmaceutical research. In the latest IMI report, published on December 17<sup>th</sup>, BTCure, a project aimed at a deeper understanding of

the pathology of rheumatoid arthritis, and coordinated by CMM Group Leader Lars Klareskog, continued to be the most productive IMI-funded project in terms of publications. Michael Sundström is the scientific director of ULTRA-DD, aimed at identification and validation of under-explored novel targets in auto-immune and inflammatory diseases, as well as one of the scientific directors of EUbOPEN, a project that aims at creating open access libraries of annotated drug targets and corresponding chemical probes. ULTRA-DD and EUbOPEN reached the 3<sup>rd</sup> and 7<sup>th</sup> best position, respectively, in this year's IMI ranking.

Lars Klareskog and Michael Sundström. Photos: Private and AnneLi Engström, respectively.





## **CMM Events and Outreach**

### **CMM Seminar with Lars Fugger**



Some glimpses from the CMM Seminar with professor Lars Fugger. Photos: Magdalena Lindén and Kristina Edfeldt.

The second seminar 2024 within the CMM Seminar Series was held on November 19<sup>th</sup> by professor Lars Fugger from the Nuffield Department of Clinical Neurosciences, University of Oxford. The talk, titled "Ancient DNA reveals evolutionary origins of autoimmune disease", presented and discussed findings published in a recent Nature paper. It took place in a fully booked CMM Lecture Hall, followed by a networking reception.

#### **CMM Core Facility Day**





Pictures from some of the core facilities at CMM and a screenshot showing the complex tour schedule. The "tour guides" were wearing special CMM t-shirts. Photos: Petter Stahre, Peri Noori, Vladana Vukojevic and Michael Sundström.

On December 9th CMM opened up the doors for everyone in- and outside of CMM who was interested in learning more about the core facilities offered at and by CMM.

The day started with a lunch seminar that included an overview of CMM's core facility strategy and short presentations of the main facilities and their different research applications. Next, the participants were offered tours of the core facilities, guided by some CMMers.

A special thanks to all people who were involved in making this to a successful day and showing the possibilities and usefulness of the CMM core facilities.



## CMM Lucia celebration and Photo Contest 2024

CMM EVENT



Choir performance, lussefika and photo viewing at CMM on the 13th of December. Photos: Kristina Edfeldt and Magdalena Lindén.

On December 13<sup>th</sup>, the traditional Swedish Lucia celebration to place at CMM.

All CMMers were invited to experience traditional Swedish Lucia songs and Christmas carols performed by the *A Scalpella* choir and enjoy saffron buns (lussekatter), ginger snaps, glögg, coffee and tea together with other CMM colleagues.

The event concluded with the announcement of the winners in the yearly CMM Photo Contest.



## The winners of the CMM Photo Contest 2024

CMM EVENT



#### 1<sup>st</sup> prize

Author: Erik Holmgren, affiliated researcher, Hans Grönlund Group Title: Double Helix Description: Two Helix snails could be called a double Helix. Their motility is unique.



#### 2<sup>nd</sup> prize

Author: Skip Middelhoff, affiliated researcher, Maja Jagodic Group Title: Let go and float Description: In research there is a constant flow of inspiration, ideas, and plans. Often chaotic and unpredictable, no one manages to be fully in control. You have to keep your mind open and sometimes be guided towards a certain outcome. Just like the river in the photo.



### 2<sup>nd</sup> prize

Author: Eric Herlenius, CMM Group Leader Title: Mobile Soap Bubble frozen in time!

## The winners of the CMM Photo Contest 2024

CMM EVENT



#### 3<sup>rd</sup> prize

Author: Ingrid Kockum, CMM Group Leader Title: Mobility transformation Captured while moving from CMM to KI campus early in the morning in December this year. This to me illustrates the increase in mobility and movement around us over the past few years but also the work to increase it even further with the building of a new subway station near us.



### Honourable mention

Author: Kang-cheng Liu, Postdoc, Michael Sundström Group

Title: Resting Tools: Pause in Motion

Description: A pair of wall-painting gloves were left on the floor of the staircase, symbolizing a moment of stillness amidst work. The scene reflects the interplay between motility (paints and human effort and precision) and mobility (tools facilitating movement and creation) in the act of painting and transformation.



## Explora Nobel: A dream come true for some Chilean researchers at CMM

#### CMM OUTREACH

During the Nobel Week 2024, three Chilean public school students from underprivileged areas got the opportunity to visit Sweden, experience the world of scientific research and meet Nobel laurates. The project was made possible thanks to the initiative and efforts of some CMMers and their colleagues.

Explora Nobel is an initiative that aims to inspire the new generation of Chilean scientists and break traditional barriers to science and academia. For a week, three Chilean public school students experienced a transformative journey in Sweden through the new "Explora Nobel: from Chile to Sweden" program. This initiative not only brought young talents closer to Sweden's scientific ecosystem but also served as a bridge for significant scientific agreements.

#### How it all started and how it became a reality

The idea originated from a tweet by the Swedish ambassador in Chile about a project where Chilean children would travel to Sweden for a football tournament. Inspired by this, CMMer Gustavo Monasterio, Vice President of the Association of Chilean Researchers in Sweden (AICHiS), envisioned a similar project focused on science. The goal was to provide a unique experience for Chilean students and open up spaces in science and academia, typically restricted to certain elites.

This novel project required coordination with key actors, securing funding, forming alliances, and managing logistics. Access to the Nobel Forum, usually reserved



Francisca Castillo showing her labwork to the Chilean students. Photo: Private.



The guests from Chile together with CMMers during the visit to CMM. Photo: Private.

for advanced researchers, was secured through direct efforts by Gustavo Monasterio and CMM Group Leader Eduardo Villablanca. Ensuring an inclusive and decentralized selection of students was also crucial, representing various regions of Chile.

#### The experience

The program included scientific and cultural activities, such as visits to CMM, SciLifeLab and Biomedicum. The students also visited Scania Sweden's facilities to see innovative solutions for global challenges. The highlight was meeting the 2024 Nobel Prize winners in Physiology or Medicine, Gary Ruvkun and Victor Ambros, who engaged with the students and shared insights about their work. During the stay, Dr. Sergio Lavandero, representing the Chilean Academy of Sciences, signed a collaboration agreement with AICHiS to promote joint projects and knowledge exchange between Chile and Sweden, strengthening Chilean science internationally.



From left to right: Sergio Lavandero, Gary Ruvkun, Francisca Ulloa, Michelle Manzanares, Yamil Niño de Guzmán de Camiña and Gustavo Monasterio. Photo: Private.



## A digital translation tool tailored for healthcare receives the Athena Prize 2024

#### CMM OUTREACH

Martin Schalling, CMM Group Leader and Professor at Karolinska Institutet, is one of the founders of Care to Translate, a digital translation tool that has been developed to empower patients from different language backgrounds to communicate effectively with healthcare providers.

On November 13<sup>th</sup> it was announced that Care to Translate are the recipients of the Athena Prize 2024. The purpose is to recognize and reward research and innovations that have taken place in collaboration between academia, healthcare and business.

The Athena Prize is sponsored by Dagens Medicin, Lif, the Swedish Research Council and Vinnova.



From top left to bottom right: Martin Schalling, CEO Maja Magnusson, MD Linus Kullänger Schalling, CTO Alexander Gyllensvärd and MD Annie Backman. Photo: Sara Damne, Bildbyrån.



## The Cilla Weigelt Award 2024

AWARDS



Ervin Ascic with CMMer Alexandra Argyriou (left) and Mireia Cruz de Los Santos (right), the 2022 and 2023 Cilla Weigelt Awardees. Photo: Private



From left: Olav Fromm, Claes Andersson (both at Chiesi), Ervin Ascic, Johan Weigelt (VD KI Holding AB), Pia Hydén (Chiesi) and Marianne van Hage (KI/CMM, the selection committee). Photo: Chiesi Nordic

Ervin Ascic, a 3<sup>rd</sup> year PhD student at Lund University, has been honoured with the Cilla Weigelt Award for outstanding research concerning molecular mechanisms in rare and undertreated diseases. Erin receives SEK 50,000 during an award ceremony held on November 4<sup>th</sup> in the Chiesi R&D site at Campus Solna.

Ervin is awarded for his research on foundational applications of gene therapy to rare diseases and cancer.

#### About the Cecilia Weigelt Prize:

The Cilla Weigelt Prize has been established by Chiesi (her employer), the Structural Genomics Consortium (SGC), as well as by friends and family in her memory to support and inspire young doctoral students and to honor her legacy. The prize is administered by the Center for Molecular Medicine Foundation (CMM) at Karolinska Institutet and Karolinska University Hospital. Additional contributions to the prize have been made by Aled Edwards (Toronto, Canada), Johan Weigelt (Stockholm), and MRCS AB (Michael Sundström, Stockholm).



## Holiday greetings from the CMM Director

#### Dear CMMer,

Another year has soon passed, we are approaching the winter holiday season, and I hope you all will have a relaxing and joyful time during the break. Please prioritise being with your friends and family during the break, and get back fresh, rested and full of energy for 2025.

In 2024, quite a few things happened including the move in of many new groups from Bioclinicum. We are very happy to see a large proportion of the Division for Immunology and Respiratory Medicine joining us.

This was a long and complicated process, and also one of the first major developments I got involved with as new Director for CMM. Now, around 2.5 years from the first initial discussion, we have more than 80 new scientists of very high-quality being part of the CMM team. This has taken some effort, and we have therefore been forced to de-prioritize other matters during this time period, which we now finally can turn our attention to. As part of this endeavour, we also made quite major adaptations of the building, especially on floor 00, but also other areas were affected. In addition, some existing groups had to compromise, and in some cases also move to other parts of the building. My most sincere thanks to all involved and affected, enabling this quite major upgrade of our building, as well as to our collective experiences, skills and competitiveness in translational medical research.

Our restaurant since many years, 'Gladan', could not sustain its operation any longer and was closed in May 2024. In discussions with the Hospital (considering that most of the restaurant was located in the adjacent building to CMM), we jointly agreed to not attempt to establish a new restaurant, in part due to that the situation around the campus so drastically has changed with numerous new restaurants within 5-10 minutes' walk. The positive part is that we regained full control over the café area on floor 00, and as a first step we have now installed automated vending machines for food, drinks and snacks. Further improvements of this area will happen during the first half of 2025.

Kristina Edfeldt joined the Service Center team, and helps out with various functions and CMM projects, often together with Magdalena and Maria. She is a most welcome addition.



Photo: iStock

In 2025, which we hope will be a bit calmer year than this one, we will still see some major developments to come. We are e.g. preparing for a full network upgrade in the building, including both wired and wireless solutions.

Finally, we will be arranging the first CMM Day in the 2020's. We will perhaps call it the CMM Research Day, as we will be focusing on our internal research, with presentations from scientists that has been with us for a while, as well as the newly arrived research groups, to get to know each other and create synergies and collaborative efforts. Last time we had a similar event was in 2018, so it's about time for sure! Mark 14 May in your calendars.

Once again, wishing you all the best for the remainder of the year, and truly Happy Holidays!

Michael Sundström



## **Upcoming Events**

**CMM SEMINAR SERIES** 

#### CMM Seminar, Thursday 23<sup>rd</sup> of January at 15:00

# William Nyberg: "Enhancing T cell therapies for cancer with precise gene editing"

Speaker: William Nyberg, Assistant Professor, Department of Medicine, Huddinge, Karolinska Institutet.

Title of the talk: Enhancing T cell therapies for cancer with precise gene editing

Date and time: Thursday 23 January, 15:00

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

After the talk there will be a networking reception with some drinks and light bites.

Recipient of the European Research Council (ERC) starting grant 2024, <u>William Nyberg</u> is now back at Karolinska Institutet after some years at UCSF. His research lab mainly focuses on cell therapies against cancers, CAR-T cells and T cell engineering.



#### CMM BIOINFORMATICS HUB

CMM Bioinformatics Hub meeting, Wednesday 29th of January at 12:00

### "Methylation Data Analysis"

Dear CMMers,

We're pleased to invite you to the second session of CMM Bioinformatics Hub. Following the success of the recent Olink Data Analysis Workshop, we are now diving into a new topic: Methylation data analysis, led by our very own Methylation Wizard, Maria Needhamsen.

Topic: Methylation Data Analysis Date: January 29, 2025 Time: 12:00 – 13:00 Location: CMM Lecture Hall, Ground Floor With limited spots available for just 30 participants, we would like to encourage you to register early on a firstcome, first-served basis.

Sign up before January 15th at 17:00

We're pleased to offer free registration for this event, which includes lunch. Please note that if you've registered but cannot attend, kindly inform us at least a week in advance. If we do not receive a notification and you do not show up, you'll receive a no-show mark, and we'll prioritize other participants for future sessions. Thank you for your understanding!

The Organizing Committee: Ana Cristina Gonzalez Sanchez, Lina Diaz-Gallo, Narsis Kiani

Sign up here:





## **Upcoming Events**

CMM EVENT

### CMM Junior seminar series starting in January 2025

#### Dear CMMers,

We are thrilled to announce the launch of the CMM Junior Seminar Series, starting in January 2025!

As the story goes, the CMM was established with the clear intent of bringing together groups from diverse scientific niches to foster interdisciplinary collaborations. However, true collaboration cannot happen if we are unaware of what's happening around us.

With this in mind, the CMM Junior Seminar Series was created to provide a platform for young researchers primarily PhD students and postdocs—to showcase the exciting work being done within the CMM community. We hope this series will spark fresh, "out of the box" ideas and inspire innovative approaches.

We also recognize the already heavy presentation load many of us face, so these seminars are designed to be informal and relaxed. There's only one key requirement for presenters: ensure that everyone can understand what you're working on, regardless of their specific expertise.

We're looking forward to seeing the creativity, insights, and collaborations that this series will inspire! More details on scheduling and participation will follow soon. What to Expect:

Frequency: Monthly (on a fixed date). Speakers: Young researchers who would like to share their story (on a voluntary basis). Format: In-person, one presentation of 25-30min, Q&A sessions.

Following the presentation we will have a "Snacking while Mingling" kindly provided by CMM.



Illustration: Pixabay

The inaugural seminar will begin in January 2025, date to be determined, and will be communicated as soon as possible.

As stated before, the speaker selection will be on a voluntary basis, so we depend on your willing to participate. Our motto is "Don't be shy and apply". If you're interested in sharing your story, don't hesitate to reach out—we'd be happy to further discuss the expected for each presentation. Additionally, we welcome your suggestions for future seminar topics or speakers.

We look forward to your participation in making the CMM Junior Seminar Series a dynamic and engaging part of our community activities.

#### Best regards,

The CMM Junior Seminar Series Committee: Chantal Reinhardt, Luis Miguel Santos, Xiaowei Bian, Berenice Fischer, Stefan Bencina, Sofija Vuckovic



## **Upcoming Events**

CMM EVENT

### **CMM Research Day**

This event will focus on translational research at CMM, with scientific presentations, networking opportunities and more. Save the date in your calendars and stay tuned for more information!



## Happy Holidays!

Next deadline for sending in contributions to CMM News: 22<sup>nd</sup> of January

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