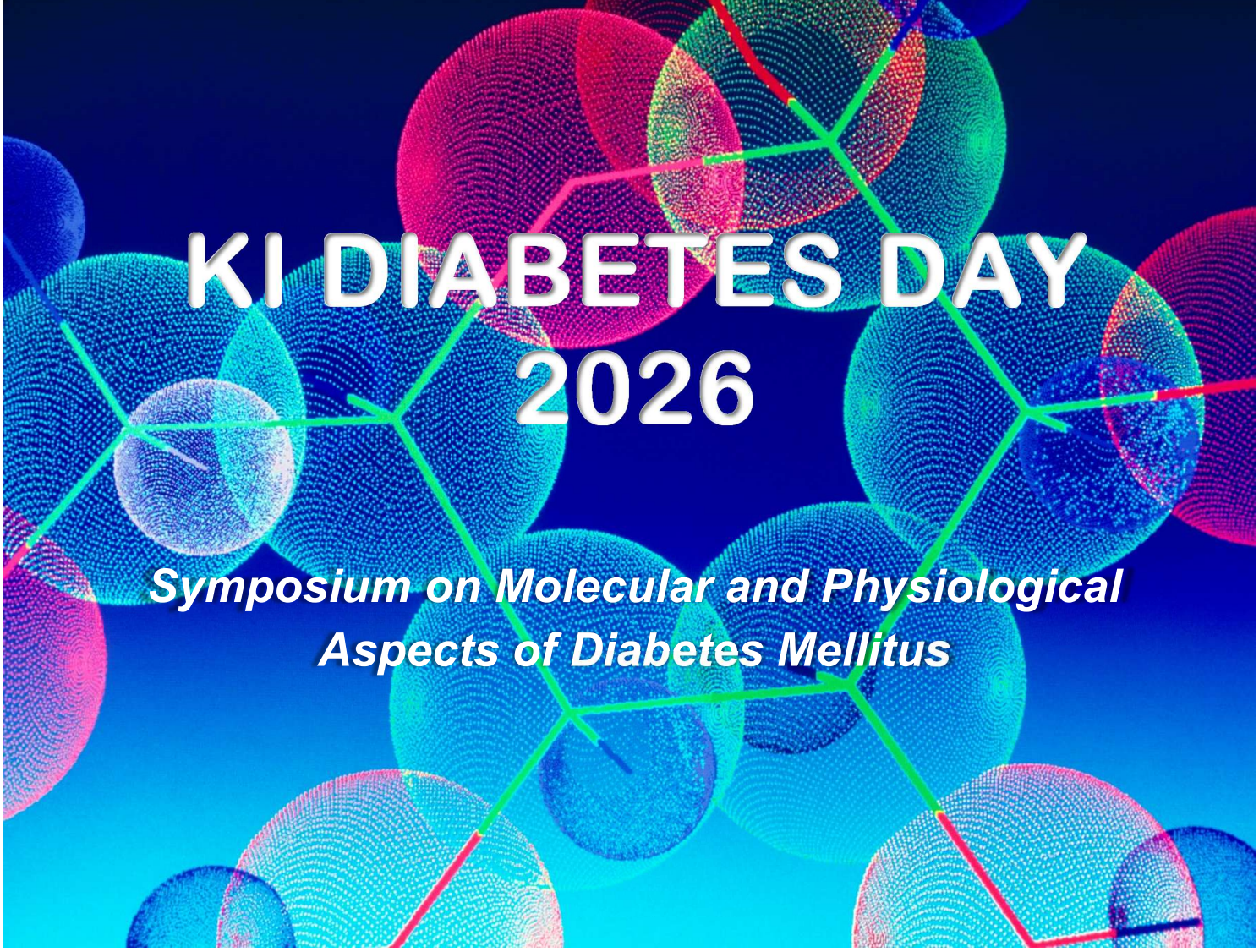


November 13, 2026 | Karolinska Institutet

PROGRAMME

world diabetes day

SRP DIABETES

Karolinska Institutet

Organiser:

Strategic Research Programme in Diabetes at Karolinska Institutet (SRP Diabetes).

https://ki.se/en/srp-diabetes

SRP Diabetes is an integrated research environment in the diabetes and metabolism area with some 400 affiliated researchers at both Karolinska Institutet and Umeå University. Results are translated between basic and clinical science with the aim to improve both prevention, care and treatment of people with diabetes.

Specifically, SRP Diabetes activities aim to:

- Develop and support technical platforms important for researchers at KI and UmU. These platforms include a Metabolic Phenotyping Centre for Diabetic Animal Models, a Centre for Clinical Metabolic Research in Diabetes, Beta Cell in-vivo Imaging/ Extracellular Flux Analysis (Seahorse) and Spatial Transcriptomics.
- Support for critical instrumentation to group leaders
- Support the next generation of scientist: postdoctoral fellowship program
- Increase interactions between the research teams of the programme by supporting collaborative projects and arranging common symposia, meetings and seminars
- Support undergraduate and graduate education within the research areas connected to the programme
- Increase translational research by supporting collaborative projects between experimental and clinical researchers
- Facilitate international contacts
- Support interactions with the biotech and pharmaceutical industry
- Support innovation and commercial utilization by liasing with Karolinska Institutet Innovations
- Increase public awarness and inform about current diabetes related research

The programme coordinates laboratories possessing substantial expertise and unique technical resources, thus affording a natural point of contact for collaboration within the diabetes area, both for researchers within Karolinska Institutet and Umeå University as well as with external researchers.

SRP Diabetes Management:

Director: Mikael Rydén (Karolinska Institutet)
Vice-Director: Thomas Nyström (Karolinska Institutet)
Helena Edlund (Umeå University)
Malin Flodström Tullberg (Karolinska Institutet)
Carolina Hagberg (Karolinska Institutet)
Harriet Wallberg (Karolinska Institutet)
Elisabet Stener-Victorin (Karolinska Institutet)
Sofia Carlsson (Karolinska Institutet)
Niklas Mejhert (Karolinska Institutet)
Stefano Romeo (Karolinska Institutet)

Venue: Eva and Georg Klein Hall, Biomedicum, Karolinska Institutet, Solna

Web: https://ki.se/en/srp-diabetes/diabetes-day

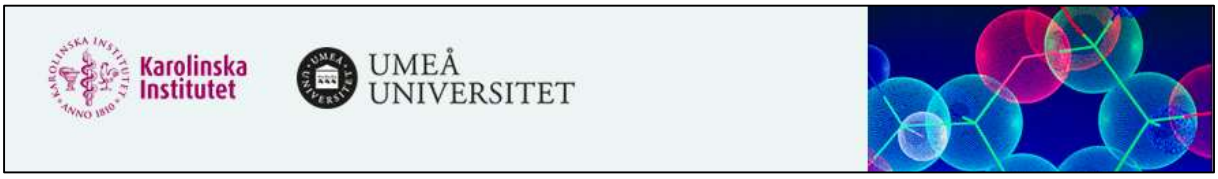
08:30 – 09:00	REGISTRATION	
09:00 - 09:10	Welcome Note: **Mikael Rydén**	
SESSION 1	Single-cell approaches in diabetes	Chair: Sontje Krupka
09:10 - 09:45	"The hidden benefits of weight loss on fat tissues." **William Scott,** *Imperial College London*	
09:45 - 10:20	"Human Adipose Tissue Vasculature: A Niche Shaped by Metabolic State" **Joanna Kalucka,** *Aarhus University*	
10:20 - 10:50	COFFEE BREAK	
SESSION 2	Spatial proteomics in metabolism	Chair: Abigail Dove
10:50 - 11:25	"Elucidating cellular processes in metabolic liver disease via organelle proteomics" **Natalie Krahmer,** *Helmholtz Munich*	
SESSION 3	Flash talks	Chair: Abigail Dove
11:30 - 12:00	6 x 3 min flash-talks	
12:00 - 13:00	LUNCH (Posters to be mounted)	
SESSION 4	Type 1 Diabetes	Chair: Pere Rehues Masip
13:00 - 13:35	"Hypoimmune Islet Transplantation in Type 1 Diabetes: From First-in-Human Proof of Concept to Clinical Translation" **Hanne Scholz**, *University of Oslo*	
13:35 - 14:10	"Insulin lost in translation" **Bart Roep**, *University of Leiden*	
14:10 - 14:40	COFFEE BREAK	
SESSION 5	Systemic metabolism and interorgan communication	Chair: Katharina Schormair
14:40 - 15:15	"Modulation of Glucagon Receptor Family Signalling by Lipid and Protein Interactions" **Alejandra Tomás-Català,** *Imperial College London*	
15:15 - 15:50	"From Beats to Metabolism: Unveiling the Heart's Metabolic Power" **Guadalupe Sabio,** *CNIO*	
15:50 - 16:00	Closing Remarks	
POSTER SESSION	Mingle	
16.00-18.00	Drinks and light bites served in the foyer by the entrance while posters are presented.	

FLASH TALKS

Presenter	Title
Joaquín Ortiz de Zevallos	Dysregulated Inflammatory Response to Exercise in Type 2 Diabetes: A Role for CXCL12 in Hypoxia-Induced Signaling
Emmy Keysendal	Low birthweight, genetic susceptibility and risk of type 2 diabetes subtypes and LADA
Georges Kiriako	Imaging insulin receptor activation states with single-molecule resolution
Bingran Xie	Systematic Screening Identifies Candidate Regulators of Insulin Responsiveness
Joakim Lehrstrand	Employing 3D mesoscopic imaging to describe the human pancreatic endocrine mass composition and distribution
Clara Sánchez	Caudal Raphe Serotonergic Neurons Regulate Energy Balance and Adipose Tissue-Specific Remodeling

Diabetes Day 2026

Posters



Poster #1

Type 2 diabetes, blood-based Alzheimer's disease biomarkers, and dementia risk: a population-based study

Abigail Dove, PhD; Giulia Grande, MD, PhD; Laura Fratiglioni, MD, PhD; Martina Valletta, MD; Claudia Fredolini, PhD; Stefano Volpato, MD; Weili Xu, PhD; Davide Liborio Vetrano, MD, PhD

Aging Research Center, Karolinska Institutet

Background: Blood-based biomarkers of Alzheimer's disease (AD) have great potential for non-invasive detection of AD-related neuropathology in the population. However, it is unclear how type 2 diabetes modifies the concentration, predictive performance, and associated dementia risk of blood AD biomarkers.

Methods: The study included 2,167 dementia-free older adults (age ≥60) from the Swedish National Study on Aging and Care, Kungsholmen, followed for 16 years. Serum concentrations of Aβ42/40, total tau, p-tau181, p-tau217, NfL, and GFAP were measured using Simoa assays. Diabetes was diagnosed based on medical history, medication use, and HbA1c. Dementia was clinically diagnosed following DSM-IV criteria.

Findings: At baseline, 186 participants (8.6%) had diabetes. Over a mean follow-up of 8.3 years, 331 (15.3%) developed dementia. Diabetes was cross-sectionally associated with higher p-tau181 and p-tau217. P-tau181, p-tau217, NfL, and GFAP showed strong predictive performance for dementia in people with and without diabetes (AUC, 0.72–0.79). In joint exposure analyses, the highest dementia risk was observed among participants with both diabetes and elevated total tau (HR 2.14), p-tau181 (2.74), NfL (2.90), p-tau217 (3.60), or GFAP (4.03) vs. those with neither exposure.

Interpretation: Diabetes appears not to modify the predictive performance of AD biomarkers for dementia, but its co-occurrence with elevated biomarker levels marks a particularly high-risk state for dementia.

Poster #2

Secretin-like peptides from Túngara frog skin modulate energy balance in mice

Ho Yan Yeung, Thomas Lund Koch, Abigail E. Jackson, Sophie L. Stephens, Rebecca McIntyre, Aymeric Rogalski, Meghan C. Curtin, Keren Hilgendorf, Sihem Boudina, Michael J. Ryan, Mónica A. Alomoto, Marcos Gridi-Papp, Zachary Gerhart-Hines, Helena Safavi-Hemami

Novo Nordisk Foundation Center for Basic Metabolic Research, University of Copenhagen; University of Utah

Hormonal control of energy balance is a key evolutionary adaptation. Although endocrine hormones are classically made by specialized tissues, bioactive metabolic peptides can emerge from unexpected sources. A notable precedent is exendin-4, a GLP-1 receptor agonist from Gila monster saliva, which inspired exenatide for the treatment of type 2 diabetes. Here we identify túngarins (TGRs), a novel class of secretin-like peptides in the skin secretion of the Túngara frog (Engystomops pustulosus), a species with energetically demanding courtship. TGRs arose by duplication of the secretin gene, followed by recruitment to the skin and diversification. They act with picomolar potency and distinct selectivity profiles across human class B1 G protein-coupled receptors (GPCRs), including the secretin receptor (SCTR), vasoactive intestinal peptide receptors 1 and 2 (VPAC1R and VPAC2R), and the pituitary adenylate cyclase-activating polypeptide type I receptor (PAC1R). TGRs stimulate lipolysis in primary mouse white adipose tissue, oxygen consumption in brown adipose tissue, and insulin secretion in rat INS-1 832/13 β cells. In vivo, they increase whole-body energy expenditure and promote weight loss in lean mice. Together, these findings reveal an unexpected metabolic function for amphibian skin and establish TGRs as evolutionarily optimized secretin-like peptides, highlighting non-canonical tissues as a source of candidates with translational potential for cardiometabolic disease.

Poster #3

Polypharmacy and use of prescription drugs with potential for misuse in individuals with type 2 diabetes: a Swedish cohort study, 2007–2024

Antonietta Anatriello, Laura Pazzagli

1. Centre for Pharmacoepidemiology, Clinical Epidemiology Division, Department of Medicine Solna, Stockholm, Sweden
2. Regional Center of Pharmacovigilance and Pharmacoepidemiology of Campania Region, Naples, Italy
3. Department of Experimental Medicine, University of Campania "Luigi Vanvitelli", Naples, Italy

Objective: to investigate the prevalence of polypharmacy and potential drug misuse in T2DM individuals, to focuse on the most involved pharmacological classes and to characterize patient profiles at higher risk of inappropriate medication use.
Patients: adults with T2DM in Sweden.

Methods: a nationwide register-based cohort study from 2007 to 2024. Polypharmacy and hyperpolypharmacy were defined as concomitant use of at least 5 and 10 medications for at least 90 days. Prevalence was assessed by year, age, and sex.

Results: 562,668 adults with T2DM were included; 307,149 (54.6%) experienced polypharmacy. Hyperpolypharmacy was less frequent (9.4%) but showed similar age-, sex-, and time-related patterns. Both outcomes were more common among older women. Prevalence remained relatively stable during most of the study period. Cardiovascular and cardiometabolic medications were the main contributors to polypharmacy. The polypharmacy group showed higher exposure to drug classes commonly associated with potential misuse (43.8%), especially opioids, sedative-hypnotics, anxiolytics.

Conclusion: polypharmacy was highly prevalent among adults with T2DM in Sweden. Although part of this medication use may reflect appropriate multimorbidity management, the high polypharmacy burden and greater exposure to drugs with potential for misuse urge structured medication review and individualized prescribing strategies.

Poster #4

Environmental Microbial Diversity in Early Childhood Settings and Possible Links to Type 1 Diabetes Risk

Marianne Nymark (1), Emma Ringqvist (1), Anirudra Parajuli (1), Marta Butrym (1), Virginia Stone (1), Marja Roslund (2), Olli Laitinen (3), Aki Sinkkonen (4), Malin Flodström-Tullberg (1).

Department of Medicine, Huddinge, Karolinska Institutet, Huddinge, Sweden.

The incidence of immune mediated diseases such as type 1 diabetes (T1D) is increasing in urbanized countries. The biodiversity hypothesis proposes that early-life exposure to microbially rich natural environments promotes healthy immune development and reduces disease risk. To test this, we will compare environmental microbial exposure in children from urban and rural settings and examine whether early-life exposure to a nature-based material modulates the gut microbiome and protects against T1D in a disease model.

We will present preliminary data analyzing microbial richness and diversity from 162 preschool playgrounds in urban and rural areas across Sweden. Furthermore, we will present data from preclinical studies involving the exposure of non-obese diabetic (NOD) mice to a rich, nature-based compound.

Preliminary results support broad analyses of microbial composition and diversity across environmental contexts and seasons, and the collected data will enable future comparisons of T1D incidence across different geographical environments and their associated environmental microbiota. The experimental studies suggest that exposure to an inactivated natural material induces beneficial shifts in gut microbiota, suggesting potential to delay or prevent T1D without the need for live microbial interventions. Understanding how environmental biodiversity affects T1D risk may guide strategies to promote early-life microbial diversity and reduce disease incidence.

Poster #5

Human vaccine derived CVB neutralizing antibodies prevent acute CVB3 infections and CVB3-induced diabetes in an experimental mouse model

V.M Stone (1) , B.Koxha (1), N.Sleiers (1), J.E. Laiho (2), H.Hyöty (2,3,4), M. Flodström Tullberg (1)

[1]Department of Medicine, Karolinska Institutet, Stockholm, Sweden, [2]Faculty of Medicine and Life Sciences, Tampere University, Tampere, Finland, [3] Department of Pediatrics, Tampere University Hospital, Tampere, Finland, [4]Fimlabs Laboratories, Tampere, Finland.

Coxsackievirus B (CVB) infections have been linked to islet autoimmunity preceding type 1 diabetes (T1D). Vaccination provides an opportunity to prevent infection and investigate the role of CVBs in T1D. A pentavalent CVB1-5 vaccine (PRV-101) recently completed a phase I trial (PROVENT), inducing strong neutralizing antibody (nAB) responses against all five serotypes. The current study tested whether PRV-101-induced nABs protect against CVB infection and CVB-induced diabetes.

A model of CVB-induced T1D (SOCS-1-tg mice) was used for passive immunization. Passive immunization was performed using pre- and post-vaccination sera from PROVENT participants or control serum containing nABs acquired after natural infection. Viraemia, diabetes incidence, nAB levels and pancreas pathology were evaluated.

PRV-101 was well tolerated, induced nABs and protected against viraemia, diabetes and pancreas damage. Pre-vaccination sera had no protective effect, whereas post-vaccination sera provided complete protection against viraemia and virus-induced diabetes, comparable to naturally acquired immunity.

These findings suggest that PRV-101-induced nABs protect against CVB infection and disease, supporting nABs as a functional correlate of protection and further clinical development of the vaccine. The study supports the investigation of CVBs as triggers of T1D, for which vaccination could offer a preventive strategy in at-risk populations.

Poster #6

Characterization of MTMR3, a novel regulator involved in skeletal muscle remodeling

Alesandra A. Marica, Xue Yu, Kirstin A. MacGregor, Juleen R. Zierath, Anna Krook, and Nicolas J. Pillon

Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden

One of the earliest detectable signs of insulin resistance preceding T2D is reduced glucose uptake in skeletal muscle. T2D is also closely associated with impaired skeletal muscle regeneration. However, the molecular mechanisms underlying this relationship remain incompletely understood. Here, we seek to characterize the role of novel myogenic regulators, including MTMR3, in skeletal muscle metabolism and remodeling.

Ten publicly available scRNA-Seq datasets comprising cells from human skeletal muscle were integrated using standardized bioinformatic pipelines. Primary cells isolated from vastus lateralis skeletal muscle biopsies were transfected with siRNA to target MTMR3. The expression profile of myogenic gene markers was assessed by qPCR.

Our meta-analysis of 71,443 quality-filtered cells segregated six major clusters spanning myogenesis from quiescent skeletal muscle stem cells to fully mature myotubes. We identified MTMR3 as a novel regulator of myogenesis. Upon MTMR3 silencing, we detected a reduction in the expression of MKI67, MSTN and MYF5. Conversely, silencing of MTMR3 upregulated the expression of CKM, DES, MYH1 and MYH7.

Our results suggest that MTMR3 coordinates the progression of human skeletal muscle differentiation, acting as a brake on myogenic maturation. These findings provide a foundation for future studies investigating whether MTMR3 modulation influences skeletal muscle mass and function in T2D.

Poster #7

Effect of circadian rhythm and physical exercise on metabolism in overweight type 1 diabetes patients

C. Högardh, I. Dahlman, E. Toft, V. Qvisth, T. Gustafsson, G. Jörnåker

Department of Clinical Science and Education, Karolinska Institutet, Stockholm, Sweden

Background: Individuals with type 1 diabetes (T1D) and overweight are at increased risk of cardiovascular disease and insulin resistance. High-intensity interval training (HIIT) improves cardiometabolic health, but its effects in T1D and the influence of exercise timing remain unclear. As circadian rhythms regulate metabolic processes and exercise responses, this study investigated whether time of day modulates metabolic responses to acute HIIT in individuals with overweight and T1D.

Materials and methods: Twenty-five healthy controls and 25 individuals with T1D (BMI 25-30 kg/m^2) completed one morning (09:30) and one afternoon (16:30) HIIT session in randomized order. Blood samples and skeletal muscle biopsies were collected before and after exercise, with an additional blood sample obtained 1 hour post-exercise.

Results: Several metabolic and hormonal biomarkers demonstrated time-dependent responses to HIIT. Markers of glucose regulation were influenced by both participant group and exercise timing, with significant group differences before and after exercise ($p = 0.002$ and $p < 0.001$) and a time-of-day effect post-exercise ($p = 0.048$). TSH showed significant timing effects ($p < 0.001$), while triglycerides demonstrated differential timing responses between T1D and controls (interaction $p = 0.005$).

Conclusion: These findings suggest that biological timing influences acute metabolic and endocrine responses to HIIT in individuals with overweight, with and without T1D.

Poster #8

Exercise-induced epoxy fatty acid accumulation improves immunometabolic responses in skeletal muscle

Xue Yu, Anna Krook, Juleen R. Zierath, and Nicolas J. Pillon

Karolinska Institutet

Background. Dysregulated inflammation contributes to metabolic dysfunction in obesity and type 2 diabetes. Soluble epoxide hydrolase (sEH) converts anti-inflammatory epoxy fatty acids into diols, modulating immunometabolism. We investigated the exercise-induced responses of these lipids and how they affect glucose homeostasis and skeletal muscle metabolism.

Methods. Plasma epoxy fatty acids and the corresponding diols were quantified in people with type 2 diabetes and healthy volunteers before and after acute exercise. Metabolic effects of epoxy fatty acids were tested in primary human myotubes. Glucose tolerance, immune cell composition, and skeletal muscle fiber morphology were assessed in high-fat diet (HFD)-fed mice treated with or without the sEH inhibitor TPPU.

Results. Women with type 2 diabetes showed more sustained post-exercise-induced elevations of plasma epoxy fatty acids than healthy volunteers. In human myotubes, epoxy fatty acids enhanced glucose utilization and glycogen storage. In HFD-fed female mice, TPPU improved glucose tolerance without altering insulin levels, and increased muscle fiber size and the proportion of natural killer cells in skeletal muscle.

Conclusions. Epoxy fatty acids are exercise-responsive metabolites that enhance glucose utilization in skeletal muscle. Inhibiting sEH to preserve these lipids may mimic some metabolic benefits of exercise by remodeling skeletal muscle and its immune niche.

Poster #9

Plasma proteome and miRNA analyses identify early biomarkers of enterovirus-induced type 1 diabetes

Fabian Byvald, Helena Sork, Isabel Diaz Lozano, Virginia M Stone, Emma E Ringqvist, Bleona Koxha, Maria Eldh, Metoboroghene Mowoe, Samir El Andaloussi, Lena Eliasson, Susanne Gabrielsson, Malin Flodström Tullberg

The Center for Infectious Medicine, Department of Medicine Huddinge, Karolinska Institutet

The events preceding beta cell destruction in type 1 diabetes (T1D) are not fully understood, although infections with coxsackievirus group B (CVB) have long been implicated as potential triggers of disease. Identifying biomarkers of early infection may facilitate risk stratification and open new avenues for personalised preventive interventions. Here, we used an experimental model of CVB-induced T1D to identify early infection biomarkers. Plasma samples collected early after CVB or mock infection, prior to diabetes onset, were analysed by NGS and LC-MS/MS, enabling characterisation of miRNA and protein signatures in whole plasma and EV-enriched plasma fractions. More than 800 plasma miRNAs were identified, of which over 14% were differentially expressed after infection. Complementary validation experiments confirmed six infection-associated miRNAs, one of which was particularly increased in animals with ongoing beta cell infection and destruction. Parallel proteome profiling of whole plasma and EV-enriched plasma fractions identified nearly 4,000 proteins, hundreds of which were significantly altered following CVB infection. These included interferon response proteins and an enrichment of immune- and inflammation-related pathways. In conclusion, this study identified circulating miRNA and protein signatures of early CVB infection, providing a foundation for future biomarker validation studies in at-risk individuals.

Poster #10

Adipose p53Ser18 phosphorylation links Post-prandial glucose intolerance to cardiac biology

Jack Scob, Heather L Armata, Sithara Pony, Roger J Davis and Hayla K Sluss

Univ Mass Medical School

Background: Impaired glucose tolerance is an early feature of metabolic disease, but the underlying mechanisms remain poorly understood. We investigated whether stress-responsive phosphorylation of p53 at Ser18 regulates glucose homeostasis during high-fat feeding.

Methods: Wild-type and p53S18A mice were challenged with a high-fat diet. Glucose metabolism, tissue-specific insulin signaling, adipose transcriptomics, and plasma metabolites were examined.

Results: Surprisingly, p53S18A mice developed marked glucose intolerance despite normal insulin tolerance, body weight, and food intake. Insulin-stimulated AKT activation was selectively impaired in adipose tissue but preserved in skeletal muscle. Adipose RNA sequencing revealed increased Folh1, implicating altered folate and one-carbon metabolism. Unexpectedly, plasma levels of five TCA-cycle intermediates—citrate, isocitrate, α-ketoglutarate, fumarate, and malate—were inversely associated with glucose intolerance (P = .004–.025), suggesting a relationship between circulating mitochondrial metabolites and postprandial glucose regulation.

Conclusions: Our findings uncover a previously unrecognized role for p53 Ser18 phosphorylation in maintaining glucose tolerance independently of systemic insulin resistance, linking adipose dysfunction with altered metabolic pathways.

Poster #11

Baseline gut microbiota and gastrointestinal symptoms after metformin initiation: a shotgun metagenomic study in metformin-naïve adults with newly diagnosed type 2 diabetes

Kenny Kalin, Wanli He, Karin Rådholm, Bledar Daka, Stefan Jansson, Anna Möllsten, Valentina Tremaroli, Fredrik Bäckhed, Olov Rolandsson

Umeå University

Background
Metformin-induced gastrointestinal (GI) side effects pose a challenge in clinical practice. We investigated if gut microbiota composition and function are associated with GI side effects after metformin initiation in newly diagnosed type 2 diabetes.

Materials and methods
The prospective MEMO study recruited metformin-naïve adults diagnosed within one year across four Swedish healthcare regions. Clinical data and stool samples were collected at baseline, 2 and 4 months. GI side effects were defined as worsening from mild to moderate/severe symptoms in any of six domains assessed using a validated questionnaire. Faecal DNA underwent shotgun metagenomic sequencing.

Results
We analysed 446 samples from 166 participants (mean age 63 years); 61 developed GI side effects. At baseline, this group had more uncharacterised taxa and fewer putative short-chain fatty acid (SCFA)-producing bacteria (Wilcoxon rank-sum, $p \leq 0.05$). During treatment, diversity did not change significantly and community restructuring was limited in this group, whereas changes were observed in those without side effects. Functional analyses showed enrichment of stress-response pathways and reduced fermentative functions in the side-effect group (Wilcoxon rank-sum, $p \leq 0.05$).

Conclusion
GI side effects following metformin initiation were associated with baseline microbial differences and altered functional profiles. These findings warrant further investigation as potential markers of susceptibility.

Poster #12

Whole-organ 3D imaging reveals lobe-specific heterogeneity in endocrine architecture across the C57BL/6J mouse pancreas

Björn Morén, Azam Mahmoud-aznaveh, Joakim Lehrstrand, Stefanie M.A. Willekens, Tomas Alanentalo & Ulf Ahlgren.

Department of Medical and Translational Biology, Umeå University, Umeå, Sweden.

The islets of Langerhans can contain up to five endocrine cell types: β-cells (insulin), α-cells (glucagon), δ-cells (somatostatin), PP-cells (pancreatic polypeptide) and ε-cells (ghrelin). They account for 1–2% of pancreatic volume and regulate glucose homeostasis through autocrine and paracrine communication. Understanding their distribution and composition is important for normal physiology and diabetes research.

Aim: To investigate inter- and intra-lobular differences in endocrine cell density and islet composition throughout the mouse pancreas, focusing on INS-, GCG-, SOM-, PP- and GHR-producing cells.

Methods: Whole-organ maps were generated in male and female mice using ex vivo antibody labelling, tissue clearing and light-sheet fluorescence microscopy. Three-dimensional images were processed and analysed using Imaris.

Results and conclusion: Our deep tissue ,3D imaging, of whole mice pancreata revealed marked variation in islet composition among the splenic (SL), duodenal (DL) and gastric (GL) lobes. Larger islets were found near the pancreatic centre, close to the central duct, in the SL. GCG and PP cell densities differed significantly between the SL and DL. The mouse pancreas contained numerous INS(+)GCG(−) -islets, consistent with observations in humans. These findings emphasize the importance of considering lobular origin and endocrine organization when using isolated islets or whole mouse pancreas in research.

Poster #13

Beyond Fat Mass: Treatment-Specific Adipose Tissue Remodelling in Type 2 Diabetes

Ghania H. Kara-Ali, Jesper Bäckdahl, Viktor Liénard, Lina Cordeddu, Jiawei Zhong, Jutta Jalkanen, Viggo Strömberg, Daniel Eriksson-Hogling, Daniel P. Andersson, Patrik Ståhl, Niklas Mejhert, Mikael Rydén

Karolinska Institutet, Department of Medicine/Huddinge

Although second-line glucose-lowering therapies modulate body weight, their effects on adipose tissue (AT) function remain poorly characterised. DIASPAX is a randomised, open-label trial comparing 6 months of pioglitazone (Pio), empagliflozin (Emp) or semaglutide (Sem), added to metformin, in participants with type 2 diabetes (n=8-11/arm).

After 6 months of treatment, HbA1c decreased with Sem (-10 mmol/mol, p=0.004) and Pio (-4 mmol/mol, p= 0.002), but not with Emp (-1 mmol/mol, ns). Pio was associated with a trend towards increased fat mass (+4.0 kg, p= 0.054), alongside increased gynoid fat mass (+0.65 kg, p= 0.008) and circulating adiponectin levels (p= 0.001). In contrast, fat mass decreased with both Emp and Sem (-2 kg; p= 0.02 and p= 0.008, respectively), alongside reductions in abdominal subcutaneous AT mass. Clamp-derived insulin sensitivity did not change significantly, although a trend towards improvement was observed with Pio (+0.48 mg/kg/min, p= 0.06). Ex vivo analyses revealed increased stimulated lipolysis with Sem and Emp (isoprenaline, ANP, 8-Br-cAMP), whereas basal lipolysis decreased with Pio. Adipocyte size remained unchanged.

These findings suggest distinct treatment-associated patterns of AT remodelling that extend beyond changes in fat mass alone. Ongoing single-nucleus multi-omics profiling and spatial transcriptomics of paired biopsies will further characterise the cellular states and tissue microenvironments associated with these treatment responses.

Poster #14

An arrayed CRISPRi screen reveals long non-coding RNAs involved in human adipocyte lipolysis

Katharina Schormair, Jordi Mengual Marti, Laura Daniela Martinez Rico, Kanwal Tariq, Christopher Thelin, Liyang Wu, Bingran Xie, Alastair George Kerr

Karolinska Institutet, Stockholm, Sweden

Adipose tissue is the major energy storage organ in the human body. In obesity, adipocyte lipolysis regulation dysfunctions. Importantly, basal lipolysis is elevated, and the cell becomes resistant to catecholamine, a major stimulator of lipid breakdown. Consequently, metabolic flexibility is blunted and chronic glycerol and fatty acid release into the periphery drives cardiometabolic disease progression. How regulatory RNA molecules, such as long non-coding RNAs (lncRNAs), participate in lipolysis regulation in adipocytes and how this may go awry in adipose tissue dysfunction is not well understood.

To identify lipolysis-associated lncRNAs, we examined 147 subcutaneous adipose tissue biopsies where extensive lipolytic phenotyping and parallel transcriptomics were performed. Filtering for cytoplasmic adipocyte expression, we selected 48 lncRNAs for CRISPRi screening. Each lncRNA was phenotyped for basal and stimulated lipolysis, and selected hits underwent lipid droplet morphology and proteomic profiling for a deeper characterization. We here identify 10 lncRNAs that display significant effects on the adipocyte lipolytic response that are now being investigated for their molecular mechanism of action.

Poster #15

Platelet function in diabetes

Maaike Jongen, PhD, Stephan Meinke, PhD, Sophia Rössner, Prof, Petter Höglund, Prof

Karolinska Institutet

Introduction:
Diabetes, both type 1 and 2, are associated with a high risk for cardiovascular disease and thrombosis, with some studies estimating a premature death rate of approximately 80% due to cardiovascular disease. Platelets play an important role in this increased risk and platelet hyperfunction has been described. However, there are no clinically available diagnostic platforms designed to measure overactive platelets.

Aim:
We aim to develop a methodology for enabling better understanding and ultimately better risk stratification for thrombosis.

Methods:
We have so far included 4 diabetes type I patients. We have applied an 18-colour panel and stimulated the platelets with increasing concentrations of agonists including CRP-A, a collagen related peptide.

Results:
We were able to pick up platelet hyperfunction in these type I patients. Phenotypically, there were some interesting changes as well.

Conclusion:
Diabetes is associated with platelet hyperfunction that can be picked up and studied with our new 18-colour flow cytometry panel and associated methodology.

Future work:
We aim to include 20 type I, 20 type II and 20 healthy volunteers. In addition to the 18-colour panel we aim to study procoagulant platelets, overall responses with multiplate, single platelet responses with droplet microfluidics, platelet-leukocyte aggregate formation and extracellular vesicle composition.