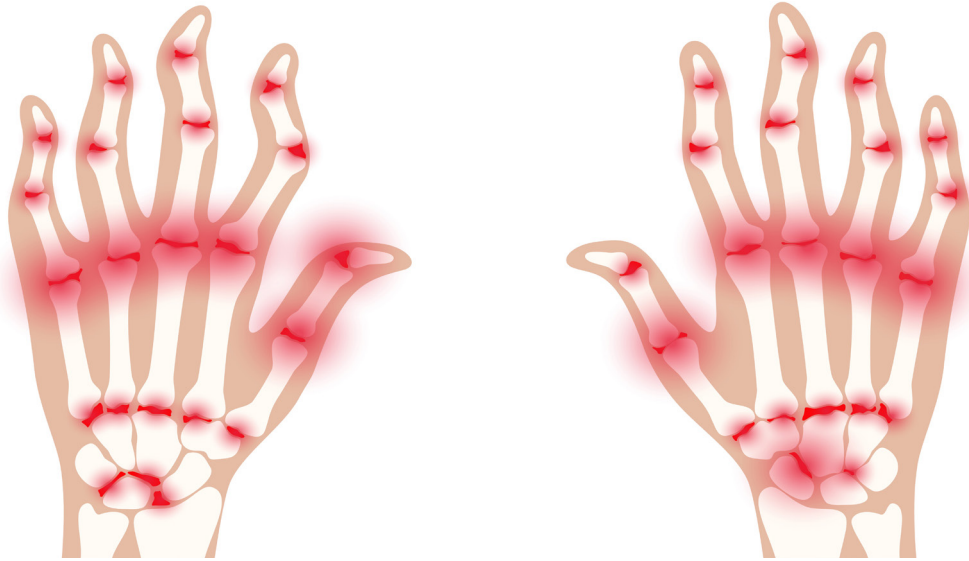
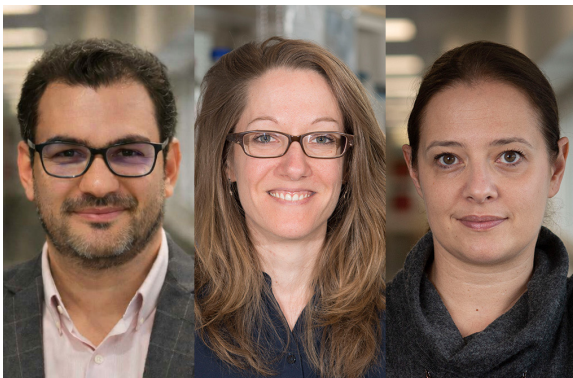


# CMM News



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**Study of a potential new treatment for rheumatoid arthritis receives private donation.**



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**Publication: CRISPR epigenome editors show complex on- and off-target effects**



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**How is CMM organized?**



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newsletter here

Editor: Magdalena Lindén  
Layout: Edna Fagerstedt

# Study of a potential new treatment for rheumatoid arthritis receives private donation

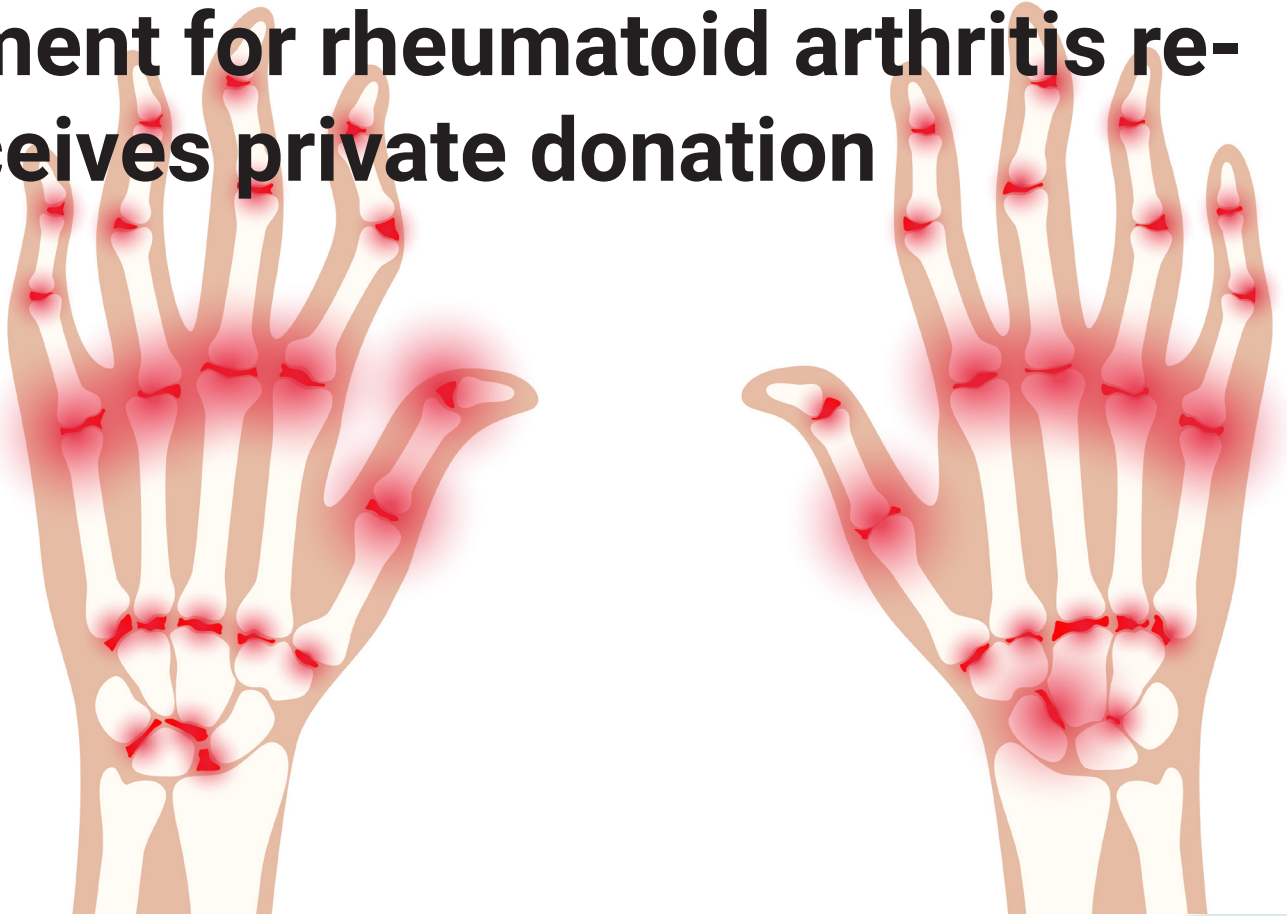


Image: iStock.

## FUNDING AND GRANTS

**A private donation from Sally Cahill, USA, to researchers at CMM, Karolinska Institutet and the Karolinska University Hospital could make a new treatment for severe rheumatoid arthritis a reality. The method, which involves stimulating a nerve in the ear with a weak electric signal, has so far delivered promising results.**

CMM Team Leader Jon Lampa, professor of rheumatology at Karolinska Institutet, and his research

group have received a donation from Sally Cahill, USA, mediated by the Feinstein Institutes, a medical research centre in New York with which the group is collaborating. The donation is worth almost SEK 10.8 million and is earmarked for the TRAVAGA clinical study.

“The donation means a great deal to us and means that we can carry out this valuable study,” says Professor Lampa at KI’s Department of Medicine in Solna, and clinical manager at Karolinska University Hospital, as well as Team Leader at CMM.

The study currently comprises six clinics in Sweden: Karolinska University Hospital, the Rheumatology Centre in Stockholm and rheuma-

tology clinics in Umeå, Örebro, Lund and Malmö. Launched last March, the study, which is coordinated by the Department of Medicine in Solna, is expected last two years.

### **Stimulated vagus nerve suppresses inflammation**

The background to the study is the discovery that the nerve and immune systems are closely linked. Back in the early 2000s, research showed that the vagus nerve, which runs from the brain stem, down through the neck and on to the heart and guts, can affect inflammatory processes.

Stimulating the nerve can activate the inflammatory reflex, a communication pathway that helps the body to suppress inflammation.

“We need to find out if this non-invasive therapy can have positive effects and suppress the morbid activity and pain of rheumatoid arthritis. If it does, it can be an important component of other treatments, some of which aren’t sufficiently suppressive.” - *Jon Lampa*



Jon Lampa. Photo: Stefan Zimmermann.

A published phase 3 study in the USA called RESET-RA, which involves patients with severe rheumatoid arthritis that have not responded to drugs, tested if a surgically implanted stimulator placed on the vagus nerve in the neck could suppress chronic inflammation. After the first three months of the study, the researchers could see distinct differences in effect in treated patients compared to controls – 35 and 24 per cent respectively. All patients then received the treatment. A year later, almost 60 per cent of them had attained the therapeutic objective and their disease had become approximately 20 per cent less active.

**A possible alternative to surgery**

This technique is easier on the body

than drugs but requires surgery. The researchers are therefore examining whether the vagus nerve can be stimulated instead with a weak electric current via the skin of the left outer ear. The nerve is stimulated for five minutes morning and night, with the control group receiving sham stimulation on a part of the ear that lacks contact with the vagus nerve.

“We’re now trying to ascertain if this also has an anti-inflammatory effect,” says Professor Lampa. “We also need to clarify the effect of the treatment on pain and fatigue, disease parameters that were not evaluated in the previous study.” The study is randomised and placebo-controlled and recruits patients with rheumatoid arthritis who have

not responded adequately to currently available treatments.

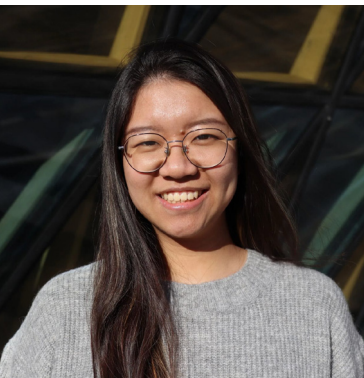
“We need to find out if this non-invasive therapy can have positive effects and suppress the morbid activity and pain of rheumatoid arthritis. If it does, it can be an important component of other treatments, some of which aren’t sufficiently suppressive,” Jon Lampa concludes.



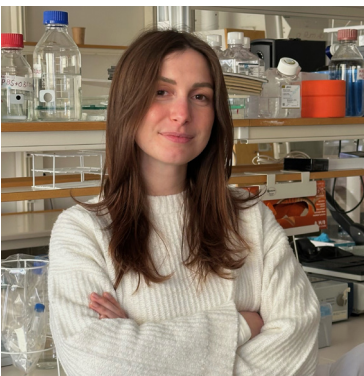
# New CMMers



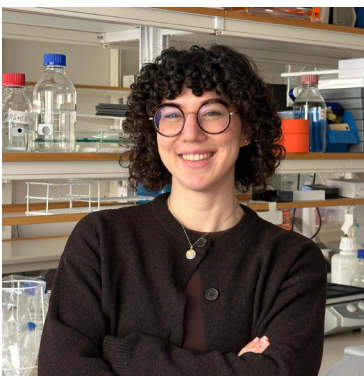
**Dima Khalil**, is a medical student who has started to work in the team of Hanna Brauner. Dima will perform an exam work project during spring 2026 and will investigate the role of macrophages in cutaneous lymphoma with 2D and 3D models.



**Jingyi Zhang** is a new PhD student in Associate Professor Hanna Björck's CMM Group. She graduated from the Master's Programme in Biomedicine at Karolinska Institutet, Sweden. Her PhD project involves ascending aortopathy and associated aortic valve disease and focuses particularly on the role of extracellular vesicles in disease development and progression.



**Susanna Parolaro** is a second-year PhD student in Pharmacological Biomolecular Sciences at the University of Milan and a visiting researcher in Ida Nilsson's Team. Her six-months stay at CMM aims to deepen her research employing in vitro assays and human-derived cell models for translational approaches. Her research investigates the role of microglia cells in the molecular mechanisms underlying AN, aiming to uncover how neuroinflammatory processes contribute to synaptic alterations.



**Barbara Eramo** is a new postdoctoral researcher in Ida Nilsson's group at CMM. She obtained her PhD in Pharmacology at Sapienza University of Rome, where she investigated neurobiological mechanisms regulating feeding behavior in obesity and eating disorders. At CMM, her research will focus on how oxytocin signaling modulates microglial function and synaptic remodeling in anorexia nervosa. Using a patient-derived cellular model, her work aims to uncover mechanisms underlying the disorder and inform future therapeutic strategies.

# New Team Leader

**Assistant professor Elisabeth Nyström was appointed a CMM Team Leader as of December 2025.**

Team Nyström relocated from University of Gothenburg to CMM in January 2026, and is now integrated to the VENoM (Villablanca, Engblom, Nyström and Monasterio) environment led by CMM Group Leader Eduardo Villablanca.

This is Elisabeth's introduction:

Our research focuses on the function and regulation of the intestinal mucus layer. As the interface between the gut epithelium and the vast microbial community, the mucus barrier plays a central role in host–microbiota interactions and tissue protection.

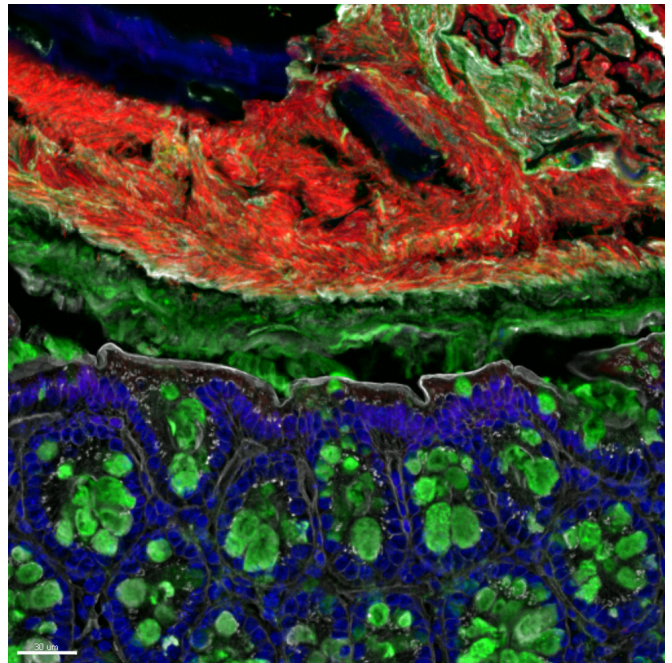
Our aim is to understand how mucus and mucus-producing goblet cells dynamically shape host–microbiota interactions as an innate immune interface in health and disease. For this, we take an interdisciplinary approach, combining cell and protein omics, targeted *in vivo* cell manipulation, specialized mucus analysis pipelines, and protein biochemistry.

We are particularly interested in how post-translational protein modifications regulate these processes and to develop *ex vivo* live tissue imaging to study host–microbe interactions in real time.

You can find us on floor 3 in the CMM L8 building. Please reach out if you are interested in our methods, or if you would like to discuss mucus biology. We are especially keen to expand our research to other mucosal tissues, and explore links between extraintestinal inflammatory conditions and intestinal health.



Elisabeth Nyström. Photo: Emelie Asplund.



Representable image of Elisabeth Nyström's research: Mucus (green) separates luminal bacteria (red) from the underlying host epithelium (blue/grey). Photo: Confocal image by Elisabeth Nyström.

# Eurostars/Vinnova grant for study and treatment of obesity

## FUNDING AND GRANTS



Carolina Hagberg. Photo: Stefan Bladh.



Volker Lauschke Photo: Erik Flygh.

**CMM Group Leaders Carolina Hagberg and Volker Lauschke labs are part of a large European project on obesity that has been awarded with a substantial grant from Eurostars/Vinnova.**

3D Perfusable Living Adipose Tissue for Model for Study and Treatment of Obesity (3DPERLAT) is a project that was recently awarded

with a EUR 1,393,192 grant from the Eurostars/Vinnova Consortium. Carolina Hagberg's and Volker Lauschke's research groups will collaborate, together with other European centers on the development of better models for studying obesity.

Carolina's group studies the cellular mechanisms of our major lipid storing cell types – adipocytes, hepatocytes and macrophages - that contribute to the development of obesity-induced metabolic and cardiovascular disorders. They focus

on how lipids are taken up, stored, and used by these cells in health and disease.

Volker's group integrates 3D cell culture systems of primary human cells, microfluidics and comprehensive molecular profiling technologies to discover novel therapeutic strategies

Carolina's and Volker's labs will receive approximately EUR 120,000 each.

# CMMers received stipends at Queen Silvia's award ceremony

## FUNDING AND GRANTS



Award ceremony March 19, 2026. Ulf Hedin and Sebastian Lewandowski, second and third from the top left, respectively. Photo: Fru Bergkvist.

On 19 March, HM The Queen presented research grants from the King Gustaf V and Queen Victoria Freemason Foundation, which supports research on ageing in the areas of neurodegenerative diseases, cardiovascular diseases, and nursing research.

CMM Group Leader Ulf Hedin and Team Leader Sebastian Lewandowski received funding from the foundation for their projects on precision medicine in stroke prevention and decoding ALS mechanism using multiomics integration, respectively.

The ceremony, held at the Bååtska Palace in Stockholm, included the presentation of diplomas to 25 researchers in geriatrics and the event concluded with a lecture by Professor Ulf Hedin, who presented his research on the risks of heart attack and stroke.

# Some Publications

## CMMers IN BOLD

AlZaim I, Hassan MN, Schröter M, Mannino L, Dragicevic K, Sjøgaard MB, Festa J, Dokshokova L, Weinbrenner S, Ayllon BT, Hansen B, Rasmussen RK, Christensen JN, Wagman O, **Schipper R, Cai M**, Dheedene W, Bohn AB, Farup J, Lin L, Soraggi S, Thorsen AD, Baek A, Thomsen HH, von Heesen M, Conradi LC, Evans P, **Hagberg CE**, Heeren J, Emont M, Rosen ED, Luttun A, Etzerodt A, Massier L, Rydén M, Mejhert N, Blüher M, Khodosevich K, Fenton RA, Sheikh BN, Jessen N, de Rooij LPMH, Kalucka J. Defining the vascular niche of human adipose tissue across metabolic states. *Nat Metab.* 2026 Mar;8(3):722-740.

Folkesson E, **Forough F, Kleberg L, Kjellgren V, Jakobsson M, Grunewald L, Hellberg J, Ryberg J, Maher Z, Silva CS, Gower MS, Grönlund H**, Correia-Neves M, Makower B, **Källenius G**, Bruchfeld J, **Sundling C**. A multiplex Mtb-specific FluoroSpot assay measuring IFN $\gamma$ , IL-2, and TNF-secreting cells can improve accuracy and differentiation across the tuberculosis spectrum. *J Clin Microbiol.* 2025 Dec 17;63(12):e0089425.

**Maestri A, Cai M\*, Schipper R\*, Backman J**, Vannay A, **Olsson A, Ehrenborg E, Nilsson R, Hagberg CE**. Aerobic glycolysis drives differentiation of unilocular adipocytes. \*Equal contribution. *J Lipid Res.* 2026 Mar 16:101023.

**Pahlevan Kakhki M, Rangani F, Ewing E, Starvaggi Cucuzza C, Zheleznyakova G, Kalomoiri M, Kenny L, Raghavan A, Rao Prakash C, van den Hoeven G, Venkata S. Badam T, Covacu R, Andreou I, Needhamsen**

**M, Kular L\* & Jagodic M\***. Comprehensive profiling of CRISPR/dCas9 epigenome editors indicates a complex link between on- and off-target effects. *Genome Biol.* 27, 52 (2026).

**Papavasileiou S, Mo J, Boey D, Wu C, Tronstad M, Margerie L**, Olsen RA, Bachmann JA, Low JH, Ong J, Blom LH, Andiappan AK, **Nilsson G, Dahlin JS**. Single-Cell Omics Analysis of Human Basophils Reveals Two Transcriptionally Distinct Populations. *Allergy* 2026, 1-10.

Wagner A, Lautaoja-Kivipelto JH, Pehkonen K, Hassinen A, Kuusela M, Röttger L, Herbers E, **Ioannidou A**, Mädler S, Rothenaigner I, Srinivasan S, Laasonen S, Rahman MT, Elomaa P, Kortetjärvi S, **Olsson A**, Ukkola O, Hadian K, Mann M, Peltoniemi H, Pietiläinen KH, Klingenspor M, Virtanen KA, **Hagberg CE**, and Pirinen E. In vitro model of human subcutaneous adipocyte spheroids for studying mitochondrial dysfunction and mitochondria activating compounds. *iScience* 29(2) 114480 (2026)

**Shavva VS, Tarnawski L, Dai W**, Moruzzi N, Haller AS, Borg F, Hansson S, **Guo Q, Min C**, Fekete E, **Vacquié JJ, Maestri A, Liu T**, Vimaladithan RS, **Malin SG**, Saliba-Gustafsson P, Berggren PO, **Hagberg CE, Ahmed O, Olofsson PS**. Proliferation of Activated Hepatic Stellate Cells Requires REST. *Mol Med* 32(1):28 (2026)

**Van Gompel E, Galešić M**, Delarogue N, Kern K, **Stålesen R, Nottarnicola A, Demirdal D, Hansson M, van Vollenhoven A, Wigren E, Gräslund S**, Szardenings M, **Malmström V, Lundberg IE, Horuluoglu**

**B, Grönwall C, Chemin K, Joshua V**. Anti-MDA5 monoclonal antibodies from patients with dermatomyositis - B cell characteristics and differential targeting of the helicase domains. *J Autoimmun.* 2026 Feb 19;159:103536.

**Wangriatisak K, Huang W, Sechi G, Oke V, Chemin K, Grönwall C, Gunnarsson I, Malmström V, Faustini F**. CD72 downregulation on DN2 B cells is associated with disease activity and resistance to rituximab in systemic lupus erythematosus. *Rheumatology (Oxford).* 2026;65(3):keag097.

**Wangriatisak K, Faustini F, Filipovic M, Wähämaa H, Malmström V, Gunnarsson I, Oke V.** Interleukin 16 in lupus nephritis-a role for Th1 and CD8+ T cell migration. *Clin Exp Immunol.* 2025;219(1):uxaf068.

Wanjiku P, Orindi B, Mwacharo J, Chemweno J, Karanja HK, Kronsteiner B, Kai O, Wright D, Ochola-Oyier LI, **Sundling C**, Dunachie S, Warimwe GM, **Färnert A**, Bejon P, **Ndungu FM**, Nduati EW. Pre-COVID-19 ex vivo cross-reactive IFN- $\gamma$  cellular response to SARS-CoV-2 spike overlapping peptides is more prevalent among Kenyan compared to Swedish adults. *BMC Infect Dis.* 2026 Jan 17;26(1):174.

# Transcriptionally distinct populations of human basophils

## PUBLICATION & OUTREACH

The journal *Allergy* has published a summary of the paper on their YouTube channel, presented by the first author Sofia Papavasileiou.

Since the publication is also a public resource, the research team is hosting an interactive website via CMM where users can analyze the published data without needing to be bioinformaticians,

<https://dahlinlab.cmm.se/>.

**PUBLICATION:** Papavasileiou S, Mo J, Boey D, Wu C, Tronstad M, Margerie L, Olsen RA, Bachmann JA, Low JH, Ong J, Blom LH, Andiappan AK, Nilsson G, Dahlin JS. Single-Cell Omics Analysis of Human Basophils Reveals Two Transcriptionally Distinct Populations. *Allergy* 2026, 1-10.

**Conclusions**

- Two novel transcriptionally distinct basophil populations were identified through single-cell omics.
- The available resource constitutes a cellular and molecular reference for future studies of basophils.

**Study design**

Healthy subjects → Blood → Single-cell omics (RNA sequencing, Large-scale immunophenotyping) → Omics integration

**Identified populations**

UMAP 2 (Population 2), UMAP 1 (Population 1)

**Gene expression** (Low to High scale)

**Protein expression** (Low to High scale)

Online resource

scRNA-seq reveals two transcriptionally distinct basophil populations

**Thank you!**

inflammatory conditions and that the available research will be a valuable tool for the research

Single-Cell Omics Analysis of Human Basophils Reveals Two Transcriptionally Distinct Populations

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Screenshot from YouTube summary presented by Sofia Papavasileiou.



# CRISPR epigenome editors show complex on- and off-target effects

Image: iStock.

## PUBLICATION

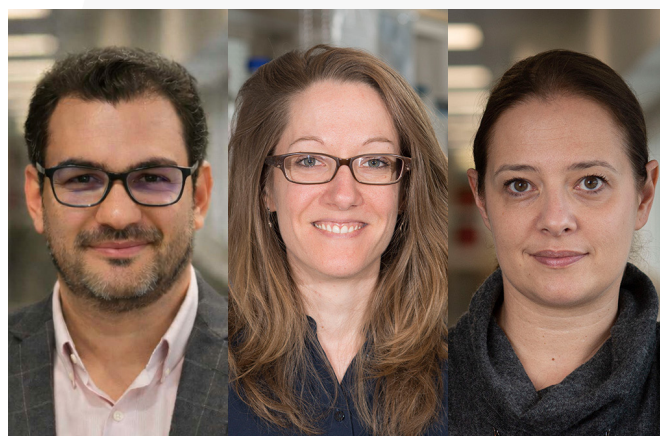
**New research from CMM reveals that advanced CRISPR-based epigenome editors may influence the genome more broadly than previously understood. The study shows that even highly sequence-specific targeting cannot fully prevent unintended epigenetic changes – a finding with important implications for both fundamental research and future therapeutic applications.**

Advanced CRISPR/dCas9-based epigenome editors are designed to precisely alter DNA methylation at specific genomic regions without introducing double-strand breaks, offering promising strategies for research and future therapies. A new study from researchers at Center for Molecular Medicine (CMM) and Karolinska Institutet, published in *Genome Biology*, shows that the relationship between intended (on-target) and unintended (off-target) effects is more complex than previously appreciated. While these systems are widely used to study gene regulation and disease mechanisms, their broader impact on the epigenome has not been comprehensively profiled.

The researchers benchmarked multiple CRISPR/dCas9 epigenome editing platforms. Using complementary

genome-wide high-resolution approaches, they demonstrate that off-target DNA methylation changes can occur even when targeting is highly specific at the DNA sequence level. Importantly, the extent and pattern of these off-target effects varied depending on the effector domain and experimental context.

“Our results show that epigenome editing is not simply a local event at the intended locus. There can be broader epigenetic consequences, and these need to be carefully evaluated, especially if these tools are to be translated into clinical applications,” says the study’s



Majid Pahlevan Kakhki (Photo: Private), Lara Kular, Maja Jagodic (Photos: Stefan Zimmerman).

# CRISPR Epigenome Editing: Balancing Potency and Precision

**POTENCY:**  
Performance Benchmarks & Stability

**PRECISION:**  
The Challenge of Specificity



## Multimerization Boosts Potency



**68%**

Average DNA methylation increased by fusing multiple catalytic domains



## Rapid On-Target Editing

Significant on-target methylation occurs within just 24 hours post-transfection.



## CRISPRoff: The Gold Standard for Stability



Emerges as the most efficient tool for maintaining stable gene silencing.

## Pervasive Early Off-Targeting



**89%**

On average, 89% of early off-target methylation changes are shared across different tools.

### Epimodifier Performance Comparison: Time & Precision

	On-Target Stability (Day 30)	Off-Target Intensity (Day 3)
CRISPRoff	High	Moderate
dCas9-3A3L	High	High
dCas9-3A	Low	High

Comparing the most potent epimodifiers on their performance over time.

## gRNA-Independent Side Effects

Most off-target activity is driven by the editing platform itself, not the gRNA.



## Methylation-Independent Transcriptional Noise

Non-targeting gRNAs can cause long-lasting alterations in energy metabolism genes without changing methylation.

first author, Majid Pahlevan Kakhki, research specialist at the Department of Clinical Neuroscience at Karolinska Institutet.

Beyond methodological benchmarking, the study provides conceptual insight: on-target efficiency and off-target activity are not independent phenomena. Instead, they appear to be linked through complex chromatin and regulatory network dynamics. These findings highlight the need for standardized validation pipelines when applying epigenome editing in functional genomics or therapeutic development.

“Our work highlights that careful and rigorous evaluation of specificity is essential to ensure accurate interpretation of functional studies and further optimizations can hopefully bring this exciting frontier to safe clinical translations in the future,” says Professor Maja Jagodic, who led the study with Dr. Lara Kular.

The research was conducted at CMM and Karolinska Institutet and has been funded by, among others, Swedish Research Council, EUBOPEN consortium, Swedish Brain Foundation, Knut and Alice Wallenberg Foundation and European Research Council (ERC).

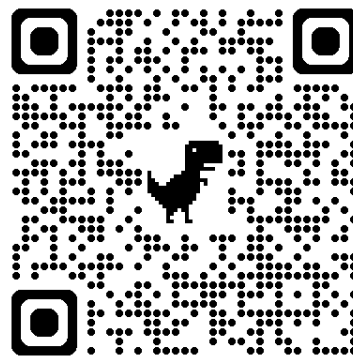
**PUBLICATION:** Majid Pahlevan Kakhki, Fatemeh Rangani, Ewoud Ewing, Chiara Starvaggi Cucuzza, Galina Zheleznyakova, Maria Kalomoiri, Lea Kenny, Anika Raghavan, Chandana Rao Prakash, Gabe van den Hoeven, Tejaswi Venkata S. Badam, Ruxandra Covacu, Ioanna Andreou, Maria Needhamsen, Lara Kular\* & Maja Jagodic\*. Comprehensive profiling of CRISPR/dCas9 epigenome editors indicates a complex link between on- and off-target effects. *Genome Biology*, 27, 52 (2026). <https://doi.org/10.1186/s13059-026-03967-6>  
\*The authors contributed equally.

Infographic explaining the study.

# How is CMM organized?

What exactly is CMM? How is it organized? We often get asked that question.

Some people think CMM is a department at Karolinska Institutet. Others even think it's a clinic at Karolinska University Hospital. Neither is correct, however. With the help of this infographic, we hope to provide a quick overview of CMM and its organization. We have also produced a document titled "Welcome to CMM" with detailed and practical information about what you need to know when working at CMM. You find the document [here](#) or by scanning the QR code.



Welcome to CMM



## How the Center for Molecular Medicine is Organized

The Center for Molecular Medicine (CMM) is a foundation established by the Stockholm County Council (now Region Stockholm).



CMM is an ecosystem - not merely a physical space - providing a nexus for intellectual stimulation and innovation.



Our mission is to support excellent translational medical research.



We bring together basic science and clinical researchers across different departments from Karolinska Institutet and Karolinska University Hospital



CMM provides a purpose-built research building and research infrastructures.

### Board



- The Board of Directors is responsible for 1) strategic decision-making, 2) overseeing management and governance, 3) ensuring the financial health of the CMM Foundation and 4) fulfillment of the by-laws and original mission of the foundation.
- It continuously evaluates CMM's activities, supported by a Scientific Advisory Board (SAB) of internationally recognized experts, and ensures evaluations lead to concrete actions.
- [Members](#) are appointed by Region Stockholm and meet 4-6 times per year.



### Steering Group



- Oversees CMM's research activities.
- Advises the Director and supports decision-making during monthly meetings.
- Presents major issues to the Board and implements Board decisions.
- Maintains dialogue across researchers, staff, management, and the Board.
- Communicates pressing issues to the Director and Board.
- Facilitates implementation of decisions and executes agreed activities.

[Contact the Steering Group:](#)



### Research Groups & Teams



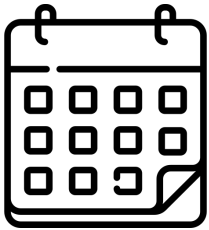
- The core and primary stakeholders of CMM.
- Researchers are employed by Karolinska Institutet or are affiliated.
- Group Leaders are appointed by the Steering Group.
- Team Leaders are nominated by their Group Leader and appointed by the CMM Director.
- The appointment processes thus differ from those at Karolinska Institutet.

Find out more about the [research Groups and Teams:](#)



Download infographic:





# Save the date:

## “Welcome to CMM” – May 6, 15:00

### UPCOMING EVENT

**We are pleased to announce that a “Welcome to CMM” event will take place on May 6 at 15:00 in the CMM Lecture Hall.**

The event is primarily intended for new members of CMM, but other CMM colleagues are also welcome to join (subject to available space).

The purpose of the event is to provide an introduction to what CMM is, help newcomers navigate the organization, find out what support there is available for their research work, and clarify where to turn for different types of questions.

The event is expected to last 1–1.5 hours.

#### Preliminary program:

- **Introduction to CMM**  
*Liselotte Jansson (Chair of the CMM Board) & Michael Sundström (CMM Director)*
- **CMM Service Center**
  - **Communication & Coordination**  
*Magdalena Lindén & Kristina Edfeldt*
  - **IT**  
*Olle Gartell*
- **Core Facilities**  
*Maja Jagodic*
- **MINGLE**

More information and a sign-up link will follow within short. We look forward to welcoming you!



Next deadline for sending in  
contributions to CMM News:  
30<sup>th</sup> of April.