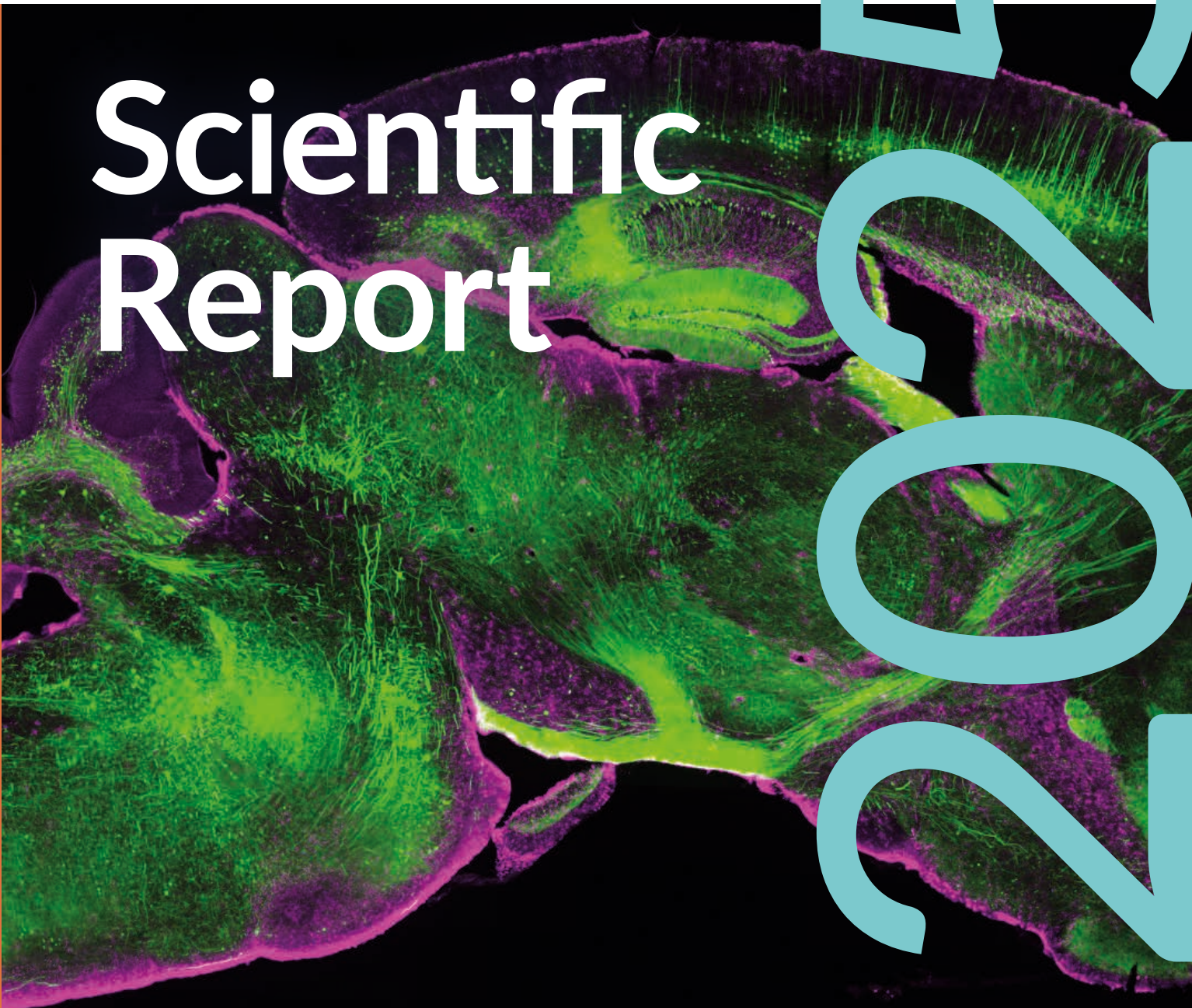
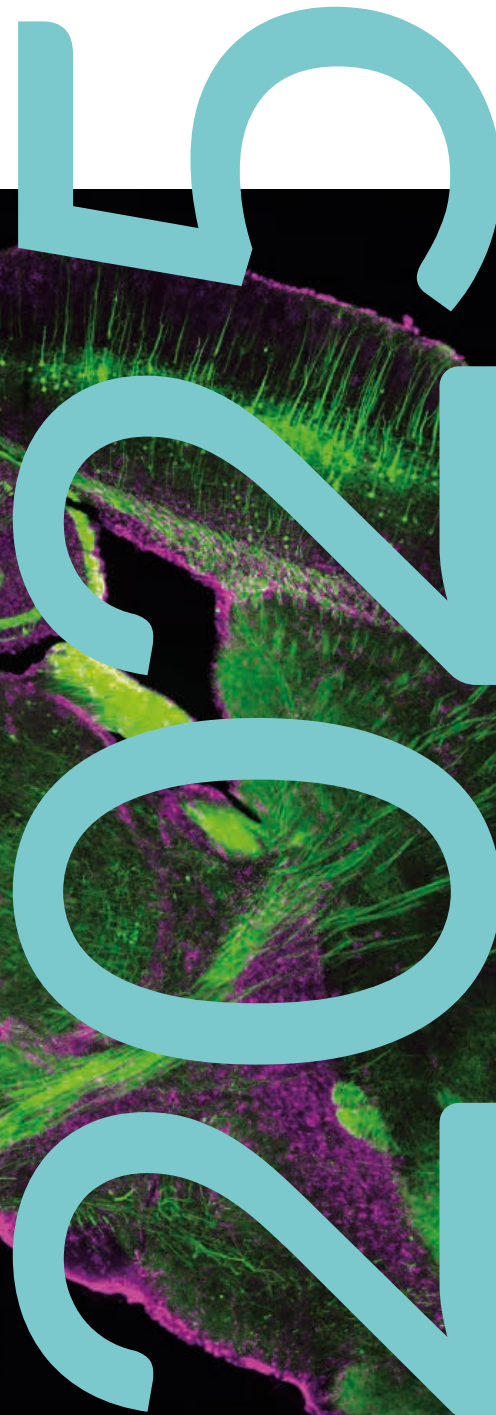




Minerva Foundation &
Minerva Foundation Institute
for Medical Research

Scientific Report





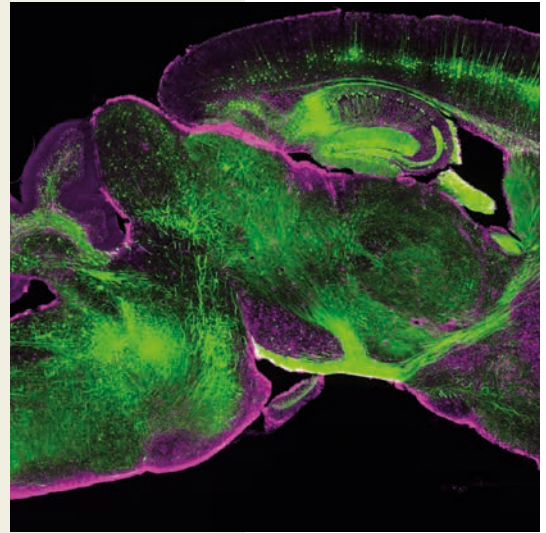
Front page Image: Mouse brain slice cut in the middle of the brain from back to front. Selected neuron populations, mainly in cortex and hippocampus, express GFP and are shown in green. Astrocytes are visualized with GFAP-antibody staining, here shown in purple. Courtesy of Emilia Toissalo (Cellular Neuroscience).

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Summary of research and activities in 2025

Minerva Foundation Institute for Medical Research is a privately owned research institute located at Biomedicum, Academic Medical Center, Helsinki, Finland. The Institute, the history of which dates back to 1959, combines basic biomedical research with clinical investigation relevant to common diseases. The overarching aims of Minerva Institute are to generate 1) new fundamental knowledge and mechanistic insight, 2) innovations for the development of future diagnostic approaches, and 3) preventive measures and treatments for common diseases. The Institute's focus areas are metabolic and cardiovascular diseases, fatty liver disease, and neurodegenerative or neuropsychiatric disorders. The research undertaken in the groups of the Institute during 2025 is outlined in this report.

The financial resources of Minerva Foundation are directed at maintaining and further developing a research infrastructure that serves, in the most effective way possible, the work of the nine research groups. The groups are responsible for acquiring external funds to cover the costs of special reagents, the stipendium or salary support of students, and the salaries of other personnel. The external, competitive research funds acquired by the groups amounted to € 1 481 000 during 2025 and covered 55% of the Institute's budget. During 2025, a total of 67 articles were published, 53 of which were original articles in international peer-reviewed journals. The median impact of all the published articles was 5.7. Moreover, five students at the Institute, David Micinski, Abel Szkalicity, Hannes Bode, Lauri Vanharanta and Sami Qadri, defended their doctoral theses in 2025. The Institute hosted five international special seminars (Professor Matthew Grubb, King's College London, UK, Professor Meredith Hawkins, Albert Einstein College of Medicine, New York, USA, Professor Mette Sørensen Thinggaard, The University of Southern Denmark, Odense, Denmark, Professor Robin Klemm, University of Oxford, UK, and Doctor Merja Joensuu, The University of Queensland, Australia).

In October 2025, the Institute organized with the support of Minerva Foundation a two-day symposium under the title "From Genetic Observations to Functional Insights and Therapy Development." This event, which took place at the Hanasaari conference center in Espoo, hosted a series of global leading experts and turned out to be a great success. Furthermore, a project aimed at increasing the public visibility of the Institute continued: During the year, special attention was focused on reporting significant events in the Institute's research groups on the web pages and as press releases, as well as on gaining increased attention for the prizes and grants awarded by Minerva Foundation. Moreover, the visibility of the Institute in social media was enhanced. Major events included the awarding of the prestigious Matti Äyräpää prize to a senior researcher at the Institute, Professor Hannele Yki-Järvinen, the Ella & Georg Ehrnrooth Foundation science award to a Minerva group leader, Professor Elina Ikonen, and the J.W. Runeberg prize to a Minerva-associated group leader, Professor Dan Lindholm.

To summarize: The Institute thrived in 2025 both scientifically and financially, and moves into 2026 with optimism and determination.

Seminars, prizes, grants & theses

Minerva special seminars

March 21, 2025

Professor Matthew Grubb

Centre for Developmental Neurobiology
Institute of Psychiatry, Psychology and Neuroscience (IoPPN)

King's College London, UK

Strikingly different neurotransmitter release strategies in dopaminergic subclasses

May 23, 2025

Professor Meredith Hawkins

Albert Einstein College of Medicine
New York, USA

Type 5 diabetes – A new global challenge

October 2, 2025

Professor Mette Sørensen Thinggaard

The University of Southern Denmark
Odense, Denmark

Molecular epidemiological studies of human aging – data and studies from the University of Southern Denmark and the Danish Registry

November 21, 2025

Professor Robin Klemm

Department of Physiology,
Anatomy and Genetics
University of Oxford, UK

Lipid exchange between mitochondria and lipid droplets drives metabolic flexibility and cell survival

December 2, 2025

Dr Merja Joensuu

Australian Institute for Bioengineering and
Nanotechnology

The University of Queensland, Australia

Endogenous fatty acid metabolism: A new paradigm in brain energy, memory and therapeutics

Prizes and Grants

MEDIX PRIZE OF THE MINERVA
FOUNDATION

Award Ceremony and Prize Lecture, October
6, 2025

The winning article: Multiparameter imaging reveals clinically relevant cancer cell-stroma interaction dynamics in head and neck cancer. Punovuori K, Bertillot F, Miroshnikova

YA, Binner MI, Myllymäki SM, Follain G, Kruse K, Routila J, Huusko T, Pellinen T, Hagström J, Kedei N, Ventelä S, Mäkitie A, Ivaska J, Wickström SA. Cell. 2024; 187(25):7267–7284.e20.

Read more on pages 8–9.

BROR-AXEL LAMBERG PRIZE IN ENDOCRINOLOGY

Professor Outi Mäkitie, University of Helsinki

Read more on pages 10–11.

SELMA AND MAJA-LISA SELANDER'S FUND FOR RESEARCH IN ODONTOLOGY

From Selma and Maja-Lisa Selander's fund 21 grants were awarded 2025, in all €119.000.

The following theses were accepted at the University of Helsinki in 2025

DOCTORAL THESES

David Micinski: The actin cytoskeleton and axon initial segment function. March 21, 2025.

Ábel Szkalisity: Computational techniques in lipid metabolic studies. July 1, 2025.

Hannes Bode: Epigenetics of environmental risk factors for breast cancer in Cancer-Discordant Twin Pairs. October 1, 2025.

Lauri Vanharanta: Mechanisms of cellular cholesterol storage. November 21, 2025.

Sami Qadri: Regulation of human liver metabolism in MASLD: Genetics, insulin resistance, and nutrition. December 12, 2025.

MASTER'S THESES

Nisa Pitafi: Characterization of CNPY2 isoforms in ER stress, Resolution and neuronal survival. July 1, 2025.

Outi Rahikkala: Development of the Healthy Weight Management Index and its association with biological aging: A Cross-Sectional Study. July 31, 2025.

Veera Häkkinen: Gut hormone receptor agonist drugs: Their receptor expression and functional effect on adipocytes and adipose tissue endothelial cells. September 11, 2025.

Laura Biskop-Lindman: Hjärtats struktur och funktion hos prepubertala barn från preeklampiska graviditeter. October 9, 2025.

Jenny Illman: The metabolic effects of incretin mimetics in L6 skeletal muscle cells. December 19, 2025.

Emma Lindfelt: Peripapillary retinal nerve fiber layer thickness and cerebral microbleeds in type 1 diabetes. December 19, 2025.

Administration

The Minerva Foundation

The main purpose of the Foundation is to promote research in medicine and biosciences by maintaining the Minerva Foundation Institute for Medical Research. This scientific review covers the period from January 1 to December 31, 2025.

During this period, the following persons served as trustees:

Board of Trustees

Professor Caj Haglund, chair
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Professor Per-Henrik Groop
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The Minerva Foundation Institute for Medical Research

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Professor Dan Lindholm
Associate professor Panu Luukkonen
Docent Miina Ollikainen
Docent Taisto Sarkola
M.Sc. Cia Olsson

**News and events
throughout the year**

Minerva Foundation Symposium 2025

The Minerva Foundation Symposium 2025 gathered leading experts in medical research to discuss the latest advancements in research to understand and treat various diseases. The event was held in Hanasaari, Espoo on the 23rd & 24th October, 2025.

Over the course of two days, researchers from around the world shared their insights on how genetic discoveries can be transformed into therapeutic approaches and clinical applications. The event welcomed researchers, academics, doctors, and other professionals in medical research and related fields, as well as students and the general public.

Professor Vesa Olkkonen, the Director of Minerva Institute, described the event as a great success: "We had a good number of audience, and the superb lectures by global leaders in their fields evoked lively discussions."

The two-day event consisted of four sessions, two each day, plus a panel discussion at the end of the second day. The topics and speakers selected for this year's symposium sessions were:

Steatotic liver disease – Leveraging genetics for therapeutic insight

- Panu Luukkonen, Minerva Foundation Institute for Medical Research
- Russell Goodman, Harvard/Massachusetts General Hospital, Boston, USA
- Shawn Burgess, UT Southwestern, Dallas-Fort Worth, USA
- Sami Qadri, Minerva Foundation Institute for Medical Research

Incretins – Bench to bedside

- Petter Bjornstad, University of Washington, Seattle, USA
- David Cherney, University of Toronto, Canada
- Ian de Boer, University of Washington, Seattle, USA

Bone and mineral metabolism, its genetic components and therapeutic approaches

- Wim van Hul, University of Antwerp, Belgium
- Harald Jüppner, Harvard/Massachusetts General Hospital, Boston, USA
- Outi Mäkitie, Folkhälsan, University of Helsinki, Helsinki University Hospital, Finland
- Heikki Koistinen, Minerva Foundation Institute for Medical Research

Genetics and pharmacogenetics in personalized medicine

- Vilma Lammi, FIMM, University of Helsinki and Broad Institute of MIT and Harvard, Cambridge, MA, US



MINERVA FOUNDATION
Institute for Medical Research

Welcome to the

Minerva Foundation Symposium

Financed by the
Minerva Foundation

- Adrian Krainer, Cold Spring Harbor Laboratory, NY, USA
- Mikko Niemi, University of Helsinki, Finland
- Elisabeth Widen, FIMM, University of Helsinki, Finland

The symposium concluded with a panel discussion about *Emerging new therapies: The path from innovation to cost-effective benefit to the patients* with panelists Ian de Boer, Petter Bjornstad, Daniel Gordin, Harald Jüppner, Adrian Krainer and Wim van Hul. Sami Pakarinen acted as the moderator of the panel discussion.

Minerva Foundation and Research Institute actively follow the hottest, fastest developing fields of biomedical science, also relevant for the Institute's own research. The next Minerva Foundation Symposium will be held in 2027.



Members of Professor Sara Wickström's research team.

Finnish research achieves breakthrough in cancer diagnostics – awarded the 2025 Medix Prize

The 2025 Minerva Foundation's Medix Prize has been awarded to Professor Sara Wickström's research group at the University of Helsinki. The prize is awarded annually to Finnish research in biomedical or clinical medicine that has been published in an international peer-reviewed scientific journal.

In the award-winning article, researchers at the University of Helsinki used an AI-powered imaging analysis method to study hundreds of biobank patient samples at single-cell resolution. The work was carried out in collaboration with researchers from the University of Turku and the Max Planck Institute in Münster, Germany.

Recognition for long-term research work

Sara Wickström emphasizes that research is often a long-term effort spanning many years, which makes this recognition especially meaningful.

- It is wonderful that the members of the research group receive such a concrete acknowledgment of their work, says Research Director Sara Wickström.
- I am inspired by creating new knowledge and by understanding how the body and the environment work together. It is rare in research to discover something that can have an immediate benefit for patients. The possibility of improving people's quality of life brings extra

motivation and makes the work especially rewarding, Wickström says.

Decoding the complexity of cancer behavior at the cellular scale

The research team's article offers a new perspective on the diagnosis of head and neck cancers, specifically squamous cell carcinomas. This cancer type ranks among the ten most common worldwide, with 700–900 new cases diagnosed annually in Finland.

Cancer tumors often consist of heterogeneous cell populations that behave in different ways, potentially making the disease aggressive and resistant to treatment. Wickström's team succeeded in combining artificial intelligence and machine learning with spatial biology methods to study tissue architecture. Using this approach, the researchers analyzed hundreds of biobank patient samples at single-cell resolution and created a kind of "fingerprint" for each patient, enabling the assessment of cancer prognosis and treatment response.

This breakthrough narrows a significant knowledge gap: it helps to understand how the diversity of cancer cells influences disease progression and offers patients new opportunities for more precise diagnostics and personalized treatment.

- The method we have developed makes it possible to analyze individual cells both in cancer tissue and in the surrounding healthy tissue. We are able to identify which combinations of cells drive aggressive cancer and which predict a more favorable disease course, Wickström summarizes.

International recognition and scientific acknowledgment

Following its publication in autumn 2024, the study attracted attention both in the Finnish media and within the international cancer research community. It was reported by outlets such as ScienceDaily, and it was highlighted by the European Association of Cancer Research as a "Highlight in Cancer Research". The research is an excellent example of how basic and clinical research can converge. Behind it is a broad network of scientists combining expertise in bioinformatics, artificial intelligence, pathology, and clinical oncology.

- From the very beginning, the research has been basic science, not classically applied. Now, however, it has given rise to a spinout company that already employs four people and brings the results closer to patient care. This is a great example of how long-term research can also lead to practical applications, Wickström explains.

Innovation in cancer diagnostics – from research to spinout company

The research group has not stopped at scientific findings alone. Patent applications have been filed for the technology, and the discovery has led to the founding of the spinout company MultivisionDx, which aims to bring the method into clinical use.

The new analysis method and platform makes it possible to study millions of cells in patient samples with subcellular precision – providing a way to identify aggressive disease forms already at an early stage. The company's goal is to develop a diagnostic tool suitable for clinical practice, one that can accelerate care pathways and improve treatment outcomes.

- The company's ambitious goal is to have a fully developed software in use within 4–5 years, capable of automatically analyzing cancer samples. The aim is for a preliminary version to be available to other researchers as early as 2026, Wickström says.



From left to right: Professor Per-Henrik Groop, a member of the Minerva Foundation's Board of Trustees, Professor Sara Wickström, Head of the Award-Winning Research Team, Professor Johanna Arola, Dean of the Medical Faculty, and Professor Vesa Olkkonen, Director of the Minerva Foundation Institute. Photographer Corinne Grönholm.

Recognition for Finnish medical science

The Medix Prize, valued at 20,000 euros, founded by the Minerva Foundation, has been awarded annually since 1988 and is one of the most significant recognitions in Finnish medical science. The award to Wickström's group underlines that research conducted in Finland is not only of the highest scientific quality but also internationally pioneering.

The justification for the winning article states that the study narrows a significant knowledge gap in understanding the mechanisms underlying cancer heterogeneity. For a long time, cancer research has faced two unresolved key questions: what cellular mechanisms explain the aggressiveness of heterogeneous tumors, and how heterogeneity can be reliably quantified to support diagnosis and prognosis.

The award-winning study was published in the fall of 2024 in *Cell* under the title "Multiparameter imaging reveals clinically relevant cancer cell-stroma interaction dynamics in head and neck cancer." The authors are Karolina Punovuori, Fabien Bertillot, Yekaterina A. Miroshnikova, Mirjam I Binner, Satu-Marja Myllymäki, Gautier Follain, Kai Kruse, Johannes Routila, Teemu Huusko, Teijo Pellinen, Jaana Hagström, Noemi Kedei, Sami Ventelä, Antti Mäkitie, Johanna Ivaska and the Research Director Sara A. Wickström.

Professor Outi Mäkitie awarded the Bror-Axel Lamberg Prize 2025

The Minerva Foundation's Bror-Axel Lamberg Prize in Endocrinology 2025 was granted to Professor Outi Mäkitie on the 30th of October. The prize, worth 10,000 €, is presented every two years at the annual meeting of the Finnish Endocrine Society to a distinguished Finnish or Nordic researcher in the field of endocrinology.



Professor Outi Mäkitie

Professor Mäkitie is a paediatric endocrinologist and internationally recognised expert in metabolic bone diseases. She serves as Professor of Paediatric Endocrinology at the University of Helsinki, Chief Physician at the Helsinki University Hospital, Senior Researcher in Clinical Genetics at the Karolinska Institute, and Group Leader at the Folkhälsan Research Center, Biomedicum.

From Lamberg's mentorship to research career

Professor Mäkitie describes herself as deeply honoured by the prize, noting its significance given that previous recipients have been pioneers in the field.

– It is a great privilege to join the ranks of previous pioneers. This prize is especially meaningful for me since my own research career began under the supervision of Bror Axel Lamberg, Mäkitie notes.

During her medical studies, Mäkitie completed a research project under Lamberg's guidance – an experience that sparked her interest in research even more and left a lasting impression of the importance of scientific research in medicine.

Diversity and international support as an asset

Based on her positive experience with mentorship, Mäkitie truly knows the importance of including researchers from different ages and tenures into a research group. Throughout her career, Mäkitie has noticed how demographic diversity plays a key role in a group's success. She sees diversity, especially in terms of age, as a significant strength.

– When a research group includes both younger and more experienced researchers, the research work can be inspiring and stimulating, and you can really enjoy it.

Young people inspire the more experienced ones, which makes the research even more meaningful, Mäkitie explains.

Mäkitie wants to encourage younger researchers to network internationally. She has noticed that the support from international research networks has been absolutely vital during her career.

– It's not possible to conduct extensive research alone in a small country, which is why international cooperation is essential, Mäkitie notes.

Groundbreaking discoveries in paediatric bone diseases

Mäkitie's research has focused particularly on early-onset osteoporosis and skeletal dysplasias as well as their underlying genetic mechanisms. Her group was the first to demonstrate that osteoporosis can also occur in children – a finding that permanently changed clinical practice and contributed to the inclusion of paediatric osteoporosis in Finland's national Current Care Guidelines in 2014.

She has also contributed to the discovery of several novel inherited bone diseases. Each genetic discovery has advanced the field significantly.

– Genetic discoveries are increasingly leading us towards understanding disease mechanisms and developing targeted therapies. We have already witnessed the impact of breakthrough precision medicines – and more are urgently needed, Mäkitie notes.

Prize acknowledges pioneering genetic research

Professor Mäkitie's research groups, in collaboration with international partners, have identified several previously unknown rare disorders, including a growth failure syndrome with compromised immune function linked

to a gene involved in G-protein signalling, a skeletal dysplasia caused by mutations in the ribosomal protein RPL13, and a monogenic skeletal disorder that can range in severity from childhood-onset osteoporosis to lethal skeletal dysplasia, caused by variants in the KIF24 gene.

By awarding the Bror-Axel Lamberg prize to Mäkitie, the Minerva Foundation wants to recognise Mäkitie's pioneering work that uniquely combines clinical practice, basic research, and international collaboration. Minerva Foundation highlights that Mäkitie's contributions have significantly advanced paediatric endocrinology and the diagnosis and treatment of rare bone diseases, while inspiring new generations of researchers in Finland and internationally.

Bror-Axel Lamberg (March 1, 1923 – May 4, 2014)

Bror-Axel Lamberg received his MD degree in 1949, after which his career continued in the Fourth Department of Internal Medicine at the University of Helsinki. Professor Johannes Wahlberg led Lamberg to study the thyroid-stimulating hypophysis hormone TSH. Lamberg was a pioneer in radioimmunoassays, and he defended his doctoral thesis in 1953 on using radioactive phosphorus to measure TSH.

After his defense, Lamberg and his co-workers studied the lack of iodine in the Finnish population. His studies played an important part in having iodine added to common salt in Finland, which led to the eradication of endemic goiter. In 1971, Lamberg was appointed professor of endocrinology at the University of Helsinki. He performed his clinical work primarily at the HUS clinics in Meilahti.

Professor Bror-Axel Lamberg was awarded many prizes, including the Matti Äyräpää prize in 1979 and the J.W. Runeberg prize in 1985. During his active career, he acted as a chair and a member of many societies and foundations. He was also granted honorary membership of several societies.

Professor Bror-Axel Lamberg was one of the founders of Minerva Foundation in 1959. The Foundation was formed to maintain the activity of the Minerva Foundation Institute for Medical Research. His endocrinological research team was one of the first to start their research at the newly founded institution at a small hospital, Konkordia, in Helsinki. Professor Bror-Axel Lamberg was the first head of the Institute, from 1959 to 1970.

Professor Lamberg was also one of the founders of the clinical service laboratory Medix Ltd. in 1964, which played an important role in creating the financial basis for the Minerva Foundation and the Research institute.

J.W. Runeberg Prize awarded to Dan Lindholm



Professor Dan Lindholm

The 2025 J.W. Runeberg Prize has been awarded to Professor Dan Lindholm for his groundbreaking contributions to neuroscience and neurodegenerative diseases. In its justification, the Prize Committee highlights Dan Lindholm's research

on neurotrophic factors and the roles of mitochondria and the endoplasmic reticulum in brain diseases such as Huntington's, Parkinson's disease, and Amyotrophic Lateral Sclerosis (ALS). He has also explored the identification of potential pharmacological molecules and the development of therapeutic strategies to prevent and mitigate neuronal damage in the brain.

"I am deeply honored by the award and want to extend my warm thanks to all my colleagues and members of the research group who contributed to the work" says Dan Lindholm. Professor Vesa Olkkonen, director of the Minerva Foundation Institute for Medical Research, states, "it is excellent that preclinical research of this kind is being recognized, as it may ultimately benefit many patients."

Dan Lindholm has served as group leader at the Max Planck Institute of Psychiatry in Munich, professor of neurobiology at Uppsala University, professor of cell and molecular biology at the University of Helsinki, and visiting professor at Harvard Medical School in Boston and at Linköping University. He has also held the position of director and research group leader at the Minerva Foundation Institute for Medical Research.

The J.W. Runeberg Prize

The Finnish Medical Society awards the J.W. Runeberg Prize every second year for outstanding scientific achievement. The prize consists of a medal and a monetary sum. Johan Wilhelm Runeberg, the third son of the national poet, was a surgeon and professor of clinical medicine at the University of Helsinki, and he donated funds for this prize in 1902. Today, the prize is one of the most prestigious medical honors in the country.

Hannele Yki-Järvinen, who has researched the link between fatty liver and diabetes, receives the Matti Äyräpää Award



Professor Hannele Yki-Järvinen

Professor Hannele Yki-Järvinen, an internationally respected physician-scientist, has been awarded the prestigious Matti Äyräpää Award for her groundbreaking work on fatty liver disease and type 2 diabetes, which has transformed patient care and clinical practice.

On April 10, 2025, the Finnish Medical Society Duodecim presented the award – one of Finland’s most esteemed medical honors – to Professor Yki-Järvinen.

“Yki-Järvinen has made significant advances in diabetes research and treatment. Fatty liver, often associated with obesity and its complications, is a timely and crucial issue. More so, she has played a vital role in educating a new generation of Finnish physician-researchers in her capacity as professor of internal medicine,” says Markus Perola, chair of the award committee.

Breakthrough in Type 2 Diabetes Treatment

Yki-Järvinen’s research team was the first to demonstrate that excess fat in liver cells impairs insulin function and is a key factor in the development of metabolic syndrome – characterized by elevated blood sugar and fat levels, hypertension, and often, overweight.

Her interest in this phenomenon began in the early 1990s while she was specializing in internal medicine at Meilahti Hospital. She already understood that suppressing the liver’s sugar production was essential to treating type 2 diabetes. Working with Finnish colleagues, she was also the first to show that this could be most effectively achieved through a simple combination of basic insulin and oral medication. This approach has now become part of international treatment guidelines. At the time, however, she did not yet understand why patients responded so differently to insulin.

“I remember a diabetes patient on the ward whose liver was so enlarged it filled the entire abdominal cavity. The patient didn’t drink alcohol, and no amount of insulin could control their blood sugar. Suddenly, I realized that fat in the liver was probably preventing insulin from working. In such cases, sugar, fats, and clotting

factors are released excessively into the bloodstream, significantly increasing the risk of cardiovascular disease.”

It was later discovered that one in four Finns has fatty liver, and for most, it is not caused by alcohol. This condition, now known as metabolic fatty liver disease, is the most common liver disease globally. It is especially prevalent among those who consume large amounts of saturated fat and engage in little physical activity. Interestingly, obesity accounts for only 25% of all fatty liver cases.

Common Genetic Variant in Finns Increases Risk of Liver Damage

In 2008, the Dallas Heart Study identified a genetic variant that explains a substantial portion of fatty liver and cirrhosis cases.

“About 40% of Finns carry the PNPLA3 gene variant, which increases the risk of liver damage. Interestingly, this hereditary form of fatty liver does not elevate the risk of cardiovascular disease,” Yki-Järvinen explains.

Her team was the first to observe that liver fat in individuals with this gene variant differs from that found in people whose fatty liver is caused by metabolic syndrome. In gene variant carriers, the liver fat resembles healthy fats, like canola oil, whereas metabolic fatty liver contains harmful fats similar to those in butter.

“Initially, fatty liver was always associated with alcohol. Then we realized it could occur without alcohol. Today, metabolic fatty liver disease is recognized as the most common form among Finns. Now we know this public health issue is even more complex than previously thought.”

Understanding the specific type of fatty liver a patient has can influence both treatment and prognosis. In the future, medication choices may be tailored according to the underlying cause of the condition.



About 40% of Finns carry the PNPLA3 gene variant, which increases the risk of liver damage.”

“If the patient has gene-related fatty liver, we need to monitor liver health carefully, but the cardiovascular risk is lower. In metabolic fatty liver, on the other hand, cardiovascular disease is the leading cause of death – so prevention is critical.”

Finland as a Leader in Patient-Based Research

“The willingness of Finnish patients to participate in research is outstanding. This has played a major role in allowing us to lead globally in metabolic research.”

The Matti Äyräpää Award holds special significance for Yki-Järvinen, who has received widespread international acclaim.

“The award meant a great deal to me, as I have spent most of my career working in Finland, developing diagnostics and treatments for Finnish patients alongside incredibly talented young researchers and healthcare professionals.”

About the Matti Äyräpää Award

Named after one of the founding members of the Duodecim Society, the Matti Äyräpää Award is valued at €20,000 and is presented annually to a Finnish physician who has made significant contributions to research.

Ella & Georg Ehrnrooth Foundation Research Prize to Elina Ikonen



Professor Elina Ikonen

The leader of the Minerva research group focusing on membrane biology, Professor Elina Ikonen, has been awarded the Ella & Georg Ehrnrooth Foundation Research Prize, valued at €25,000. As the research group leader, Ikonen is broadly responsible for her group’s operations, everything from creating project ideas and securing funding, to coordinating the work.

Ikonen is delighted to receive the award

– This is a wonderful recognition of the long-term work of our entire research group. This type of research is very much a team effort, with each member contributing their own expertise. The knowledge and skills of each individual complement each other.

Ikonen was recognized for her internationally significant research in the field of cholesterol and other lipids at the Ella & Georg Ehrnrooth Foundation’s 90th-anniversary celebration, held at the University of Helsinki on October 30, 2025. Foundation Chairman, Professor Henrik Meinander, presented the €25,000 prizes to a total of four scientists who have received both national and international recognition for their long-standing and significant scientific achievements. The Ella and Georg Ehrnrooth Foundation annually distributes over €3 million in grants to promote scientific research and literary activity.

Professor Elina Ikonen, MD, PhD, leads cell and tissue biology research at the University of Helsinki’s Faculty of Medicine and is particularly known for her significant breakthroughs in cholesterol research. She is also the director of the University of Helsinki’s Bioimaging Service Unit and a member of the Academy of Finland’s Centre of Excellence in Metabolic Integration. Her multidisciplinary work combines, among other things, lipid metabolism, cell membrane structure, and intracellular transport.

The objective of Ikonen’s research group, which operates under Minerva and consists of 13 researchers, is to determine how the most important membrane and storage fats, such as cholesterol and triacylglycerols, move within the intracellular environment and how their distribution between cellular compartments is regulated. In addition, the research group aims to determine how changes in this balance lead to human diseases and how such diseases could be detected and treated better than at present.

– The Ella & Georg Ehrnrooth Science Prize motivates us even more to continue our research in cell physiology and the mechanisms of metabolic diseases. Understanding these will help us create the treatments of tomorrow, Ikonen comments.

Research groups

Cardiorenal diabetes

Current Projects

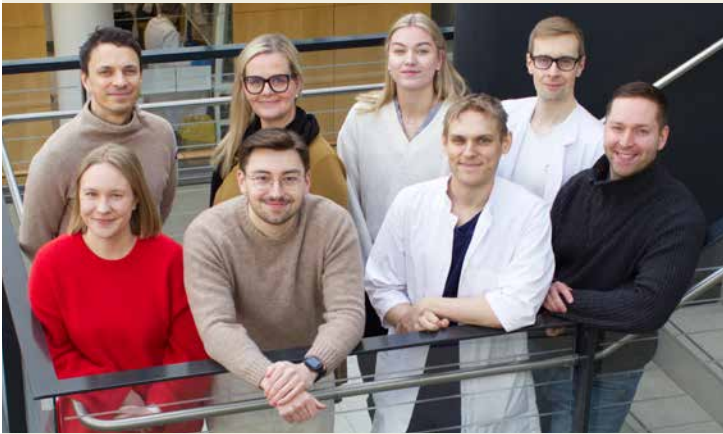
Renal studies

Rare kidney diseases are a group of often genetic conditions with no targeted therapies. These are under-studied because of their rarity, thus their inadequate sample sizes and statistical power. Autosomal dominant polycystic kidney disease (ADPKD) is the most common hereditary kidney disease. IgA Nephropathy (IgAN) in turn, has the highest prevalence of primary glomerulonephritis. We will study these diseases in a large (>550,000) patient-enriched sample of the Finnish population (finngen.fi). The goal of this study is to improve understanding of ADPKD and IgAN by assessing clinical and genetic tools, as well as systems biology. Matti Senturk has started his Ph.D. thesis studies as part of this project.

Renal diseases are major drivers of cardiovascular morbidity, early mortality, and poor quality of life. Our group utilizes methodology including measurement of iohexol glomerular filtration rate, effective renal plasma flow, renal imaging by blood oxygenation level dependent magnetic resonance imaging (MRI) studies, and positron emission tomography/computed tomography, has been set up within the FinnDiane (finndiane.fi) study to investigate renal diseases. Rasmus Simonsen has been instrumental in setting up the lab. Karoliina Ahtola is coordinating the studies.

Cerebrovascular study in type 1 diabetes

Participants in this FinnDiane sub-study underwent brain MRI, genetic analyses, metabolomic profiling, cognitive testing, and retinal imaging using optical coherence tomography angiography. The aim is to investigate structural-functional relationships between the brain, eye, and cognition. Jussi Inkeri and Aleksis Tarkkonen are finalizing their Ph.D. theses, while Iiris Kyläheiko and Emma Lindfelt are preparing theirs as part of this work.



Group members

Daniel Gordin, M.D., Dr.Med.Sci., Docent, Head
 Rasmus Simonsen, M.D., Dr.Med.Sci.
 Jussi Inkeri, M.D.
 Aleksi Tarkkonen, M.D.
 Anni Heiskala, M.Sc., Biostatistician
 Iiris Kyläheiko, M.A.
 Emma Lindfelt, M.Bs.
 Matti Sentürk, M.Bs.
 Karoliina Ahtola, Research nurse

External funding

Medical Society of Finland (Finska Läkaresällskapet)
 Medicinska Understödsföreningen Liv och Hälsa r.f.
 Research Council of Finland
 Research Funding of the Helsinki-Uusimaa Hospital District
 Sigrid Jusélius Foundation
 Wilhelm and Else Stockmann Foundation

Awards, honors and positions of trust

M.D. Aleksi Tarkkonen:
 Abstract prize in the Progress Report Meeting of the Finnish Society of Angiology.

Thesis completed in the group in 2025

The following Master's thesis was accepted at the University of Helsinki this year:

Emma Lindfelt. Peripapillary retinal nerve fiber layer thickness and cerebral microbleeds in type 1 diabetes. December 19, 2025.

Selected publications 2025

Claesson TB, Mutter S, Putaala J, Salli E, **Gordin D**, Groop PH, Martola J, Thorn LM. Age at type 1 diabetes onset does not influence attained brain volume. *BMC Endocr Disord.* 2025; 25:43.
 Januszewski AS, Snaith JR, Grzelka-Wozniak A, Simonsen JRA, Sachithanandan N, Ward GM, O'Neal DN, **Gordin D**, Thorn LM, Groop PH, Uruska AA, Zozulinska-Ziolkiewicz DA, Jenkins AJ, Greenfield JR. No evidence from euglycaemic-hyperinsulinaemic clamp studies for greater insulin sensitivity in adults with type 1 diabetes using insulin pump versus multiple daily insulin injections-Post hoc meta-analysis. *Diabetes Obes Metab.* 2025; 27:5322-5326.

Kakaletsis N, **Gordin D**, Martinez-Majander N, Joutsu-Korhonen L, Salopuro T, Adeshara K, Sibolt G, Curtze S, Pirinen J, Soenne L, Sairanen T, Suihko S, Lehto M, Sinisalo J, Tatlisumak T, Groop PH, Putaala J. Insights into the vascular aging burden in young adults with embolic stroke of undetermined source. *J Neurol Sci.* 2025; 476:123642.
 Rimpeläinen K, Jansson Sigfrids F, **Gordin D**, Klemetti MM, Harjutsalo V, Groop PH, Thorn LM; FinnDiane Study Group. Impact of different hypertensive disorders of pregnancy on cardiovascular disease risk and all-cause mortality in women with type 1 diabetes. *Cardiovasc Diabetol.* 2025; 24:255.
Tarkkonen A, **Kyläheiko I**, **Inkeri J**, Eriksson MI, Thorn LM, Summanen PA, Tatlisumak T, Groop PH, Putaala J, **Gordin D**, Martola J; FinnDiane Study Group. Progression of cerebral small vessel disease among neurologically asymptomatic middle-aged individuals with Type 1 Diabetes. *Diabetes Care.* 2025; 48:776-780.

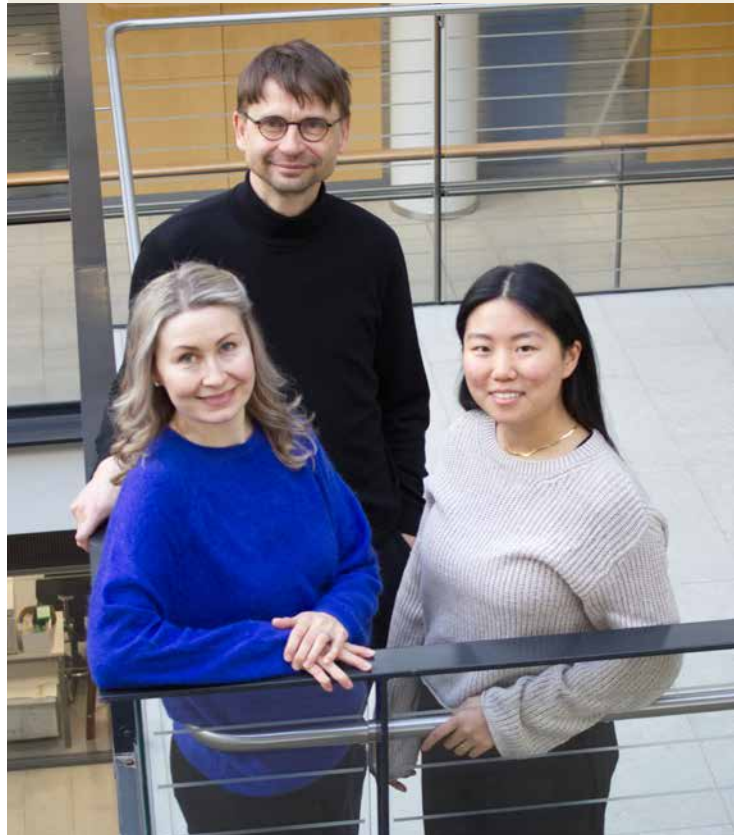
Cardiovascular research in the young

Main research activities

During the year, main research activities remained in the project domains of fetal cardiovascular programming and prevention of cardiovascular disease. The FINNCARE project (A lifestyle intervention for families with a history of pre-eclampsia – primary prevention of cardiovascular disease; NCT04676295) study visits were completed in 2023 and the project is currently in the data analysis and manuscript writing phase. In addition, the work to update the clinical research database (2021–) for fetal congenital heart disease (previously established for 2010–2020) was initiated by medical student Lili Pusa.

One article from FINNCARE with Ph.D student Anni Kivelä as first author has been published. The study concluded that women with history of pre-eclampsia and gestational diabetes and with superimposed pre-eclampsia exhibit an adverse cardiometabolic profile characterized by high body mass index. This highlights the need for targeted cardiovascular prevention. Women with de novo PE should undergo regular blood pressure monitoring. In December 2025, M.Sc Anni Kivelä defended her Ph.D. thesis at the Medical Faculty at the University of Helsinki within the collaboration of her supervisors, Professor Hannele Laivuori and Docent Tiina Jääskeläinen. Medical student Laura Biskop-Lindman completed her Master's thesis and Karita Hyvönen continued finalizing her Master's thesis within the FINNCARE project. During the year, M.D. Anna Savolainen actively continued her work as an M.D-Ph.D. student in the FINNCARE project supervised by Taisto Sarkola with a presentation provided in the Minerva scientific seminars in autumn 2025.

Taisto Sarkola continued his active collaboration within the pediatric thoracic Scandiatransplant organization. One register study article describing children's heart transplantation within the Scandiatransplant region over 38 years was published. The study concluded that the number of pediatric heart transplants in the Scandiatransplant region per year is low but has increased over time. There has been a significant decrease in waiting list



Group members

Taisto Sarkola, M.D., Dr.Med.Sci., Docent, Head
My Blomqvist, D.D.S., Dr.Med.Sci.
Michelle Renlund-Vikström, M.D., Dr.Med.Sci.
Mari Ylinen, M.D., Dr.Med.Sci.
Anna Savolainen, M.D.
Laura Biskop, Medical student
Karita Hyvönen, Medical student
Lili Pusa, Medical student
Maria Finne, M.Sc., Research coordinator
(maternity leave 02-12/2025)

External funding

Foundation for Pediatric Research
Medical Society of Finland (Finska Läkaresällskapet)
Medicinska understödsföreningen Liv och Hälsa r.f.
Stiftelsen Dorothea Olivia, Karl Walter och
Jarl Walter Perklés minne

mortality over time, whereas improvements in post-transplant outcomes have been less evident, most likely due to the excellent short-term outcomes for the first graft recipients in the region. Two scientific poster abstracts were presented at the ISHLT 2025 congress in Boston, USA.

Taisto Sarkola continued as Chair of the European Society AEPC Fetal Cardiology working group council. A survey describing the status of fetal echocardiography imaging and fetal counseling fellow training in 29 European countries was published with Sarkola as first author. The survey concluded that there is substantial variation in advanced fetal cardiology training practice in Europe, suggesting a need for further clarification of training criteria and structure. Trainee assessment is mainly verbal and based on direct observation. There seems to be a need to strengthen the fetal cardiology module in core pediatric cardiology training and to improve the quality assessment of the clinical service provided. The survey results were also presented as an oral abstract by Sarkola at the Nordic Pediatric Cardiology Meeting, September 2025 in Stockholm. One brief fetal cardiology review and one case report describing the first intrauterine fetal balloon valvuloplasty performed on a Finnish citizen due to critical fetal aortic stenosis related heart failure was published in the domestic journal of the Finnish Cardiac Society, *Sydänääni*. The same journal also published an interview highlighting Sarkola's collaborative work within pediatric cardiology in Europe. Taisto Sarkola continued as Editor of the ISUOG journal Ultrasound in Obstetrics and Gynecology, covering fetal cardiology.

Within the ORALPEDHEART study coordinated by My Blomqvist, one domestic review was published and two scientific abstracts presented at the International Association of Paediatric Dentistry meeting in Cape Town, South Africa.

Awards, honors and positions of trust

Docent Taisto Sarkola:

Positions of trust in the following organizations:

Association for European Paediatric Cardiology, Fetal Cardiology working group council chair 2024–2027

Editor of the ISUOG Ultrasound in Obstetrics and Gynecology journal 2024–2027, covering fetal cardiology

Scandiatransplant pediatric heart and lung group (SPeAdHLG), founding member 2020–

Gyllenberg Foundation, member of the board 2023–

Finnish Medical Ultrasound Society, member of the board 2020–

The Medical Society of Finland, Prize and Grant, board member 2025–2027

Thesis completed in the group in 2025

The following Master's thesis was accepted at the University of Helsinki this year:

Laura Biskop-Lindman. Hjärtats struktur och funktion hos prepubertala barn från preeklampiska graviditeter. October 9, 2025.

Publications 2025

Kivelä A, **Renlund-Vikström M**, Heinonen S, **Sarkola T**, Laivuori H, Jääskeläinen T. Cardiometabolic health 8–12 years after pre-eclampsia: Role of obesity and gestational diabetes (FINNCARE study). *Pregnancy Hypertens.* 2025; 41:101226.

Sarkola T, Seale AN, Tulzer A, Duignan SM, Grzyb A, Tuo G, Vanhie E, McMahon CJ; Fetal Cardiology Working Group of the AEPC. Current Status of Fetal Echocardiography Imaging and Fetal Counseling Fellow Training in 29 European Countries. *Pediatr Cardiol.* 2025 Sep 1. doi: 10.1007/s00246-025-04006-0. Online ahead of print.

van der Have O, Tran-Lundmark K, Wähländer H, Kaskinen AK, Möller T, Juul K, Jahnukainen T, Weinreich ID, **Sarkola T**, Nilsson J, Odermarsky M. Pediatric heart transplantation within the Scandiatransplant region – a multinational observational study spanning 38 years. *J Heart Lung Transplant.* 2025; 44:1597–1609.

Publications in Finnish journals 2025

Karikoski E, **Sarkola T**, Blomqvist M. Varhainen neuvonta synnynnäistä sydänvikaa sairastavien lasten suunterveyden parantamiseksi – tuloksia satunnaistetusta vertailukoikeesta. *Denstal - tiedettä pureskeltavaksi* -lehti, 04/2025.

Sarkola T. Sydänlääkärin urapolku: Suomalaiset Euroopassa (haastattelu). *Sydänääni* 2025; 31:2:247–248. https://www.fincardio.fi/site/assets/files/10476/sydanaani_2_25_netti.pdf

Sarkola T, Macharey G, Ylinen M, Räsänen J, Pitkänen-Argillander O. Ensimmäinen suomalaiselle sikiölle tehty kriittisen aorttaläpän ahtauman pallolaajennus (tapauselostus). *Sydänääni.* 2025; 31:1:48–52. https://www.fincardio.fi/site/assets/files/9941/sydanaani_1_25_netti.pdf

Ylinen M, **Sarkola T**, Pitkänen-Argillander O. Heterotaksia – monielin-epämuodostuma, jossa sydänvika usein vaikea (katsaus). *Sydänääni.* 2025; 31:1:43–47. https://www.fincardio.fi/site/assets/files/9941/sydanaani_1_25_netti.pdf

Cardiovascular research

Main research activities

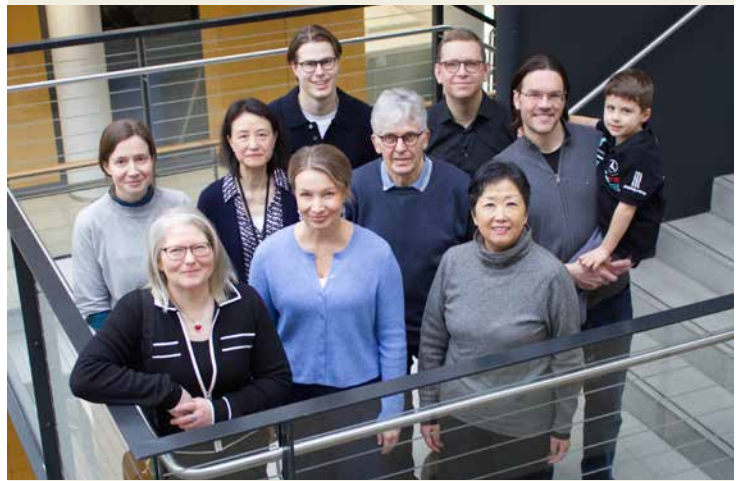
We study the molecular mechanisms of cardiac injury, repair, and regeneration in myocardial infarction and heart failure to identify potential targets for cardiovascular medicines and novel biomarkers. We are particularly interested in the role of noncoding RNAs in the development and progression of heart failure. The main projects worked on during 2025 are presented below.

New molecular mechanisms and biomarkers of heart failure

Heart failure is a significant cause of morbidity and mortality. The prognosis of heart failure remains poor, despite optimal therapy with currently available cardiovascular drugs. A better understanding of the cellular and molecular mechanisms of heart failure is needed to advance the development of novel treatments and diagnostic tools for heart failure.

We have previously used a multiomics approach to identify dysregulated signaling pathways and potential target molecules for new therapies in ischemic heart failure, in collaboration with Professor Juha Sinisalo. The most significant dysregulation was found in pathways regulating cardiac metabolism, muscle contraction, and cardiac fibrosis. During 2025, we have continued this project by investigating how specific long noncoding RNAs and microRNAs (miRNAs) regulate these pathways, and thus the development and progression of heart failure. In these functional studies, we use human cardiac cell cultures and zebrafish heart failure models.

MiRNAs are short noncoding RNA molecules that play an important role in the pathogenesis of heart failure. miRNAs have also emerged as potential diagnostic and prognostic biomarkers of cardiovascular disease. Cardiogenic shock (CS) is the most severe form of acute heart failure, with in-hospital mortality close to 40%, even with current treatment. New biomarkers to stratify CS patients according to their risk and to optimize treatment are needed. In collaboration with Professor Veli-Pekka Harjola, we have shown that higher plasma miR-20b-5p levels are associated with 90-day survival in patients with CS. Our results indicate the potential of miRNAs as biomarkers for risk assessment in CS. Our studies on novel miRNA biomarkers continue.



Group members

Päivi Lakkisto, M.D., Dr.Med.Sci., Docent, Head
Ilkka Tikkanen, M.D., Dr.Med.Sci., Professor
Mika Laine, M.D., Dr.Med.Sci., Docent
Chunguang Wang, M.D., Dr.Med.Sci., Docent
Jere Paavola, M.D., Dr.Med.Sci.
Hong Wang, Ph.D.
Mikko Hänninen, M.D.
Karri Kalervo, M.D.
Tuomas Mäntylä, M.D.
Heli Segersvärd, M.D.
Ian Hägerström, Medical student
Katariina Immonen, B.Sc., Laboratory technician
Sanni Perttunen, B.Sc., Laboratory technician

External funding

Aarne Koskelo Foundation
Finnish Foundation for Cardiovascular Research
Finnish Foundation for Laboratory Medicine
Medical Society of Finland (Finska Läkaresällskapet)
Medicinska Understödsföreningen Liv och Hälsa r.f.
Paulo Foundation
Research Funding of the Helsinki-Uusimaa Hospital District (state funding for university-level health research)

We are also investigating the origin and function of circulating miRNAs to better understand the significance of measured miRNA levels in disease pathophysiology.

During 2025, our group participated in the COST Action AtheroNET (CA21153), the Network for implementing multiomic approaches in atherosclerotic cardiovascular disease prevention and research, in which Päivi Lakkisto served as a member of the management committee.

Molecular mechanisms of cardiac regeneration

We use zebrafish models to study the molecular mechanisms of heart failure. Unlike humans, zebrafish are capable of fully regenerating their hearts and restoring cardiac function following

injury, making them an excellent model for investigating factors that regulate the development and recovery of heart failure. During 2025, we continued working on zebrafish transcriptomics data to identify and validate the functions of noncoding RNAs that regulate cardiac regeneration after injury.

Role of heme oxygenase-1 (HO-1) in cardiovascular diseases

HO-1 and its reaction products, carbon monoxide (CO), biliverdin, and bilirubin, have a variety of cardiovascular protective properties. The promoter region of *HMOX1* gene contains a guanine–thymine (GT) microsatellite repeat. A long GTn repeat decreases HO-1 expression and is associated with cardiometabolic diseases and pre-eclampsia. We have studied the role of HO-1 and *HMOX1* gene polymorphisms in the development of cardiovascular and renal complications in type 1 diabetes in collaboration with Professor Per-Henrik Groop and the FinnDiane Study Group. We found that the LL genotype of the *HMOX1* GTn repeat and the AA genotype of -413A/T SNP were associated with ischemic cardiac complications and all-cause mortality in men, but not in women. Thus, the *HMOX1* genotype may influence the development of cardiovascular complications in individuals with type 1 diabetes in a sex-dependent manner. The *HMOX1* gene polymorphisms could be utilized as possible risk factors for coronary heart disease, especially in

men. In addition, serum HO-1 concentrations were higher in men compared to women, and higher concentrations were found to be associated with the presence of cardiovascular or kidney disease. This suggests that serum HO-1 concentrations could serve as a possible tool to identify cardiovascular and kidney complications in individuals with type 1 diabetes.

Clinical hypertension

High blood pressure is the leading risk factor for death worldwide. Despite developments in antihypertensive therapies during recent years, treatment results are still unsatisfactory. Our clinical hypertension research has focused on new treatment strategies for resistant hypertension.

Publications 2025

- Mäntylä T, Wang C, Hänninen M, Immonen K, Jäntti T, Lassus J, Tikkanen I, Pulkki K, Devaux Y, Harjola VP, Lakkisto P;** CardShock Study Investigators. Circulating levels of miR-20b-5p are associated with survival in cardiogenic shock. *J Mol Cell Cardiol Plus.* 2025; 11:100284.
- Narumanchi S, Perttunen S, Laine P, Kosonen R, Lakkisto P, Laine M, Tikkanen I, Paavola J.** Tricaine, eugenol and etomidate for repetitive procedural anesthesia in adult zebrafish, *Danio rerio*: effect on stress and behavior. *Front Vet Sci.* 2025; 12:1562425.
- Segersvärd H, Sandholm N, Harjutsalo V, Tikkanen H, Kosonen R, Laine M, Tikkanen I, Groop PH, Lakkisto P;** FinnDiane Study Group. Heme oxygenase-1 polymorphisms associate with ischemic cardiac complications and all-cause mortality in type 1 diabetes. *Cardiovasc Diabetol.* 2025; 24:339.

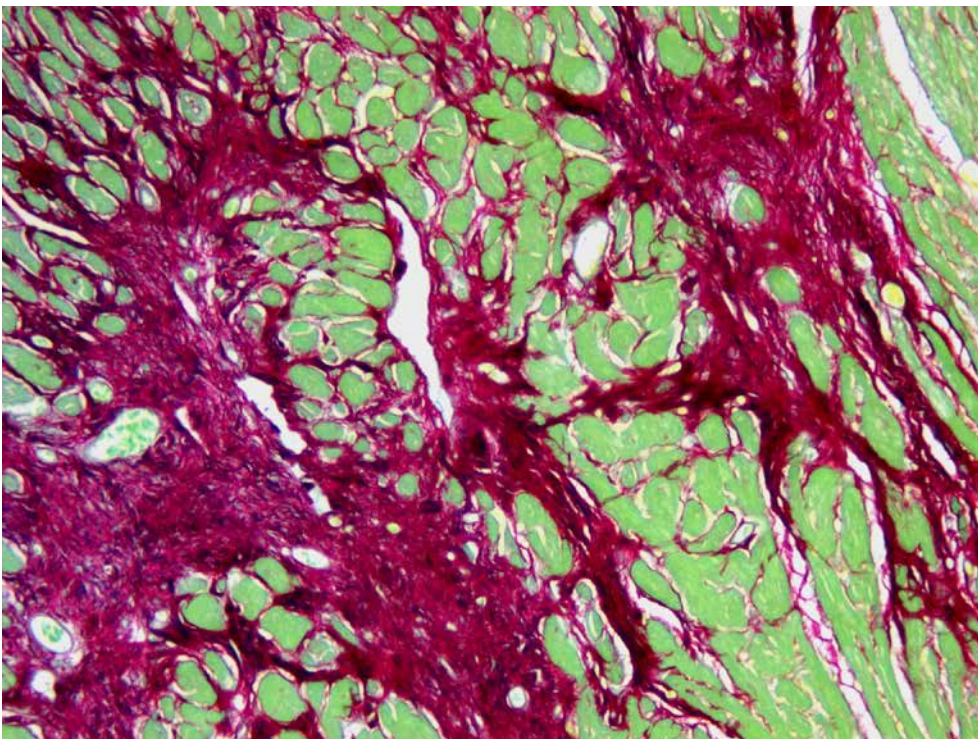


Figure. Sirius Red and Fast Green staining of rat heart showing fibrotic areas in red and cells in green. Courtesy of Katariina Immonen.

Cellular neuroscience

Main research activities

In 2024, we initiated a new project examining the long-term effects of transient peripheral inflammation on the brain, and this has now become our main project. In 2025, we confirmed that peripheral inflammation affects the brain and transient joint inflammation leaves long-term changes. The brain does not appear damaged, but rather reshaped. This work helps us to understand why infections or severe inflammations in the body increase the risk for neurological and psychiatric diseases later in life. It seems that short-lived peripheral inflammation leaves a “neuroimmune memory” that increases vulnerability to later challenges.

In 2025, we also finalized studies on our long-term interests focusing on neuronal structures called dendritic spines and the axon initial segment (AIS). The AIS is a specialized compartment that separates the axonal and somatodendritic components. Dendritic spines are small protrusions along dendrites where excitatory synapses are located. Our research in recent years has elucidated the mechanisms of actin cytoskeleton regulation in dendritic spines and the AIS, in health and disease.

Regulation of dendritic spine initiation

Spine initiation factors are proteins that interact with the plasma membrane and actin cytoskeleton to push out the first protrusion from the neuronal dendrite. Spine formation is linked to various neuronal functions including learning. Understanding the mechanisms and regulation of spine initiation is necessary to understand the changes in neural networks in health and disease.

To date, we have identified two spine initiation factors – MIM (Saarikangas et al., 2015) and Gas7 (Khanal et al., 2023). Aqsa Jabeen continued the work started by Pushpa Khanal to characterize the expression pattern and function of a close MIM homologue called ABBA. This work was published at the end of the year in *Molecular Neurobiology*.

ABBA has gained broader interest due to two significant findings: first, its mRNA expression increases upon exercise-induced activation of granule neurons in the dentate gyrus of the hippocampus, and it is required for exercise-induced increases in dendritic spine density; second, a missense mutation in MTSS2, the human gene encoding ABBA, was found to cause intellectual disability syndrome.

As a novel discovery, we found that ABBA is highly expressed in GABAergic inhibitory neurons, such as



Group members

Pirta Hotulainen, Ph.D., Docent, Head
David Micinski, M.Sc., Ph.D. in spring 2025
Aqsa Jabeen, M.Sc.
Jaan Korpikoski, M.Sc.
Matilda Kuusi, M.Sc.
Emilia Toissalo, M.Sc.
Vilja Salmi, B.Sc.
Eevi Rautjärvi, B.Sc.
Veera Syrjäniemi, B.Sc.
Ioanna Kastanioti, Erasmus student
Tiia Parmanen, Laboratory assistant
(shared with Hanna Ollila)

External funding

Medicinska Understödsföreningen Liv och Hälsa r.f.
Sigrid Jusélius Foundation
University of Helsinki, Doctoral Education Pilot
(Jaan Korpikoski)
University of Helsinki, The Doctoral Programme
Brain & Mind (Matilda Kuusi)

parvalbumin-positive interneurons in the hippocampus. Through live-cell imaging, we demonstrated that ABBA facilitates spine initiation by clustering on the plasma membrane before a new filopodium appears. However, our live-cell imaging data also revealed that ABBA localized not only on small focal points typical for filopodia formation on the plasma membrane, but also more broadly on the edges of lamellipodial structures. Compared to its close homolog MIM, ABBA appears to be a more general facilitator of protrusion formation, from dendritic filopodia

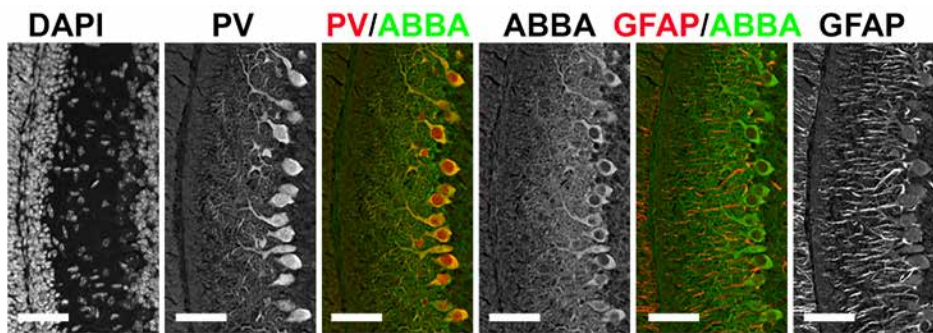


Figure. Cerebellum area of the sagittal section of the P11 mouse brain. At the cerebellum, ABBA showed high expression, especially in Purkinje cells and radial glial cells at P11. We stained Purkinje cells with anti-parvalbumin (PV) antibody and radial glial cells with anti-Glial Fibrillary Acidic Protein (GFAP) antibody. DAPI staining shows nuclei of cells. Scale bar, 50 μm .

to lamellipodial structures. Altogether, our findings provide insights into which cells and processes might be dysfunctional in mutation-carrying patients.

Regulation of axon initial segment plasticity

The axon initial segment (AIS) contains a high density of ion channels that control the initiation of action potentials. Our first AIS study showed that actin filaments are crucial for maintaining the high order of AIS proteins (Abouelezz et al., 2020). David Micinski, who has continued the AIS work after Amr Abouelezz, analyzed changes in the AIS actin cytoskeleton during AIS plasticity using structured illumination microscopy (SIM) imaging (Micinski and Hotulainen, 2024). In 2025, David successfully defended his PhD thesis, receiving the rare "Pass with Distinction" grade awarded only to the most outstanding doctoral research at the University of Helsinki.

Effects of peripheral inflammation in the brain

Inflammation in the brain is involved in many neurological and psychiatric disorders, but we still lack understanding of how neuroinflammation begins. Increasing evidence suggests that even short-lived inflammation outside the brain can cause long-lasting changes in brain function. This project aims to discover how transient peripheral inflammation affects the brain and how persistent these changes are.

To explore these questions, we established a rheumatoid arthritis (RA) mouse model called the collagen antibody-induced arthritis (CAIA) model. We evaluated changes using behavioral analyses, brain imaging, and cytokine measurements. The results showed that peripheral inflammation reshaped the brain, and these changes were observable a month after the transient joint inflammation has healed. Mice show more anxious behavior, including enhanced fear learning. Changes in astrocyte activity, excitatory neuron synaptic plasticity, and complement system activation correlate with these behavioral outcomes.

Furthermore, we followed cytokine dynamics in blood and the brain using a broad cytokine array.

Impact

Beyond chronic conditions, this approach has implications for acute inflammatory events (surgery, infection, trauma) where cytokine modulation during critical windows might prevent long-term neurological sequelae. The research also contributes fundamental knowledge about peripheral-brain immune communication, which remains incompletely understood despite its relevance to numerous neurological and psychiatric conditions.

Analysis of cytokine profiles will establish whether and how peripherally-acting immunomodulatory drugs can serve as neuroprotective agents – potentially repositioning existing approved therapies for new indications while informing the development of next-generation treatments optimized for CNS protection.

Awards, honors and positions of trust

Docent Pirta Hotulainen:
Chair of Brain Research Society of Finland
Chair of FENS-Kavli Network of Excellence alumni
Organizing a FENS Regional meeting in Oslo

M.Sc. Emilia Toissalo:
Organizing Brain and Mind Symposium 2025 in Helsinki

Theses completed in the group in 2025

The following Ph.D. thesis was accepted at the University of Helsinki this year:

David Micinski: The actin cytoskeleton and axon initial segment function. March 21, 2025.

The following Master's thesis was accepted at the University of Helsinki this year:

Veera Syrjäniemi: Microglial and astrocytic responses in the spinal cord following transient peripheral inflammation in the Collagen Antibody-Induced Arthritis (CAIA) mouse model. June 10, 2025.

Publications 2025

Jabeen A, Khanal P, Toissalo E, Lahti L, Minkeviciene R, Kramm A, Rivera C, Hotulainen P. Expression, subcellular localization, and mechanistic analysis of intellectual disability syndrome protein ABBA. *Mol Neurobiol.* 63:271.

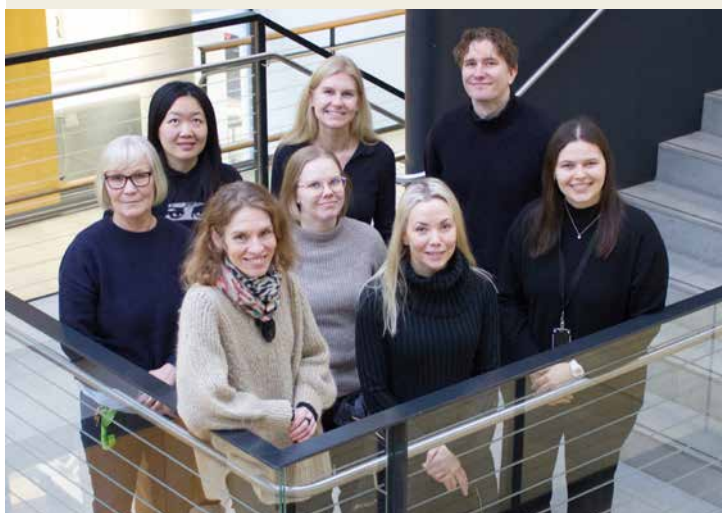
Epigenomics of complex traits

Main research activities

Our research stands at the intersection of genetics, environment, and public health, addressing some of the most pressing challenges of our time – obesity and metabolic health. Our aim is to advance understanding of how genes and environment interact to shape human health and aging, ultimately guiding strategies for healthier lives. Some of our research highlights of 2025 are described below.

Alterations in mitochondrial metabolism in obesity may indicate disrupted communication between mitochondria and nucleus, crucial for adapting to changing metabolic demands. Epigenetic modifications may influence the intricate interplay between these two. Ph.D student Aino Heikkinen examined the connections between DNA methylation, mitochondrial DNA quantity, and obesity, and tested for causal paths. She showed that reduced mitochondrial metabolism was associated with increased activity of the gene *SH3BP4*, particularly in individuals with a higher body fat percentage and reduced insulin sensitivity. This indicates a potential feedback loop where impaired mitochondrial function, possibly due to overnutrition, may contribute to obesity and altered gene regulation (Heikkinen et al., 2025). This study highlights the complex interplay between mitochondrial function, DNA methylation, and obesity, suggesting that interventions targeting these interconnected mechanisms may be beneficial in combating the obesity epidemic. Further, it contributes to understanding the causal link between mitochondrial content and epigenetics in obesity and its relevance to public health.

My group has been conducting a comprehensive and methodologically rigorous investigation of the biological correlates of epigenetic age acceleration using multiomics data in monozygotic twin pairs across distinct age groups. In a study by Ph.D student Gabin Drouard integrating proteomic, metabolomic, exposomic, and lifestyle data with withinpair analyses of monozygotic twins in young and older cohorts, he disentangled genetic, shared environmental, and individualspecific influences on biological aging. His analyses demonstrated that much of the previously reported multiomic variation associated with epigenetic aging is explained by smoking, BMI, or genetic factors. Importantly, only a limited set of associations



Group members

Miina Ollikainen, Ph.D., Docent, Head
Tianyu Zhu, Ph.D.
Hannes Bode, M.Sc., Ph.D. in autumn 2025
Aino Heikkinen, M.Sc.
Mikaela Hukkanen, M.Sc.
Caroline Högel-Starck, M.Sc.
Volter Lukander, M.Sc.
Annika Opperbeck, M.Sc.
Outi Rahikkala, B.Sc.
Mia Urjansson, Research nurse

External funding

Finnish Cultural Foundation, Kymenlaakso Fund
HiLIFE Joint Postdoc Funds
Juho Vainio Foundation
Maud Kuistila Memorial Foundation
Medicinska Understödsföreningen Liv och Hälsa r.f.
Minerva Foundation
NIH/NIDA (National Institutes of Health/National Institute on Drug Abuse, USA)
Sigrid Jusélius Foundation
University of Helsinki, Doctoral Program in Population Health
University of Helsinki, Doctoral Education Pilot in Precision Cancer Medicine (iCANDOC)

persisted within monozygotic twin pairs, indicating likely causal or individual-specific environmental effects. Replication across age groups showed that few markers are consistently associated with epigenetic age acceleration across the life course, highlighting strong agespecificity in biological aging signatures and informing the interpretation and development of aging biomarkers (Drouard et al., 2025).

With our collaborators from the UConn Center on Aging, USA, we developed and validated a novel, proteomics-based composite biomarker for human healthspan – the Healthspan Proteomic Score (HPS) – using large-scale proteomic and chronological age data from the UK Biobank Pharma Proteomics Project (Kuo et al., 2025). HPS captures years lived in good health, defined as survival without major chronic disease or disability. We demonstrated that lower HPS is strongly associated with increased risk of all-cause mortality and multiple age-related diseases, and that HPS outperforms established biological age measures in predicting healthspan-related outcomes.

To strengthen translational relevance and reproducibility, we validated HPS in the Finnish Twin Cohort. This cross-cohort validation established HPS as a robust, biologically meaningful, and generalizable biomarker of healthy aging across different European populations and study designs. The results position HPS as an actionable surrogate endpoint for geroscience research and for monitoring the effectiveness of interventions aimed at extending healthspan, with clear potential for integration with other metrics of aging such as epigenetic clocks.

Awards, honors and positions of trust

Docent Miina Ollikainen:
Co-Director of Doctoral Program in Population Health,
University of Helsinki

M.Sc. Outi Rahikkala:
University of Helsinki Research Foundation awarded
doctoral researcher position

Theses completed in the group in 2025

The following Ph.D. thesis was accepted at the University of Helsinki this year:

Hannes Bode: Epigenetics of environmental risk factors for breast cancer in Cancer-Discordant Twin Pairs. October 1, 2025.

The following Master's thesis was accepted at the University of Helsinki this year:

Outi Rahikkala: Development of the Healthy Weight Management Index and its association with biological aging: A Cross-Sectional Study. July 31, 2025.

Publications 2025

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- Drouard G, Hagenbeek FA, **Ollikainen M**, Zheng Z, Wang X, FinnGen, Ripatti S, Pirinen M, Kaprio J. Twin study provides heritability estimates for 2,321 plasma proteins and assesses missing SNP heritability. *J Proteome Res*. 2025; 24:2689–2697.
- Drouard G, Palviainen T, Kuo CL, Diniz BS, Wang X, **Ollikainen M**, Latvala A, Kaprio J. Protein associations with alcohol consumption and genetic risk for alcohol-related sociomedical conditions. *Addict Biol*. 2025; 30:e70045.
- Drouard G, Suhonen S, **Heikkinen A**, Wang Z, Kaprio J, **Ollikainen M**. Multi-omic associations of epigenetic age acceleration are heterogeneously shaped by genetic and environmental influences. *Aging Cell*. 2025; 24:e70088.
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- Kankaanpää A, Tolvanen A, Joensuu L, Waller K, **Heikkinen A**, Kaprio J, **Ollikainen M**, Sillanpää E. The associations of long-term physical activity in adulthood with later biological ageing and all-cause mortality – a prospective twin study. *Eur J Epidemiol*. 2025; 40:107-122.
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- Obeso A, Drouard G, Palviainen T, Wang X, **Ollikainen M**, Silventoinen K, Kaprio J. Proteomic associations with fluctuation and long-term changes in BMI: A 40-year follow-up study. *Diabetes Obes Metab*. 2025; 27:4192–4202.
- Ravi S, Kankaanpää A, Bogl LH, **Heikkinen A**, Pietiläinen KH, Kaprio J, **Ollikainen M**, Sillanpää E. Suboptimal dietary patterns are associated with accelerated biological aging in young adulthood: A study with twins. *Clin Nutr*. 2025; 45:10–21.
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Fatty liver disease and diabetes

Main research activities

We have continued mechanistic in vivo and in vitro studies addressing the heterogeneity of metabolic dysfunction-associated steatotic liver disease (MASLD, previously known as non-alcoholic fatty liver disease, NAFLD), with a special focus on the mechanisms underlying common risk-modifying genetic variants in humans.

We have also developed and validated new clinical scores and biomarkers to improve the early detection of liver disease in both the general population and patients. Our group has also contributed to national and international clinical practice guidelines on the diagnosis and treatment of MASLD.

In addition, we are pursuing elucidating the role of hepatic mitochondrial reductive stress (i.e. an increased ratio of reduced and oxidized nicotinamide adenine dinucleotide; [NADH]/[NAD⁺]) in the pathogenesis of MASLD. We have previously shown that common genetic risk factors of MASLD increase this stress. In addition to genetic risk factors, we hypothesize that increased hepatic mitochondrial reductive stress is a feature of other risk factors of MASLD, such as excessive metabolism of fatty acids and alcohol in the liver. We postulate that amelioration of hepatic mitochondrial reductive stress is an underrecognized characteristic of many of the currently available MASLD therapies. Ultimately, our goal is to identify novel therapeutic approaches for MASLD.

We are a partner in the EU H2020: Liver Investigation: Testing Marker Utility in Steatohepatitis. LITMUS is a project aiming at developing better biochemical and imaging tests for diagnosing various stages of NAFLD (total funding €45 million).



Group members

Panu Luukkonen, M.D., Dr.Med.Sci., Associate Professor, Head
Hannele Yki-Järvinen, M.D., Dr.Med.Sci., F.R.C.P, Professor
Kimmo Porthan, M.D., Dr.Med.Sci., Docent
Laura Granö, M.D., Dr.Med.Sci
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Noora Ahlholm, M.D.
Juho Asteljoki, M.Sc.
Mari Jokinen, M.Sc.
Sami Qadri, M.D., Dr.Med.Sci. in autumn 2025
Riikka Sane, M.D.
Nova Hongisto, B.Sc.
Sonja Laitila, Medical student
Daniel Segercrantz, Medical student
Sabrina Belgasem, Laboratory technician, Research nurse
Päivi Ihamuotila, Laboratory technician, Research nurse
Aila Karioja-Kallio, Laboratory technician, Research nurse
Saila Saarinen, Laboratory technician, Research nurse

External funding

Finnish Medical Foundation
Emil Aaltonen Foundation
Instrumentarium Science Foundation
Medicinska Understödsföreningen Liv och Hälsa r.f.
Novo Nordisk Foundation
Orion Research Foundation
Research Council of Finland
Research Funding of Helsinki-Uusimaa Hospital District
(state funding for university-level health research)
Sigrid Jusélius Foundation
University of Helsinki
Wilhelm and Else Stockmann's Foundation

Awards, honors and positions of trust

Professor Hannele Yki-Järvinen:
Matti Äyräpää Award by the Finnish Medical Society Duodecim, April 10, 2025. Read more on pages 12-13.

Thesis completed in the group in 2025

The following Ph.D. thesis was accepted at the University of Helsinki this year:

Sami Qadri: Regulation of human liver metabolism in MASLD: Genetics, insulin resistance, and nutrition. December 12, 2025.

Publications 2025

Huang DQ, Wong VWS, Rinella ME, Boursier J, Lazarus JV, **Yki-Järvinen H**, Loomba R. Metabolic dysfunction-associated steatotic liver disease in adults. *Nat Rev Dis Primers*. 2025; 11:14.

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Lam CSP, Rodriguez A, Aminian A, Ferrannini E, Heerspink HJL, Jastreboff AM, Laffin LJ, Pandey A, Ray KK, Ridker PM, Sanyal AJ, **Yki-Järvinen H**, Mason D, Strzelecki M, Bartee AK, Cui C, Hurt K, Linetzky B, Bunck MC, Nissen SE. Tirzepatide for reduction of morbidity and mortality in adults with obesity: rationale and design of the SURMOUNT-MMO trial. *Obesity (Silver Spring)*. 2025; 33:1645-1656.

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Stefan N, **Yki-Järvinen H**, Neuschwander-Tetri BA. Metabolic dysfunction-associated steatotic liver disease: heterogeneous pathomechanisms and effectiveness of metabolism-based treatment. *Lancet Diabetes Endocrinol*. 2025; 13:134-148.

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Yki-Järvinen H, **Luukkonen PK.** Function of PNPLA3 I148M-Lessons from In Vivo studies in humans. *Liver Int*. 2025; 45:e70047.

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Åberg F, Männistö V, **Asteljoki J**, Salomaa V, Jula A, Lundqvist A, Männistö S, Perola M, **Luukkonen PK.** Evidence-based criteria for identifying at-risk individuals requiring liver disease screening. *Hepatol Commun*. 2025; 9:e0679.

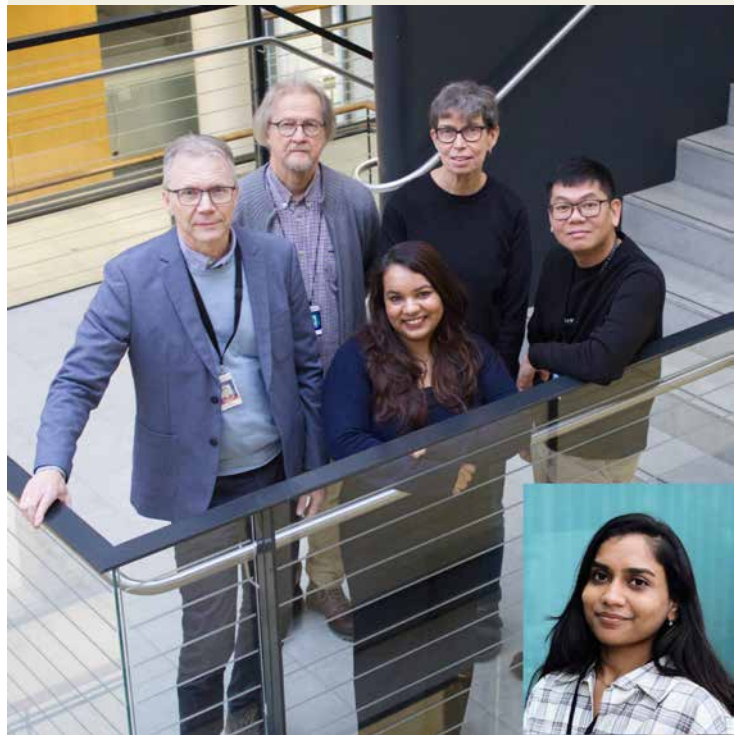


Lipid signaling and homeostasis

Main research activities

A major project in the group investigates molecular defects in the adipocytes and endothelial cells (EC) of obese white adipose tissue. We carried out omics profiling of mature adipocytes and EC isolated from obese (BMI>30) and lean (BMI<25) donors, and combined the adipocyte data with similar data of our collaborators from (1) fat biopsies of subjects after and before bariatric surgery-induced weight loss and (2) primary human adipocytes incubated with a conditioned medium of type 1 macrophages (MCM). Similarly, we investigated EC incubated with MCM or conditioned medium of inflamed adipocytes. The data suggest that the inflammatory activation of adipocytes is a major driver of white adipose tissue dysfunction in obesity. The omics data reveal aspects of mitochondrial dysfunction, dysregulation of vesicular trafficking, and cell adhesion in obese adipocytes. The adipose EC proteomics suggests that the obese EC become increasingly quiescent and display a dysbalanced mitochondrial function. The first article from these results has been submitted for publication. This project is being run as a collaboration with the unit of Doctor Francisco Ortega and Professor José Manuel Fernández-Real at the IDIBGI Institute, Girona, Spain, and that of Professor You Zhou, Cardiff University, UK. The work continues with in vitro experiments assessing the differences in signaling from adipocytes from lean or obese donors to adipose EC. Moreover, a project was launched aimed at analyzing the effects of gut hormone receptor agonist drugs on fat tissue adipocytes and EC as putative targets of their antidiabetic and anti-obesogenic action.

In a Ph.D study focusing on a protein called GOLM1/GP73, a novel biomarker for cancers and liver diseases, we carried out functional analysis of the protein in human cholangiocytes, which express the protein at high levels. The results of an interactome and functional study identified a number of putative GOLM1 interacting partners involved in essential cellular regimes such as mitochondrial and Golgi functions, ribonucleoprotein biogenesis, cell cycle, and basement membrane organization. GOLM1 silencing resulted in impaired mitochondrial function, reduced mitochondrial and P-body markers, increased apoptosis, and



Group members

Vesa Olkkonen, Ph.D., Professor, Head
Matti Jauhiainen, Ph.D., Adjunct professor emeritus
Muhammad Yasir Asghar, Ph.D.
P.A. Nidhina Haridas, Ph.D.
Dan Duc Pham, Ph.D.
Vaishali Chaurasiya, M.Sc.
Meghana Nagaraj, M.Sc.
Veera Häkkinen, B.Sc.
Riikka Kosonen, M.Sc., Laboratory technician
Sanni Perttunen, B.Sc. Laboratory technician

External funding

Diabetes Research Foundation
Jane and Aatos Erkko Foundation
Magnus Ehrnrooth Foundation
Medicinska Understödsföreningen Liv och Hälsa r.f.
Sigrid Jusélius Foundation

reduced cell adhesion, suggesting crucial roles of GOLM1 in maintaining normal cholangiocyte function and metabolism (Nagaraj et al., 2025). The final phase of this project underscored the role of GOLM1 in the proliferation and invasion capacity of lung adenocarcinoma cells (manuscript submitted). Our data reveal GOLM1 as a potential new target of cancer therapies.

One of the long-standing interests of the unit is membrane contact sites (MCS). In 2025, we finalized a study on the role of an MCS component, the lipid-transfer protein Nir2, in endothelial cell functions. We found that Nir2 knock-down (KD) inhibits angiogenic tube formation by EC and reduces cell

viability, proliferation, and migration, while Nir2 overexpression increases cell viability and overexpression of an shRNA-resistant Nir2 construct rescues it. Nir2 KD results in decreased activity of AKT and ERK signaling pathways upon VEGF stimulus, plausibly underlying the observed defects in proliferation, migration, and angiogenesis. The findings unravel new molecular mechanisms by which Nir2 regulates key endothelial functions such as angiogenesis (Poliaskyte-Prause et al., 2025).

In addition to the above work, Professor Vesa Olkkonen contributed to collaborative studies on metabolic and cellular pathways distorted in severe obesity (Dadson et al., 2025) and on the pathogenesis of monogenic *SGMS2*-related osteoporosis (Pihlström et al., 2025). An emeritus scientist in the group, Docent Matti Jauhiainen, participated in several studies focusing on lipoprotein metabolism and cardiovascular risk (e.g., Leiviskä et al., 2025; Lähteenmäki et al., 2025; Äikäs et al., 2025).

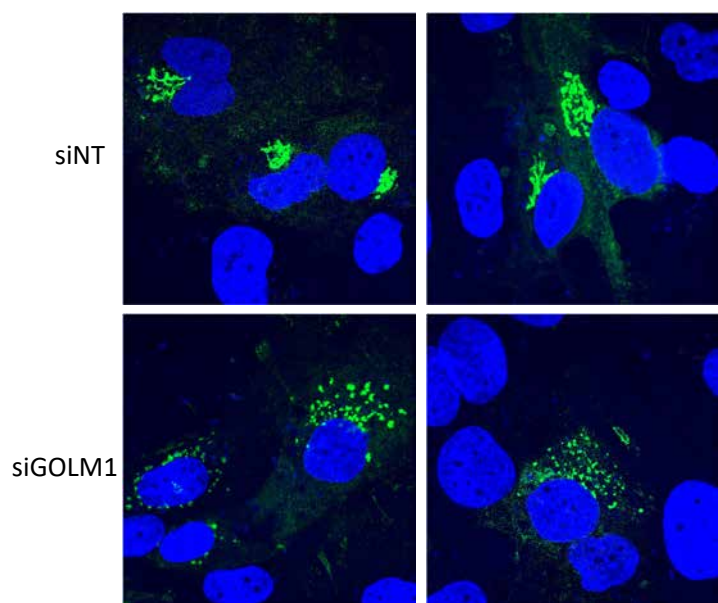


Figure. GFP-tagged vesicular stomatitis virus G3 protein (green) on the way through the Golgi complex in control MMNK-1 cholangiocytes (siNT) and ones subjected to GOLM1 knock-down (siGOLM1). Nuclei are stained with DAPI (blue). Courtesy of Meghana Nagaraj.

Awards, honors and positions of trust

M.Sc. Vaishali Chaurasiya:

Young Investigator Award for the best oral presentation at the 18th annual conference of the Finnish Atherosclerosis Society. June 12–13, 2025.

Thesis completed in the group in 2025

The following Master's thesis was accepted at the University of Helsinki this year:

Veera Häkkinen: Gut hormone receptor agonist drugs: Their receptor expression and functional effect on adipocytes and adipose tissue endothelial cells. September 11, 2025.

Publications 2025

Dadson P, Honka MJ, Suomi T, **Haridas PAN**, Rokka A, Palani S, Goltseva E, Wang N, Roivainen A, Salminen P, James P, **Olkkonen VM**, Elo LL, Nuutila P. Proteomic profiling reveals alterations in metabolic and cellular pathways in severe obesity and following metabolic bariatric surgery. *Am J Physiol Endocrinol Metab.* 2025; 328:E311–E324. – Methods and Resources

Karkamo V, Airas N, Kairento H, Nguyen SD, **Jauhiainen M**, **Metso J**, Grönthal T, Knuutila A, Kareinen L, Hytönen MK, Lohi H, Öörni K, Kareinen I. Heterozygous Korat cats with LDL receptor mutation are asymptomatic and normolipidemic. *Res Vet Sci.* 2025; 193:105784. – Original article

Lee-Rueckert M, **Jauhiainen M**, Kovanen PT, Escolà-Gil JC. Lipids and lipoproteins in the interstitial tissue fluid regulate

the formation of dysfunctional tissue-resident macrophages: Implications for atherogenic, tumorigenic, and obesogenic processes. *Semin Cancer Biol.* 2025; 114:104–127. – Review

Leiviskä J, Sundvall J, **Jauhiainen M**, Kotseva K, Tuomilehto J, De Backer G, Tokgözoğlu L, Reiner Z, De Bacquer D. Residual cardiovascular risk is tracked by apolipoprotein B in coronary patients with elevated serum triglyceride levels: the ESC EORP EUROASPIRE IV survey. *Clin Chim Acta.* 2025; 23:120653. – Original article

Lähteenmäki EI, Lehti S, **Jauhiainen M**, Kankaanpää A, Soliymani R, Baumann M, Ruhanen H, Käkelä R, Vaara J, Laakkonen EK, Öörni K, Kyröläinen H, Lehti M. Association of aerobic fitness and body composition with protein and major lipid class composition of high-density lipoprotein. *Am J Physiol Endocrinol Metab.* 2025; 329:E367–E380. – Original article

Nagaraj M, **Emmagouni SKG**, **Chaurasiya V**, Li L, Nguyen VD, Keskitalo S, Varjosalo M, Zhou Y, **Haridas PAN**, **Olkkonen VM**. Insight into the function of the Golgi membrane protein GOLM1 in cholangiocytes through interactomic analysis. *FEBS Lett.* 2025; 599:1299–1316. – Original article

Pihlström S, Oghabian A, Määttä K, Legebeke J, Mäkitie RE, Campeau PM, Terhal PA, Botto LD, **Olkkonen VM**, Mäkitie O, Pekkinen M. Transcriptomic and lipidomic profiling provide novel insight into the pathogenesis of monogenic *SGMS2*-related osteoporosis. *JBMR Plus.* 2025; 9:z1af128. – Original article

Poliaskyte-Prause Z, **Arora A**, **Taskinen JH**, **Chaurasiya V**, Keskitalo S, Tuhkala A, **Hilksa I**, Varjosalo M, **Olkkonen VM**. The role of Nir2, a lipid-transfer protein, in regulating endothelial cell functions. *Biochim Biophys Acta Mol Cell Res.* 2025; 1872:119926. – Original article

Äikäs L, Kovanen PT, Lorey MB, Laaksonen R, Holopainen M, Ruhanen H, Käkelä R, **Jauhiainen M**, Hermansson M, Öörni K. Icosapent ethyl-induced lipoprotein remodeling and its impact on cardiovascular disease risk markers in normolipidemic individuals. *JCI Insight.* 2025; 10:e193637. – Original article

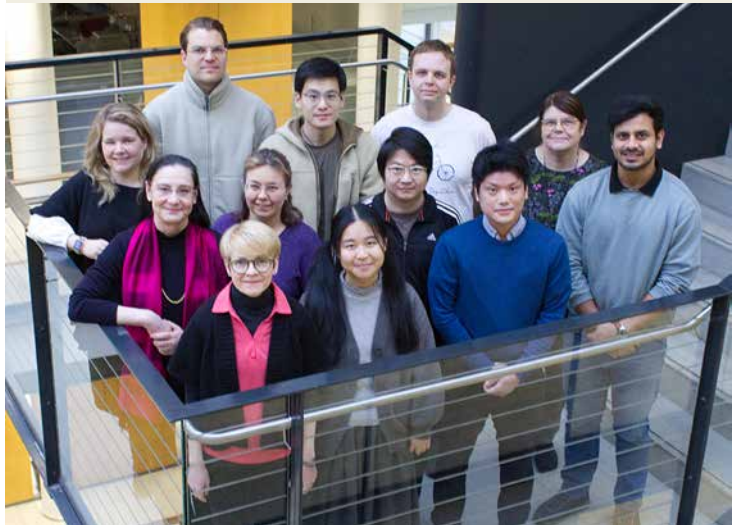
Membrane biology

Main research activities

During 2025, we reported on a novel molecular mechanism involved in generating the large lipid droplets characteristic to adipose tissue. In a collaborative effort led by Prof. Philipp Scherer at UT Southwestern, we found that the adipocyte microprotein adipogenin complexes with a key protein involved in lipid droplet formation, seipin, helping to stabilize this complex and directing additional protein and lipid cargo to the growing droplet (Li et al., 2025). Large lipid droplets enable adipocytes to efficiently store the chemical energy obtained from dietary sources as triglycerides and release this energy as fatty acids in a controlled manner during fasting.

We also found new mechanisms by which cholesterol coordinates the functions of essential membrane protein complexes, such as vacuolar ATPase (V-ATPase) and nuclear pore complexes (NPCs). Acute removal of the vital phosphatase Sac1 from human cells altered the Golgi cholesterol-phosphoinositide content, leading to the disassembly of the V-ATPase and consequent perturbation of Golgi pH and secretion (Zhou et al., 2025). On the other hand, cholesterol esterification in the nuclear envelope was found to modulate nuclear translocation of cytoplasmic proteins via the NPCs (Szkalisity et al., 2025).

We have been a partner in the Leducq Foundation "Cellular and systemic cholesterol transport in physiology and disease" Transatlantic Network of Excellence, and we were selected as a partner for the Research Council of Finland Centre of Excellence in Metabolic Integration (MetaScale) starting in 2026.



Group members

Elina Ikonen, M.D., Dr.Med.Sci., Professor (Director), Head
Maarit Hölttä, Ph.D., University lecturer
Kristiina Kanerva, Ph.D.
Aryan Kaveh, Ph.D.
Hodaka Saito, Ph.D.
Miesje van der Stoel, Ph.D.
Ábel Szkalisity, M.Sc., Ph.D. in summer 2025
Rakesh Zha, Ph.D.
Xin Zhou, Ph.D.
Haoran Li, M.Sc.
Heljä Lång, M.D.
Lauri Vanharanta, M.D., Dr.Med.Sci. in autumn 2025
Päivi Kleemola, Research assistant
Liisa Särkiö, Research assistant
Anna Uro, Laboratory technician

External funding

EU MCSA Innovative Training Network EndoConnect
EU MCSA Postdoctoral fellowship PIP-AID
Jane and Aatos Erkko Foundation
Leducq Foundation for Cardiovascular Research
Research Council of Finland
Sigrid Jusélius Foundation

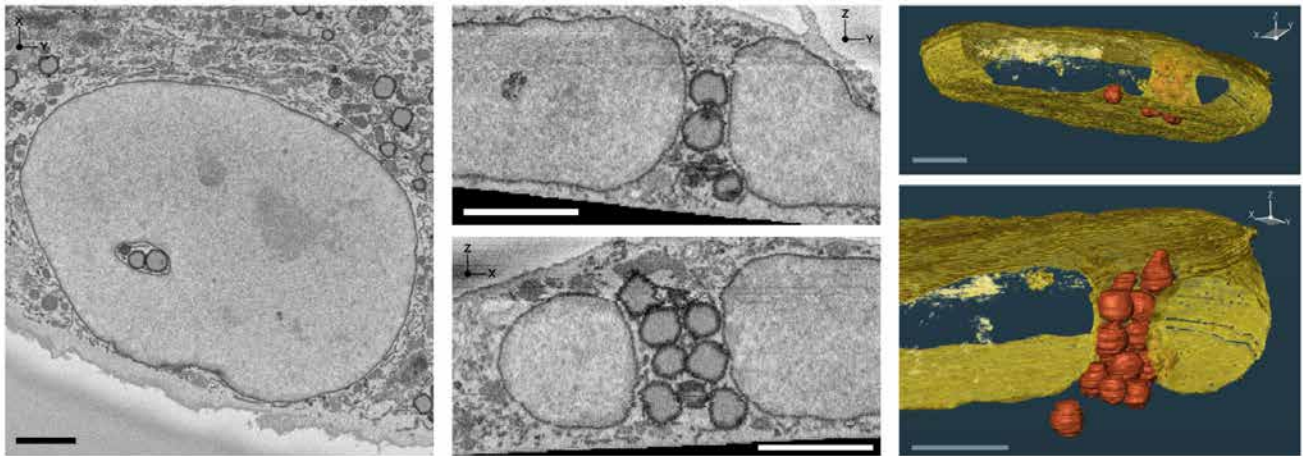


Figure. Electron micrographs and 3D model of a human primary macrophage loaded with cholesterol and oleic acid, showing nuclear-envelope associated lipid droplets in a tunnel traversing the nucleus. Courtesy of Ábel Szkalisity and Lauri Vanharanta.

Awards, honors and positions of trust

Professor Elina Ikonen:

Van Deenen Lecture and Prize, Internation Conference on the Bioscience of Lipids. September 21, 2025.

Ella & Georg Ehrnrooth Foundation Research Prize, October 30, 2025. Read more on page 13.

Theses completed in the group in 2025

The following Ph.D. theses was accepted at the University of Helsinki this year:

Ábel Szkalisity: Computational techniques in lipid metabolic studies. July 1, 2025.

Lauri Vanharanta: Mechanisms of cellular cholesterol storage. November 21, 2025.

Publications 2025

Li C, Sun XN, Funcke JB, **Vanharanta L**, Prasanna X, Gov K, Li Y, Virostek M, Joung C, Joffin N, **Kanerva K**, **Szkalisity A**, Kulig W, Straub L, Chen S, Velasco J, Cobb A, La Padula D, Wang MY, Onodera T, Vörös C, Kim DS, Kim M, Varlamov O, Li Y, Liu C, Nawrocki AR, Zhao S, Oh DY, Wang ZV, Gordillo R, Goodman JM, Wynn RM, Henne WM, Vattulainen I, Han Y, **Ikonen E**, Scherer PE. Adipogenin promotes the development of lipid droplets by binding a dodecameric seipin complex. *Science*. 2025; 390:eadr9755. – Original article

Lång HKM, Roach TG, **Hölttä M**, Keskitalo S, Varjosalo M, Heiskanen K, Collins MV, Seppänen MRJ, Capelluto DGS, **Ikonen E**, Ryhänen SJ. TOM1 G307D variant impairs interaction with TOLLIP, autophagosomal lysosome fusion and regulation of innate immunity. *Dis Model Mech*. 2025; 18:dmm052140. – Original article

Szkalisity Á, **Vanharanta L**, **Saito H**, **Vörös C**, **Li S**, Isomäki A, Tomberg T, Strachan C, Belevich I, Jokitalo E, **Ikonen E**. Nuclear envelope-associated lipid droplets are enriched in cholesteryl esters and increase during inflammatory signaling. *EMBO J*. 2025; 44:2774-2802. – Original article

Zhou X, **van der Stoep M**, Kaptan S, **Li H**, **Li S**, **Hölttä M**, Vihinen H, Jokitalo E, Thiele C, Pietiläinen O, Morioka S, Sasaki J, Sasaki T, Vattulainen I, **Ikonen E**. Control of Golgi V-ATPase through Sac1-dependent co-regulation of PI(4)P and cholesterol. *Nat Commun*. 2025; 16:7808. – Original article

Metabolism

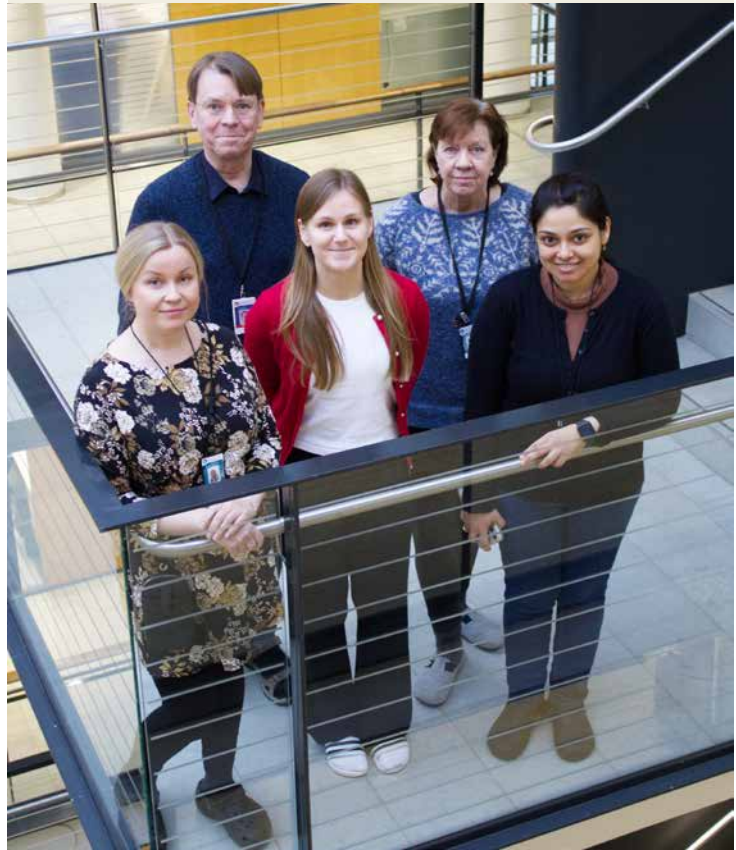
Main research activities

We are interested in the regulation of metabolism and especially in the molecular mechanisms regulating insulin action in human skeletal muscle. As a main research model, we are using primary muscle cell cultures established from muscle biopsies obtained from clinically carefully characterized volunteers. We analyze mechanisms predisposing for and leading to insulin resistance and seek novel ways to improve insulin action. We have a variety of in vitro methods for studying cell metabolism at our disposal.

The Finland-United States Investigation of NIDDM Genetics (FUSION) is an international multi-organizational collaborative project, the main goal of which is to identify genetic risk factors that predispose to T2D and related intermediate traits. We collaborate closely with the FUSION study, with the head of the group, Professor Heikki Koistinen, being one of the FUSION PIs.

In the FUSION Tissue Study, we have obtained skeletal muscle and adipose tissue biopsies from a cohort of well-characterized Finnish people. We have analyzed bulk and single-nucleus RNA sequencing (RNA-seq) and single-nucleus ATAC-seq data from 281 skeletal muscle biopsies to characterize sex differences in gene expression and regulation. We have found that more than 2,100 genes demonstrated sex-biased expression. Expression of genes involved in mitochondrial function and energy metabolism was enhanced in men, whereas expression of genes involved in signal transduction and cell differentiation was enhanced in women. Chromatin accessibility and expression of long noncoding RNAs and microRNAs were also affected by sex (Hanks et al., 2025).

In a meta-analysis of 2,344 subcutaneous adipose tissue samples, more than 30,000 conditionally distinct expression quantitative trait locus (eQTL) signals at more than 18,000 genes were identified. Colocalization of eQTLs with genome-wide association study (GWASs) signals for 28 cardiometabolic traits identified 1,835 genes (Brotman et al., 2025). In a meta-analysis of 1,002 skeletal muscle samples, colocalization of eQTL signals with 26 muscle and cardiometabolic trait GWASs identified 2,252 GWAS-eQTL colocalizations in 1,342 genes (Wilson et al., 2025).



Group members

Heikki Koistinen, M.D., Dr.Med.Sci., Professor, Head
Selina Mäkinen, Ph.D.
Sreeshya Sree, Ph.D.
Jenny Illman, Ph.C.
Leena Kinnunen, Ph.C.
Henric Kultalahti, M.B.

External funding

Finnish Cultural Foundation
Jalmari and Rauha Ahokas Foundation
Medical Society of Finland (Finska Läkaresällskapet)
Medicinska Understödsföreningen Liv och Hälsa r.f.
Research Funding of Helsinki-Uusimaa Hospital District
(state funding for university-level health research)
University of Helsinki

As part of FUSION, we have participated in a large collaborative effort to study the genetic background of obesity. We used genetic data from up to 5.1 million people from different ancestries to develop ancestry-specific and multi-ancestry polygenic risk scores (PGS) for obesity. The multi-ancestry score was able to explain up to 17.6% of BMI variation in some populations. Children with higher PGSs gained weight more rapidly from childhood to adolescence. Higher PGSs also led to a greater weight gain in adults. After lifestyle intervention, people with higher PGSs were more likely to regain lost weight (Smit et al. 2025).

Awards, honors and positions of trust

Professor Heikki Koistinen:

Co-director of Clinicum, Faculty of Medicine, University of Helsinki, 2025 onwards

Member of Steering committee on specialist training (ERJO), Faculty of Medicine, University of Helsinki, 2024 onwards

Vice-member of the Collegium of University of Helsinki, 2022–2026

Member of the scientific committee and reviewer of grant applications of the Finnish Diabetes Research Foundation 2024–2026

Member of the Board of the Finnish Society of Internal Medicine 2024 onwards

Secretary of the Finnish Society of Internal Medicine 2025–2026

Thesis completed in the group in 2025

The following Master's thesis was accepted at the University of Helsinki this year:

Jenny Illman: The metabolic effects of incretin mimetics in L6 skeletal muscle cells. December 19, 2025.

Publications 2025

Brotman SM, El-Sayed Moustafa JS, Guan L, Broadaway KA, Wang D, Jackson AU, Welch R, Currin KW, Tomlinson M, Vadlamudi S, Stringham HM, Roberts AL, Lakka TA, Oravilahti A, Silva LF, Narisu N, Erdos MR, Yan T, Bonnycastle LL, Raulerson CK, Raza Y, Yan X, Parker SCJ, Kuusisto J, Pajukanta P, Tuomilehto J, Collins FS, Boehnke M, Love MI, **Koistinen HA**, Laakso M, Mohlke KL, Small KS, Scott LJ. Adipose tissue eQTL meta-analysis reveals the contribution of allelic heterogeneity to gene expression regulation and cardiometabolic traits. *Nat Genet.* 2025; 57:180–192.

Hanks SC, Mauger AS, Varshney A, Ciotlos DL, Manickam N, Narisu N, Shumway AJ, Orchard P, Erdos MR, Sweeney MD, Okamoto J, Jackson AU, Stringham HM, Bonnycastle LL, Zhou X, Lakka TA, Mohlke KL, Tuomilehto J, Laakso M, Boehnke M, Sethupathy P, Collins FS, **Koistinen HA**, Parker SCJ, Scott LJ. Extensive differential gene expression and regulation by sex in human skeletal muscle. *Cell Genom.* 2025; 5:100915.

Smit RAJ, Wade KH, Hui Q, Arias JD, Yin X, Christiansen MR, ... **Koistinen HA**, ... Polygenic prediction of body mass index and obesity through the life course and across ancestries. *Nat Med.* 2025; 31:3151–3168.

Wilson EP, Broadaway KA, Parsons VA, Vadlamudi S, Narisu N, Brotman SM, Currin KW, Stringham HM, Erdos MR, Welch R, Holtzman JK, Lakka TA, Laakso M, Tuomilehto J, Boehnke M, **Koistinen HA**, Collins FS, Parker SCJ, Scott LJ, Mohlke KL. Skeletal muscle eQTL meta-analysis implicates genes in the genetic architecture of muscular and cardiometabolic traits. *Am J Hum Genet.* 2025; 112:2693–2707.

Preprint publications

Ciotlos DL, Hanks SC, Varshney A, Erdos MR, Manickam N, Stringham HM, Orchard P, Hill-Burns EM, Narisu N, Bonnycastle LL, Sweeney MD, Saramies J, Laakso M, Tuomilehto J, Lakka TA, Mohlke KL, Boehnke M, Collins FS, **Koistinen HA**, Parker SCJ, Scott LJ. Inverse directions of association of higher physical activity and higher insulin resistance with human skeletal muscle cell type abundance and fiber-type-level gene expression. *bioRxiv [Preprint].* 2025 Nov 28:2025.10.27.683567. doi: 10.1101/2025.10.27.683567.

Sharma M, Samra S, Liu Y, James A, Michalski C, Yousefi P, Del Bel KL, Lu HY, Sharma AA, Tarailo-Graovac M, Dalmann J, Buder L, Modi B, Drogemoller B, Blanchard Rohner G, Senger C, Rehms W, Prendiville JS, Mangino M, Ross CJ, van Karnebeek CD, Wasserman WW, Lavoie PM, Prathibha PM, Biggs CM, Boehnke M, Kinnunen L, **Koistinen HA**, McKinnon ML, Patil SJ, Bayer DK, Lyons JJ, Turvey SE. Human germline biallelic loss-of-function *OSMR* variants cause severe allergic disease. *medRxiv [Preprint].* 2025 Aug 8:2025.08.05.25332527.

Wang X, Robertson CC, Varshney A, Manickam N, Orchard P, Laakso M, Tuomilehto J, Lakka TA, Mohlke KL, Boehnke M, Scott LJ, **Koistinen HA**, Collins FS, Parker SCJ. Genetic integration with cell-specific nucleosome positioning resolves causal relationships underlying chromatin accessibility profiles. *bioRxiv [Preprint].* 2025 Oct 28:2025.09.09.674883. doi: 10.1101/2025.09.09.674883.

Zhang M, Brown MR, Bentley AR, Winkler TW, Noordam R, Nagarajan P, ..., **Koistinen HA**, ... Large-Scale Gene-Smoking Interactions and Fine Mapping Study Identifies Multiple Novel Blood Pressure Loci in over 1 Million Individuals. *medRxiv [Preprint].* 2025 Oct 7:2025.10.06.25337440. doi: 10.1101/2025.10.06.25337440.



Associated group:

Neuronal signaling

Main research activities

We study trophic factors in neurodegenerative diseases with a focus on the roles of endoplasmic reticulum (ER) stress and protein degradation pathways, including the ubiquitin proteasome and autophagy systems. We employ various biochemical, proteomic, molecular biology, and cell biology methods for our studies, such as primary neuron cultures and genetically modified mice. The majority of the group is housed in Medium, Faculty of Medicine of the University of Helsinki, and the group is actively engaged in research at Minerva.

USP14 and altered protein ubiquitination in human dopaminergic cells

Disturbances in protein homeostasis are associated with several human diseases, including cancer and neurodegenerative disorders (Lindholm et al., 2017). The deubiquitinating enzyme USP14 (Ubiquitin Specific Protease 14) is associated with the proteasome and is a major player in the control of proteostasis by influencing levels of protein ubiquitination and the activity of the proteasome (Srinivasan et al., 2020). We previously observed that USP14 plays a role in clearing of mutant Htt protein aggregates by binding to the ER protein, IRE1 α (Hyrskyluoto et al., 2014). We deleted USP14 in cells using CRISPR/Cas9 and discovered novel functions of USP14 in the regulation of mitochondria, oxidative stress, and lysosomes in human SHSY5Y dopaminergic cells (Srinivasan et al., 2025). We observed that α -synuclein (α -syn) was up-regulated in the absence of USP14, likely due to reduced degradation by proteasomes (Srinivasan et al, 2025). α -syn aggregates in Lewy bodies in Parkinson's disease (PD) and we showed that USP14 is present in human dopaminergic cells.

EN-RAGE and neuroinflammation in brain disorders

Inflammation in the brain contribute to several neurological and psychiatric disorders. Cytokines are crucial molecules in this context, and are



**Dan Lindholm, M.D., Dr.Med.Sci.,
Professor, Head**

Group members

Ove Eriksson, Ph.D., Docent
Muhammad Yasir Asghr, Ph.D.
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Chiara Scudari, M.Sc.
Anni Mäenpää B.Sc
Pyy Aunola, Medical student

External funding

Finnish Society of Sciences and Letters
Magnus Ehrnrooth Foundation
Medical Society of Finland (Finska Läkaresällskapet)
Medicinska Understödsföreningen Liv och Hälsa r.f.

produced by cells both in the periphery and the brain. Changes in cytokines in the body can signal to the brain and vice versa. In a recent collaboration, we have observed that the protein EN-RAGE/S100A12 is increased in the serum of acute psychosis patients compared with age-matched controls (Korhonen et al., 2023). EN-RAGE/S100A8/9 is a member of the S100 family of calcium-binding proteins and impacts immune responses in the body, but little is known about its effects in the brain. We hypothesize that EN-RAGE, by influencing the blood brain barrier, can also affect brain cells and instigate

neuroinflammation (see **Figure 1**). In this study, we are using the EN-RAGE recombinant protein added to brain cell cultures and then also examining the expression of its receptor in different brain regions. Preliminary results have revealed that EN-RAGE can increase dendritic spines in hippocampal neurons that are known to be affected in neurological diseases (Manuscript).

CNPY2 isoforms in neuronal and tumor cell survival

ER stress is associated with the pathophysiology of neurodegenerative diseases (Lindholm et al., 2017). We have previously cloned canopy 2 (CNPY2), an ER-resident protein found in different tissues including the brain. CNPY2 was found to be neuroprotective in cellular models of Huntington's disease (HD). CNPY2 is expressed in striatal and cortical neurons in vivo in the neuronal circuitry regulating body movements that is altered in HD (Scordino et al, 2024). The precise functions of CNPY2 in brain neurons are also currently under investigations using gene-deleted mice. We then recently cloned novel CNPY2 isoforms, arising from alternative splicing and with a different cellular location requiring further investigations (Pitafi et al., Manuscript).

We also noted that CNPY2 is present in human tumors including thyroid cancer cells. Silencing of CNPY2 by siRNA reduced cell viability and proliferation of the thyroid tumors (Manuscript). Transcriptome and proteomic analysis showed changes in specific gene products related to ER in CNPY2 downregulated cells. These studies can increase our understating of ER stress modulation in tumor growth and give insight into possible molecular targets for intervention.

Animal models for studying brain disorders including Huntington's disease

Animal models have proven useful in the study of different aspects of neurodegenerative diseases. We recently summarized available cell and animal models that have been utilized to study basic mechanisms and pathophysiology of HD (Polina et al., 2025). We also highlighted some outstanding research questions in HD research that will require further study using animal models and patient data. Along with this, we emphasized the importance and roles of specific factors including CNPY2 that can modulate ER stress and neuronal viability in neurons at risk, with the hope to alleviate the course of HD and other brain disorders.

Awards, honors and positions of trust

Professor Dan Lindholm:

The J.W. Runeberg Prize 2025 awarded by the Finnish Medical Society. Chair of Biological Section in the Finnish Society of Sciences and Letters. Read more on page 11.

Theses completed in the group in 2025

The following Master's thesis was accepted at the University of Helsinki this year:

Nisa Pitafi: Characterization of CNPY2 isoforms in ER stress, Resolution and neuronal survival. July 1, 2025.

Publications 2025

Srinivasan V, Soliymani R, Ivanova L, Eriksson O, Peitsaro N, Lalowski M, Karelson M, Lindholm D. USP14 is crucial for proteostasis regulation and α -synuclein degradation in human SH-SY5Y dopaminergic cells. *Heliyon*. 2025; 11:e42031.

Stepanova P, Voutilainen MH, Eriksson O, Lindholm D. Animal models of Huntington's disease. Pros and cons. *Brain Behav Immun Health*. 2025; 50:101149.

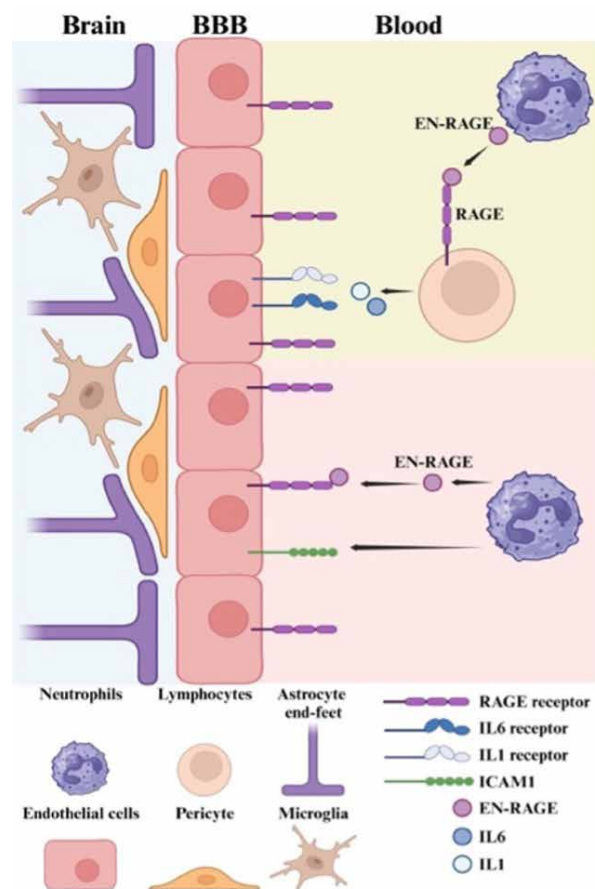


Figure. Summary of the actions of the EN-RAGE in inflammation and at the level of the BBB. EN-RAGE is produced by neutrophils and acts on other cells via its receptor RAGE. This causes an increase in cytokines such as IL-1 and IL-6 that act on the blood-brain barrier (BBB). Endothelial cells respond to EN-RAGE by increasing expression of adhesion molecules like ICAM-1 that leads to an enhanced recruitment of neutrophils and their transmigration into brain tissue.

Publications 2025

Original articles

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2. Brotman SM, El-Sayed Moustafa JS, Guan L, Broadway KA, Wang D, Jackson AU, Welch R, Currin KW, Tomlinson M, Vadlamudi S, Stringham HM, Roberts AL, Lakka TA, Oravilahti A, Silva LF, Narisu N, Erdos MR, Yan T, Bonnycastle LL, Raulerson CK, Raza Y, Yan X, Parker SCJ, Kuusisto J, Pajukanta P, Tuomilehto J, Collins FS, Boehnke M, Love MI, **Koistinen HA**, Laakso M, Mohlke KL, Small KS, Scott LJ. Adipose tissue eQTL meta-analysis reveals the contribution of allelic heterogeneity to gene expression regulation and cardiometabolic traits. *Nat Genet*. 2025; 57:180–192.
3. Claesson TB, Mutter S, Putaala J, Salli E, **Gordin D**, Groop PH, Martola J, Thorn LM. Age at type 1 diabetes onset does not influence attained brain volume. *BMC Endocr Disord*. 2025; 25:43.
4. Dadson P, Honka MJ, Suomi T, **Haridas PAN**, Rokka A, Palani S, Goltseva E, Wang N, Roivainen A, Salminen P, James P, **Oikkonen VM**, Elo LL, Nuutila P. Proteomic profiling reveals alterations in metabolic and cellular pathways in severe obesity and following metabolic bariatric surgery. *Am J Physiol Endocrinol Metab*. 2025; 328:E311–E324.
5. Davyson E, Shen X, Huider F, Adams M, Borges K, McCartney D, Barker L, Van Dongen J, Boomsma D, Weihs A, Grabe H, Kühn L, Teumer A, Völzke H, **Zhu T**, Kaprio J, **Ollikainen M**, David FS, Meinert S, Stein F, Forstner AJ, Dannlowski U, Kircher T, Tapuc A, Czamara D, Binder EB, Brückl T, Kwong A, Yousefi P, Wong C, Arseneault L, Fisher HL, Mill J, Cox S, Redmond P, Russ TC, van den Oord E, Aberg KA, Penninx B, Marioni RE, Wray NR, McIntosh AM. Antidepressant exposure and DNA methylation: Insights from a methylome-wide association study. *Nat Commun*. 2025; 16:1908.
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11. **Heikkinen A**, Esser VFC, Lundgren S, Lee SHT, Hakkarainen A, Lundbom J, Kuula J, Groop P-H, Heinonen S, Pajukanta P, Kaprio J, Pietiläinen KH, Li S, **Ollikainen M**. Twin pair analysis uncovers novel links between DNA methylation, mitochondrial DNA quantity and obesity. *Nat Commun*. 2025; 16:4374.
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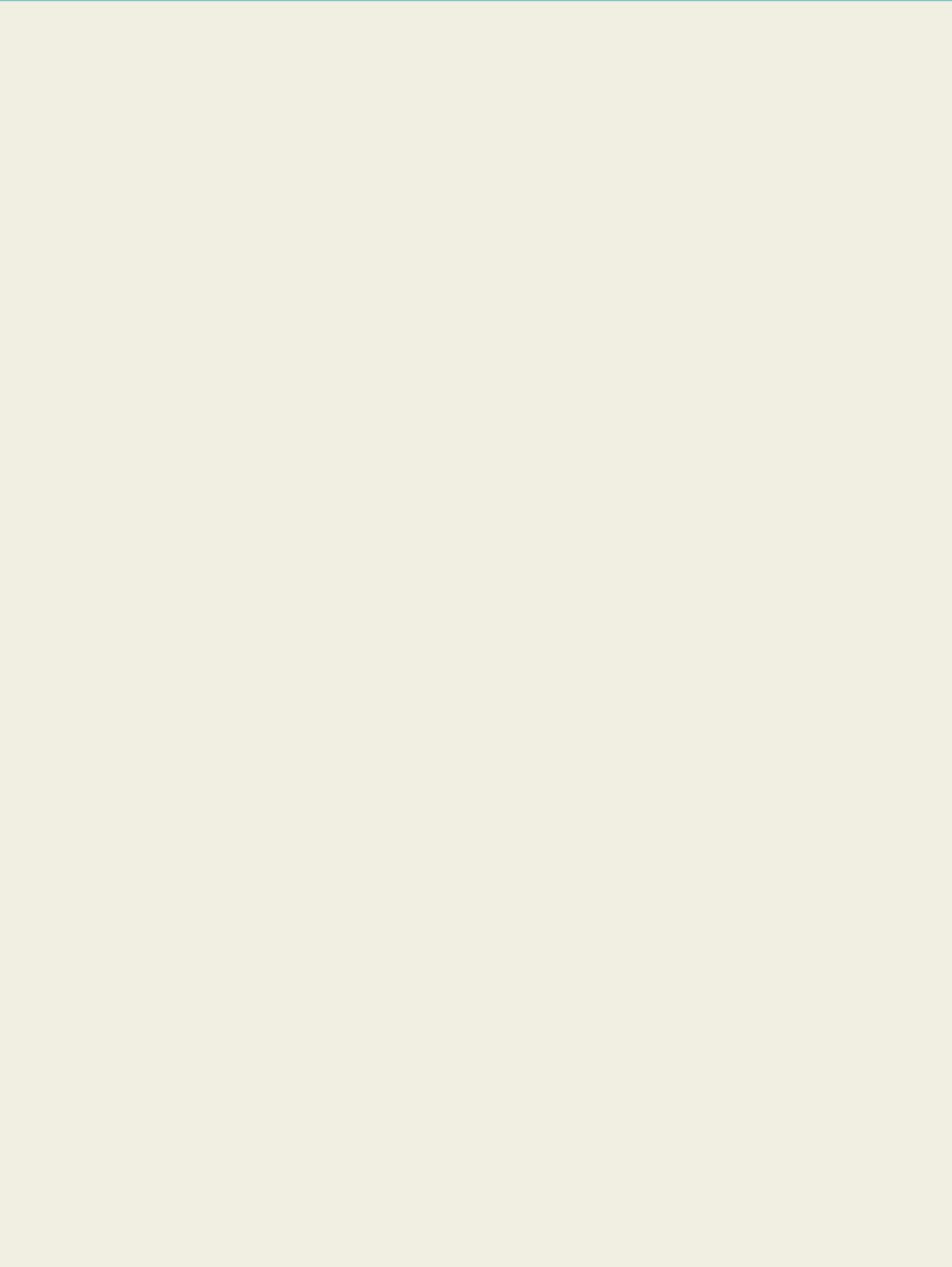
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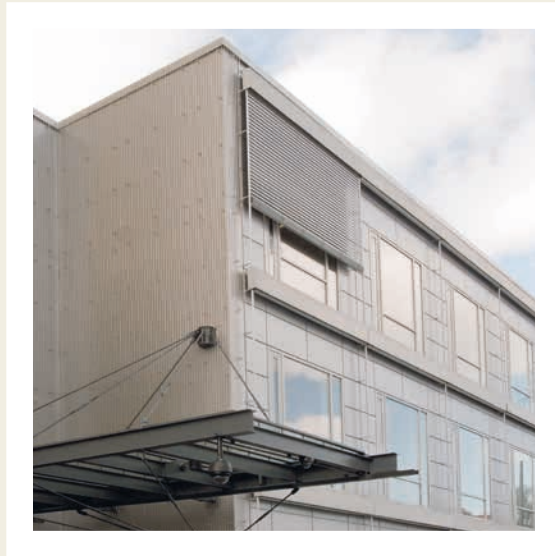
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