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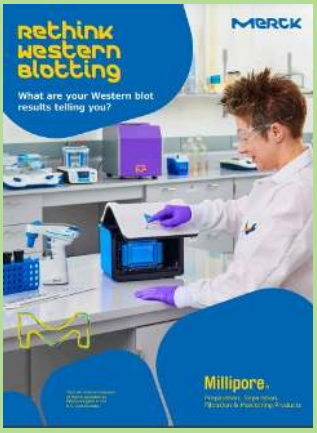

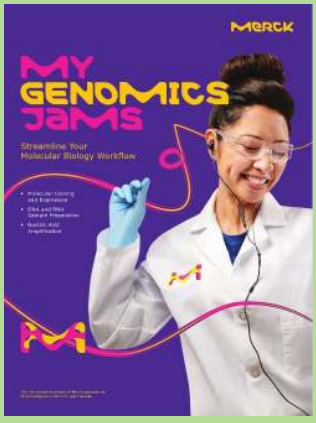

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Program

Monday 27th January	
13:00 Opening by Future Faculty	
13:15 Keynote lecture: Michael Schöll (Institute of Neuroscience and Physiology)	
14:00 Neuroscience session Chairs: Luisa Klahn and Maryam Ardalan	**14:00 Andrew Naylor** – *The differential and temporal effects of a single or dual inflammatory insult on microglial activation states* **14:15 Stamatia Karagianni** – *One modality to rule them all? Comparison of amyloid, tau, and FDG PET for the prediction of decline in different cognitive domains* **14:30 Christina Heiss** – *Neurofilament light chain clearance through microglia and the implications of microglial states for biomarker interpretation* **14:45 Melis Çelik** – *Unraveling the Impact of CACNA1C and Its Risk Variant on Neural Development in Bipolar Disorder*
15:00 Poster session 1, fika and sponsor exhibitions	
16:00 Research session 1 Chair: Rossella Crescitelli and Bingqing He	**16:00 Sara Berggren** – *Frequent pain is common among 10-11-year-old children with symptoms of attention deficit hyperactivity disorder* **16:15 Daniel Schmidt/Emilio Rundbeck** – *Advancing Clinical Microbiology: The Role of Bioinformatics in Data-Driven Insights and Public Health* **16:30 Lucia de Miguel Gomez** – *Preconditioning scaffolds for uterus bioengineering with metalloproteinases: does it affect cytocompatibility and immunogenicity?* **16:45 Wing Ki Chan** – *Perinatal exposure to Staphylococcus epidermidis as a potential factor contributing to autism later in life*
17:30 Social event at Zamenhof	

Tuesday 28th January	
09:00 Research session 2 Chairs: Francesco Longo and Lina Jonsson	**09:00 Fadi Askar** – *Women with knee osteoarthritis: the role of progesterone in a post-menopausal age window* **09:15 Andreas Törnell** – *NOX2 activity may determine disease progression in Parkison's disease* **09:30 Daniel Schmitz** – *Nallo: A Nextflow pipeline for comprehensive human long-read genome analysis* **09:45 Noor Hassan** – *The role of oxytocin in the development of social preference in zebrafish*
10:00 Sponsor presentation	AH Diagnostics
10:30 Fika and sponsor exhibitions	
11:00 Cancer session 1 Chair: Elin Bernson and Reshed Abohlaka	**11:00 Ella Äng Eklund** – *Equalizing prognostic disparities in KRAS-mutated stage III NSCLC patients: addition of durvalumab to combined chemoradiotherapy improves survival* **11:15 Lijuan Yu** – *Prostate cancer extracellular vesicles delivered miRNAs may intelligently regulate bone metastasis* **11:30 Kerryn Elliott** – *Mechanistic basis of atypical TERT promoter mutations*
11:45 Research Support Office	
11:50 Poster session 2, lunch and sponsor exhibitions	
13:15 Keynote lecture: Jenny Nyström (Dean at Sahlgrenska Academy)	
14:00 Cancer session 2 Chairs: Kerryn Elliott and Martina Sundqvist	**14:00 Sanchari Paul** – *Targeting murine metastatic cancers with adjuvanted cancer antigen vaccines* **14:15 Mustafa Kaya** – *NRF2 Signaling in EMT and Macrophage Polarization*
14:30 Fika and sponsor exhibitions	
15:00 Sponsor presentation	BD
15:30 Prize ceremony and closing	

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Academicum, 4th floor

Poster Session Schedule

Poster session	Group (Chairs)	Poster number	First name	Last name	Title
1 Monday 15:10 - 15:50	A (Martina Sundqvist & Francesco Longo)	1	Kristina	Benevides	Mito-gatk: A pipeline for comprehensive mitochondrial short-variant discovery
		3	Camilla	Locatelli	The effects of iodixanol density solution on cellular morphology and viability
		5	Lindsay	Zentveld	Pre-clinical models of osteoarthritis: effect of ovaries removal on the joint of aged mice.
		7	Andre	Hesselink	OPTIMIZING FOR VITAMIN D INTAKE AND LOW-CARBON EMISSIONS IN DIETS AMONG SWEDISH ADOLESCENTS
		9	Maja	Sandberg	Pre-pregnancy BMI and BMI Change as Predictors of Breastfeeding Duration: Findings from the Swedish CArdioPulmonary bioImage Study (SCAPIS)
		11	Lujain	Maasfeh	Identification of allergy-like mucosal immune responses mounted against local injection of dietary antigens in IBS patients
	B (Stefanie Fruhwürth & Lina Jonsson)	13	Mathilda	Forsby	The Swedish vitamin D fortification policy may benefit most pregnant women, but not equally
		15	Luiza Santos	Machado	Novel CSF astrocyte-related biomarkers for Alzheimer's disease
		17	Carl	Öberg	The microglial receptor AXL is involved in the antiviral defense against HSV-1 infection.
		19	Christoffer	Petersson	Preanalytical errors in liquid biopsies.
		21	Linnéa	Ögren	Light-based footprinting of a complete eukaryotic genome
	C (Luisa Klahn & Amina Basic)	23	Toms	Voits	Synaptic plasticity, synapse loss, and proteinopathy in mild neurocognitive disorder: Study design
		25	Gwenna	Breton	BaTwa populations from Zambia retain ancestry of past hunter-gatherer groups
		27	Tahzeeb	Fatima	Causal association between body mass index and risk of rheumatic joint disorders: A systematic review and meta-analysis of Mendelian randomization studies
		29	Cecilia	Överdahl	Metabolomics and lipidomics in juvenile localized scleroderma
		31	Nicole	Kerekes	TBA

Poster session	Group (Chairs)	Poster number	First name	Last name	Title
2 Tuesday 12:20-13:00	D (Martina Sundqvst & Francesco Longo)	2	Fredrik	Eklund	Characterization of biological nanoparticles using Dual-Angle Interferometric Scattering microscopY (DAISY).
		4	Simeon	Mavropoulos	Rapid Griess Assay (RGA): A Chairside Test for Ex Vivo Semi-Quantitative Oral Nitrite Measurement and In Vitro Assessment of Nitrite Production by Oral Bacteria
		6	Reshed	Abohalaka	Determinants affecting fractional exhaled nitric oxide in a population-representative adult sample in western Sweden
		8	Sandeep	Jha	Prospective Comparison of Temporal Changes in Myocardial Function in Women with Takotsubo versus Women with Anterior STEMI
		10	Anna	Trullenque Eriksson	Diabetes and diabetes-related complications are associated with periodontitis. Population data from Sweden.
	E (Stefanie Fruhwürth & Lina Jonsson)	12	Chiara	Badami	BAP-1 deletion disrupts IFNγ signaling and sensitizies cancer cells to NK cell cytotoxicity
		14	Sara	Schumacher	Construction of a gene panel for liquid biopsy-based diagnostics of gynecologic cancer
		16	Michael	Smith	Consequences of environmental noise and noise masking for sleep fragmentation and metabolic function
		18	Davide	Cadeddu	Nicotine-induced neuroplasticity in prelimbic cortex may drive the increased risk of alcohol misuse
		20	Nalleli	Vivanco Karlsson	A clinical guide to a Nordic adaptation of the Crohn's Disease Exclusion Diet
	F (Luisa Klahn & Amina Basic)	22	Bingqing	He	Finding new mechanisms of schizophrenia using a novel postnatal stem-cell based neuronal model
		24	Weixiao	Yuan Wahlgren	Chemical Biology and Fragment based screens using solution NMR
		26	Jessica	Berglundh Gottlieb	Coronary atherosclerosis and oral status – a case control study
		28	Agnieszka	Podraza-Farhanieh	Physical training and senolytic interventions reduce cellular senescence in skeletal muscle
		30	Kristina	Johansson	Cytokine Stimulation of Airway Mucins

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Abstracts

OP01: Neurofilament light chain clearance through microglia and the implications of microglial states for biomarker interpretation

C Heiss, L Grötschel, E Rembeza, L Montoliu-Gaya, J Gentile, S Vallabh, E Minikel, H Zetterberg, S Fruhwürth

Psychiatry and Neurochemistry, Neuroscience and Physiology

Neurofilament light chain (NfL) is a protein released by degenerating neurons and serves as a biomarker for various neurodegenerative diseases. In these diseases, microglial activation is a hallmark of disease onset or progression. Interestingly, recent studies suggest that NfL might not be such a stable biomarker as previously thought. Studies report that patients that received the antibiotic minocycline, which is known to inhibit microglial activation, showed elevated NfL levels. Similarly, mice receiving minocycline show an increase in NfL levels. Here, we investigate how microglia can affect NfL levels.

We use human iPSC-derived cell models differentiated to microglia, neurons, or astrocytes. To investigate the role of microglia in neurofilament light chain (NfL) clearance, we measure NfL levels in co-cultures of microglia and neurons across different conditions The uptake of Alexa-Fluor-488-labeled NfL was tracked via fluorescence microscopy.

We demonstrate that the presence of microglia in neuronal cultures reduces NfL levels. In co-cultures treated with minocycline, NfL levels increase. Furthermore, by tracking labelled human recombinant NfL, we observe its uptake by microglia in both monoculture and in co-culture. Pre-treatment with minocycline significantly reduces uptake of labelled NfL. Finally, RNA sequencing analysis of microglia incubated with and without minocycline reveals changes in gene expression related to microglial functions.

Our data suggest that microglia might play an active role in modulating NfL levels through uptake and the inhibition of this process by minocycline may account for the elevated NfL levels observed in patients. These findings highlight the importance of considering microglial activation states when assessing and interpreting NfL levels in patients.

OP02: Unraveling the Impact of CACNA1C and Its Risk Variant on Neural Development in Bipolar Disorder

Melis Çelik, Mahnaz Nikpour, Bingqing He, Berta Marcó de La Cruz, Vika Telle, Parvaneh Nikpour, Lina Jonsson, Carl M. Sellgren, Mikael Landén, Erik Smedler

Psychiatry and Neurochemistry, Neuroscience and Physiology

Bipolar disorder (BD) is a serious psychiatric condition characterized by episodes of depression and mania, affecting millions of people worldwide. While BD is highly heritable, its biological mechanisms remain poorly understood. Studies have identified CACNA1C, a calcium channel gene crucial for brain development and neural function, as a major genetic risk factor for BD. The strongest association is with a SNP located in the third intronic region of the gene, but its effects on brain development are still unclear.

To investigate this, we use an integrative approach combining patient-derived stem cells, CRISPR-engineered isogenic lines, and advanced 3D brain organoids and assembloids. Our findings reveal that the CACNA1C risk variant increases neural progenitor proliferation (Ki67+) and impairs neuronal differentiation (MAP2+). These results suggest that the CACNA1C variant disrupts the timing of neural progenitor development and neuronal maturation, which may contribute to the neurodevelopmental origins of BD.

By leveraging these innovative human-specific models, we aim to unravel the pathogenesis of BD and lay the groundwork for targeted therapeutic strategies. In future work, we plan to bridge molecular alterations in individual cells with network-level activity by utilizing advanced tools such as single-cell RNA sequencing, optogenetics, and multielectrode arrays.

OP03: One modality to rule them all? Comparison of amyloid, tau, and FDG PET for the prediction of decline in different cognitive domains

S Karagianni, A Moscoso, M Schöll

Psychiatry and Neurochemistry, Neuroscience and Physiology

Background:
Alzheimer's disease (AD) research leverages PET imaging—amyloid (Aβ)-, fluorodeoxyglucose (FDG)-, and tau-PET—to predict cognitive decline. These modalities align with the A/T/N framework, which categorizes AD pathology respectively into amyloidosis, tau pathology, and neurodegeneration. However, their relative predictive accuracies across cognitive domains remain unclear. Clarifying this can optimize PET use and guide personalized AD interventions.

Aims:
The study (1) compares the accuracy of the three PET modalities and (2) assesses decline rates across cognitive domains by A/T/N statuses.

Methods:
Data from 335 participants from ADNI, including CN, MCI, and AD, were analyzed. All participants had available data for all three PET modalities. Longitudinal changes in cognitive domains were assessed using linear mixed-effects models with PET biomarkers, combinations of modalities, and A/T/N profiles as predictors. The models controlled for age, sex, education, and baseline diagnosis, and included interactions with time. Marginal R^2 values quantified the variance explained by each modality and their combinations.

Results:
Tau-PET had the highest predictive accuracy for memory ($R^2 = 0.50$) and language ($R^2 = 0.29$), while tau- and FDG-PET were equally effective for executive functions ($R^2 = 0.35$) and global cognition ($R^2 = 0.40$). Aβ-PET showed the lowest predictive accuracy across domains. Combining modalities yielded minimal additional variance explained. A+T+ biomarker profiles were associated with the fastest decline across all domains ($p < 0.001$).

Conclusion:
Tau-PET demonstrated the highest predictive accuracy for memory and language, while tau- and FDG-PET performed comparably for executive functions and global cognition. The lack of significant improvements with combined PET modalities aligns with the hypothesis that single modalities, particularly tau-PET, may sufficiently capture cognitive decline in specific domains. These findings highlight how reducing reliance on multimodal imaging can streamline applications, lower costs, and simplify protocols, while emphasizing domain-specific approaches and the role of pathological processes in cognitive decline.

OP04: The differential and temporal effects of a single or dual inflammatory insult on microglial activation states

Andrew S. Naylor, Christina Heiss, Henrik Zetterberg, Stefanie Fruhwürth

Department of Psychiatry and Neurochemistry, Institute of Neuroscienceand Physiology

Objectives:
Neuroinflammation is a key defence mechanism in the brain, primarily orchestrated by microglia, which play an essential role in responding to injury and infection. However, a prolonged or excessive response by microglia to inflammation can exacerbate neuronal damage and impair synaptic plasticity, significantly disrupting brain function and contributing to the progression of neurodegenerative diseases, such as Alzheimer's and Parkinson's disease. Inflammation in the brain is typically a dynamic, multi-phase process, often involving multiple inflammatory triggers. Interferon gamma (IFNg), which has been found in the brains of Alzheimer's patients, acts as a "primer" of microglia, so when a secondary inflammatory trigger occurs, it can lead to an intensified microglial activation state. Here, we investigated the dual effect of IFNg and lipopolysaccharide (LPS) on the inflammatory activation cascade of microglia.
Methods and Results:
We used human iPSC-derived microglia in monoculture to investigate the "priming" effect of IFNg alone or in combination with LPS. Our data revealed not only a differential effect on the gene expression of several inflammatory related markers, but we also discovered temporal changes in inflammation and morphological and motility changes in microglia exposed to either a single or a dual inflammatory insult. RNA sequencing analysis of the microglia also revealed a robust and varied effect on several different molecular functions and biological processes.
Conclusion:
Taken together, these findings emphasise the importance of understanding the temporal effects, the differential response of pro-inflammatory cytokines and the diverse impact of dual inflammatory insults on the activation and response of microglia during inflammation.

OP05: Perinatal exposure to Staphylococcus epidermidis as a potential factor contributing to autism later in life

W.K. Chan, S.M.J. Shiadeh, S. Rasmusson, T. Chumak, C. Mallard, and M. Ardalan

Department of Physiology, Institute of Neuroscience and Physiology

Background and aim:
Autistic spectrum disorder (ASD) is a common neurodevelopmental disorder with a higher prevalence in boys than girls. Its aetiology is multifactorial with complex interplay of environmental influences and genetic predispositions. Recent studies revealed that Staphylococcus epidermidis (SE) infection could trigger neuroinflammation during crucial stages of brain development, thereby exacerbating the risk of neurodevelopmental impairments. Accordingly, this project aims to investigate the long-term effects of perinatal SE infection on neurodevelopment, focusing on ASD.

Material and Method:
Male and female C57Bl/6 mice were administered with sterile saline or SE intraperitoneally on post-natal day 4. At the age of 45±5 days, behavioural tests associated with autism, including examining repetitive behaviour (marble burying test and grooming scoring) and three-chamber test for sociability, direct social interaction and hyperactivity were conducted.

Results:
Sex-dependent differences in response to perinatal SE infection were observed in adolescent mice. In males, perinatal SE infection resulted in a significantly increased number of buried marbles and grooming time, indicative of repetitive behaviour. Impaired sociability was noted in infected males, as shown by the lack of preference for the chamber with a stimulus mouse. Significant impaired direct social interaction was also observed in SE-infected males, revealed by a lack of preference for sniffing the pencil cup containing a stimulus mouse. No autistic-like behaviours were observed in female mice. However, significantly increased locomotor activity indicative of hyperactivity, associated with attention deficit hyperactivity disorder (ADHD), was demonstrated exclusively in females.

Conclusion:
In conclusion, the study findings highlight sex-dependent differences in response to perinatal SE infection. Male mice displayed an increase in ASD-like behaviours, characterised by repetitive behaviours and impaired sociability, while female mice exhibited heightened hyperactivity reminiscent of ADHD. These observations underscore the implications of perinatal SE infection on neurodevelopment and the importance of considering sex-specific responses to perinatal inflammation.

OP06: BDC: Advancing microbiological methods with clinical and research applications

E. Rudbeck, D. Schmidta, S. Thankaswamy Kosalaia, S. Abrahamssona, G. P. Di Santo Meztlera

Bioinformatics and Data Centre, Gothenburg University

Bioinformatics serves as a bridge between raw sequence data and the biological understanding of organisms, enabling transformative insights into their functioning. The advent of high-throughput sequencing technologies has revolutionized microbiology by facilitating the analysis of vast genomic, transcriptomic, and proteomic datasets, uncovering patterns and mechanisms that were previously beyond reach.

At the BDC (GU), the microbiology group develops robust bioinformatics pipelines tailored for the analysis of bacterial and viral data derived from patient samples collected across hospitals in the Västra region of Sweden. These pipelines enables us to analyze viral genomes such as SARS-CoV-2, Hepatitis B and C, HIV, and Cytomegalovirus (CMV), alongside bacterial datasets, including metagenomic data and multidrug-resistant Staphylococcus aureus (MRSA).

Our presentation will feature real-world examples that demonstrate the effectiveness of our workflows. From identifying viral mutations associated with disease progression to profiling microbial communities involved in antibiotic resistance, illustrating how bioinformatics is advancing clinical microbiology and public health. Our main goal is to support clinics in improving diagnostic precision and enhancing patient care.

OP07: Preconditioning scaffolds for uterus bioengineering with metalloproteinases: does it affect cytocompatibility and immunogenicity?

De Miguel-Gómez L, Sehic E, Thorén E, Johannsson L, Hellström M, Brännström M

Obstetrics and Gynecology - Section , Clinical Sciences

Introduction:
Uterus bioengineering offers a potential treatment option for women with uterine factor infertility. Decellularized (DC) uterine tissue scaffolds have proved promising in in vivo experiments in rodent and domestic species animal models. To promote further recellularization of DC scaffolds, we have already established a pre-conditioning step using metalloproteinases (MMP2, MMP9). However, we have not yet evaluated whether this treatment can affect the scaffold's cytocompatibility and immunogenicity by generating additional damage-associated molecular patterns (DAMPs). Thus, we aimed to study these two features in MMP-treated DC uterine scaffolds from two different species, cow and baboon.

Methods:
All uteri were decellularized using a one-week sodium deoxycholate-based protocol. Half of the obtained scaffolds were further preconditioned with MMP2 and MMP9. Then, using fertilized chicken eggs, the chorioallantoic membrane assay (CAM) examined the cytotoxicity of the scaffolds. Additionally, the cow scaffolds were subcutaneously transplanted into a rat model to evaluate immune cell tissue infiltration by immunohistochemistry. In parallel, the immunogenicity of DC baboon scaffolds was assessed by in vitro co-culture with human peripheral blood mononuclear cells followed by cell phenotype identification using FACS. All scaffolds were also subjected to in vitro recellularization using mesenchymal stem cells.

Results:
The CAM assay and in vitro recellularization confirmed the scaffold's cytocompatibility. Additionally, MMP preconditioning improved the in vitro recellularization efficiency without compromising the scaffold's immunogenicity. More specifically, the cow tissue showed no differences regarding immune cell infiltration, while the baboon experiment demonstrated that MMP preconditioning generated more immune-privileged scaffolds.

Conclusion:
Preconditioning DC uterine scaffolds with MMPs increased recellularization efficiency without affecting their cytocompatibility or immunogenicity.

OP08: Frequent pain is common among 10-11-year-old children with symptoms of attention deficit hyperactivity disorder

SSB Berggren

Dep. of Paediatrics, Clinical Sciences

Background and aims:
Adults with neurodevelopmental disorders have increased risk for chronic pain. This study aimed to describe the prevalence of frequent and multisite pain among children with symptoms of attention deficit hyperactivity disorder (ADHD) and explore potential sex differences in pain prevalence.
Methods:
Children born 2008 included in the "Halland Health and Growth Study" were invited to a follow-up (n = 1,186) in 2018-19. Parents received the digital screening questionnaire, the Swanson, Nolan and Pelham Rating Scale (SNAP-IV) for ADHD, and the children answered a pain questionnaire, including a pain mannequin. The main outcome was pain experience, and children with symptoms of ADHD were compared to children without these symptoms.
Results:
In this general population of 10-11-year-old Swedish children, weekly pain was reported in 52.5% of children with symptoms of ADHD combined type, compared to 36.2% of children without these symptoms ($p < 0.05$). Hyperactivity and impulsivity were significant contributors to the increased risk for frequent pain (OR 2.33 95% CI 1.30 to 4.17, $p = 0.004$), but inattention was not a significant contributor (OR 1.17 95% CI 0.74 to 1.87, $p = 0.497$). Multisite pain was more common among girls with hyperactivity compared to boys with hyperactivity (51.4 vs. 27.9%, $p = 0.036$). Weekly headache and/or abdominal pain was reported by a quarter of girls with symptoms of ADHD combined type, and up to a fifth of boys, compared to 11-13% of children without these symptoms.
Conclusion:
Frequent pain was more common for children with symptoms of ADHD compared to children without symptoms of ADHD. Hyperactivity and impulsivity had a stronger association to pain than had inattention-related problems. Clinicians should be aware of the frequent occurrence and the association between pain and neurodevelopmental disorders among children, and that it could complicate both the clinical picture and the treatment.

OP09: Prostate cancer extracellular vesicles delivered miRNAs may intelligently regulate bone metastasis

Lijuan Yu, Roger Olofsson Bagge, Toshima Parris, Jiayun Liu, Xiaoke Hao, Lei Zheng

Sahlgrenska Cancer Centre, Institue of Clinical Science

Background:
We have previously reported that extracellular vesicles derived from osteoblastic, osteoclastic and mixed prostate cancer cells promote osteoclast differentiation and inhibit osteoblast differentiation via transferring miR-92a-1-5p. However, at the same time, osteoblastic miRNAs also exist in prostate cancer extracellular vesicles. In the present study, we focused on discovering the roles of miR-375 and miR-148a-3p delivered by prostate cancer EVs in bone homeostasis and bone metastasis, and then explaining the reason that osteoblastic miRNAs and osteoclastic miRNAs co-exist in prostate cancer EVs.

Methods:
Conditioned media, miRNA mimics and inhibitors were co-cultured with MC3T3-E1 cells. Stable prostate cancer cell lines (MDA PCa 2b) overexpressing miR-375 or miR-148a-3p were constructed by lentivirus. And miRNAs overexpressed MDA PCa 2b cells were injected into the bone. Target gene of miR-375 and miR-148a-3p was proved by a dual-luciferase reporter assay system. After weeks that miRNAs overexpressed MDA PCa 2b cells were injected into the prostate, prostate EVs were isolated and osteoblastic miR-375, miR-148a-3p and osteoclastic miR-92a-1-5p were detected by ddPCR.

Results:
Conditional media from prostate cancer culture promote osteoblast differentiation at least partly from EVs contribution, as confirmed by ALP staining and Alizarin red staining. Further, miR-375 and miR-148a-3p promote osteoblast differentiation in vitro by reducing KLF4 expression. In vivo, the miR-375 and miR-148a-3p overexpressed MDA PCa 2b cells promote osteoblastogenesis and tumor growth. siRNA targeting KLF4 resulted in similar increase in osteoblast function and tumor cells proliferation. Osteoclastic miRNAs and osteoblastic miRNAs exist in different bone metastatic phase according to the bone EVs miRNA ddPCR data.

Conclusion:
These experiments suggest that miR-375 and miR-148a-3p delivered by PCa EVs regulate osteoblast function and tumor growth via targeting KLF4. Osteoclastic miR-92a-1-5p and osteoblastic miR-375 and miR-148a-3p play their roles at different phase of bone metastasis in an intelligent way.

OP10: Equalizing prognostic disparities in KRAS-mutated stage III NSCLC patients: addition of durvalumab to combined chemoradiotherapy improves survival

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Surgery, Kliniska Vetenskaper

Introduction:
Stage III non-small cell lung cancer (NSCLC) is a heterogeneous group and identification of subgroups with differential treatment responses is crucial. Addition of durvalumab to concurrent chemoradiotherapy (cCRT) has previously been shown to improve survival outcomes. Meanwhile, subgroups harboring KRAS mutations have been shown to have worse prognosis. We investigated whether KRAS mutational status may affect survival outcomes after adjuvant durvalumab following cCRT in stage III NSCLC.

Methods:
In this multi-center retrospective study, we present a real-world dataset of all stage III NSCLC patients treated with curative-intent cCRT with molecular assessment, between 2016 and 2021 in the Västra Götaland Region of western Sweden. The study period includes the standard practice prior to the introduction of durvalumab, enabling evaluation of the potential impact of immune checkpoint blockade (ICB). Primary study outcomes were overall survival (OS) and progression free survival (PFS).

Results:
We identified 145 patients who received cCRT with curative intent, and 32% harbored an activating mutation in the KRAS gene (KRASMUT; n = 46). Compared to patients with wild-type KRAS (KRASWT; n = 99), KRASMUT had worse OS (p = 0.047) and PFS (p = 0.038). This finding persisted on multivariate analysis with OS (HR 1.703, 95% CI 1.074-2.702, p = 0.024) and PFS (HR 1.628, 95% CI 1.081-2.453, p = 0.020). Within the subgroup that received cCRT alone, KRASMUT patients (n = 35) exhibited worse OS (p = 0.036) and PFS (p = 0.037) compared with KRASWT (n = 35). However, among those who received additional durvalumab after cCRT (KRASWT; n = 99. KRASMUT; n = 11) there were no significant differences in OS (0.788) or PFS (0.855) between the groups.

Conclusions:
KRAS mutations are a negative prognostic factor after cCRT in stage III NSCLC, and the addition of durvalumab ameliorates the negative impact of harboring this mutation.

OP11: Mechanistic basis of atypical TERT promoter mutations

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Medkem, Biomedicine

Background:
Non-coding mutations in the TERT promoter (TERTp), typically at one of two bases -124 and -146 bp upstream of the start codon, are among the most prevalent driver mutations in human cancer. Several additional recurrent TERTp mutations have been reported but their functions and origins remain largely unexplained.

Aim:
To explain the frequency and basis of atypical mutations in TERTp

Materials and methods:
Analysis of whole genome and targeted sequencing cancar cohorts, in-house generated Simsen-seq of TERTp following UV exposure, in vitro UV damage assays using purified ETS protein

Results:
Here, we show that atypical TERTp mutations arise secondary to canonical TERTp mutations in a two-step process. Canonical TERTp mutations create de novo binding sites for ETS family transcription factors that induce favourable conditions for DNA damage formation by UV light, thus creating a hotspot effect but only after a first mutational hit. In agreement, atypical TERTp mutations co-occur with canonical driver mutations in large cancer cohorts and arise subclonally specifically on the TERTp driver mutant chromosome homolog of melanoma cells treated with UV light in vitro.

Conclusion:
Our study gives an in-depth view of TERTp mutations in cancer and provides a mechanistic explanation for atypical TERTp mutations which arise due to increase UV damage at the newly created transcription factor binding sites.

OP12: NRF2 Signaling in EMT and Macrophage Polarization

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Microbiology and Immunology , Biomedicine

Our research explored the role of NADPH oxidase 2 (NOX2)-derived reactive oxygen species (ROS) in breast cancer, focusing on its dual impact on epithelial-to-mesenchymal transition (EMT) and M2 macrophage polarization in the tumor microenvironment (TME).

First, we demonstrated that NOX2-derived ROS drive EMT in breast cancer, a key step in cancer metastasis. In vitro studies showed that NOX2-derived ROS induced EMT in MCF-7, T-47D, 4T1 and EO771 breast cancer cell lines, and our results suggest that this induction was via NRF2-mediated upregulation of SNAI transcription factors. In vivo, using orthotopically implanted 4T1 breast cancer cells, we showed that stimulation of NOX2 in tumor-infiltrating myeloid cells via intratumoral WKYMVm injection, enhanced tumor growth, EMT marker expression, and lung metastases, effects reversed by the NOX2 inhibitor histamine dichloride (HDC). Similarly, in the EO771 breast cancer model, tumors grown in WT mice exhibited elevated EMT marker expression, further amplified by WKYMVm, while tumors grown in NOX2 knock out (Nox2-/-) mice showed reduced expression of EMT markers. Additionally, high NOX2 expression correlated with EMT gene signatures and poor metastasis-free survival in human breast cancer datasets.

Second, we investigated effects of NOX2-derived ROS on M2 macrophage polarization. Analyzes of scRNA-seq data from 100 human breast cancer tumors showed that M2 macrophages expressed significantly higher levels of NOX2 compared with other myeloid subsets. In vitro, NOX2 inhibition impaired monocyte differentiation into M2 macrophages, and Nox2-/- mice exhibited fewer M2 macrophages in tumors. Mechanistic studies suggested that NOX2-driven NRF2 activation is critical for M2 polarization. These findings highlight NOX2-derived ROS as key drivers of EMT and M2 polarization, identifying NOX2 as a promising therapeutic target to mitigate metastasis and immunosuppression in breast cancer.

OP13: Targeting murine metastatic cancers with adjuvanted cancer antigen vaccines

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Department of Microbiology and Immunology, Institute of Biomedicine

Metastasis has been deemed as the cause for most cancer-related deaths as it is difficult for the immune system to eliminate the cells that disseminate from their microenvironment to distant organs. Vaccines represent one of the greatest avenues of training the immune system towards eradication of diseases. However, success of vaccines is critically dependent on immunomodulation using adjuvants and preservation of the tumor-specific T cells. Efficient targeting of the dendritic cell (DC) population responsible for processing and presentation of antigens is a key aspect of such vaccines. Cholera toxin-based adjuvants have shown good effect in vaccines for infectious diseases, but their role in cancer treatment remains under explored. In this study, we investigated the potential of cholera toxin A1 (CTA1)-based adjuvants to enhance anti-tumor T cell responses and protect against metastasis. We report that an adjuvant where CTA1 is fused to a dimer from Staphylococcus aureus protein A (DD) stimulates immune responses against the tumor associated antigens TRP2 and Twist1 in mice, providing protection against murine B16F1 melanoma and 4T1 breast cancer metastasis, respectively. Both mucosal (intranasal) and systemic (intraperitoneal) vaccine delivery conferred protection from intravenously injected tumor cells. When comparing the efficiency of antigens mixed with CTA1-DD relative to those fused with a CTA1-based adjuvant, the fusion construct exhibited the strongest regulation of T cells. But administration of a 20-fold higher antigen dose in the mixed-setting provided efficient protection from metastasis.

OP14: The role of oxytocin in the development of social preference in zebrafish

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Social abilities, like attention to faces, and joint attention are established very early in human infants. Whereas the fetal environment is difficult to access and manipulate in mammals, zebrafish (Danio rerio) larvae are directly after hatching fully accessible for behavioral and neuroscientific experiments. At about three-weeks of age the zebrafish larvae relatively abrupt start to attend to other conspecifics. This provides a rather unique possibility to investigate the development of the social brain, and, hence, the emergence of social preference behavior. Zebrafish also holds additional advantages for neuroscience research. They are highly social, mainly relying on their vision, and their visual system connects with other brain regions that are active during social behavior. Furthermore, zebrafish possesses high genetic homology with humans, an evolutionarily conserved brain, and a broad behavioral repertoire, making it a good model to study brain function. Taken together, the zebrafish model provides a rather unique possibility to investigate the development of the social brain using various experimental approaches. In the current study, we investigate the development of oxytocin neurons at several time points from one-week-of-age to adulthood using Light-Sheet microscopy of whole-brains from oxtl:EGFP transgenic zebrafish, expressing green-fluorescent protein in oxytocin neurons. Furthermore, we used mutant fish lacking either or both of the two oxytocin receptors, oxtr and oxtrl, to investigate the functional importance of oxytocin for social preference in different developmental stages. The number of oxytocin neurons increased substantially from the larval stage to adulthood, with the major increase seen at the juvenile stage. Whereas oxytocin receptor mutant zebrafish display substantially less social preference behaviour compared to sibling controls in adulthood, they show the same preference for social stimuli at four-weeks-of age. In conclusion, our results indicate that oxytocin plays a crucial role for social preference specifically in adults, which is not seen in larval zebrafish.

OP15: Nox2 Activity may Determine Disease Progression in Parkinson's Disease

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NOX2 (NADPH oxidase type 2) is an enzyme complex mainly expressed by myeloid immune cells and by central nervous system resident microglia, that produces reactive oxygen species (ROS) to aid pathogen clearance. Dysregulated NOX2 has been implicated in neurodegenerative diseases, but direct evidence for its role in humans is lacking. We aimed at determining the potential impact of genetic variation encoding NOX2 activity on disease progression in Parkinson's disease (PD). The single nucleotide polymorphisms (SNP) rs4673 and rs1049254 in CYBA, encoding the functional NOX2 subunit p22phox, regulates the magnitude of NOX2-derived ROS formation. Using TaqMan SNP genotyping assays, we genotyped a cohort of 93 patients with idiopathic PD, with up to 42 years follow-up from onset of PD, for rs4673 and rs1049254. Through patient journal review, time from onset of disease to the occurrence of 25 milestones of disease progression was determined in a blinded fashion. Using a linear mixed-effects model, we analyzed the impact of CYBA SNP genotypes on PD progression determined by a composite measure of all milestones. Data were censored when 50% of events within each milestone had occurred to reduce contribution of normal aging. We found that rs1049254 (P=0.009) as well a combination of each SNP (P=0.01) impacted on disease progression measured by accumulation of milestones over time. These effects remained significant in multivariable analysis when adjusting for potential confounders. Ten years after onset of PD, patients homozygous for alleles associated with high ROS formation at both SNP locations had reached a mean of almost three times as many milestones as patients with a low-ROS genotype. These results propose a role for NOX2 in progression of PD, and suggest pharmacological targeting of NOX2 as a strategy to reduce progressive neurodegeneration.

OP16: Nallo: A Nextflow pipeline for comprehensive human long-read genome analysis

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Whole-genome sequencing has been a well-established method in research and clinical application for several years. While the dominant short read-based technology has allowed for sweeping improvements in the discovery of clinically relevant single-nucleotide variants and short indels, it struggles with many kinds of potentially deleterious variations, such as complex rearrangements, tri-nucleotide expansions and large insertions and deletions.

Long-read sequencing technologies are becoming more common in research due to their ability to detect variations that short reads cannot. They also make complex analyses, like haplotype phasing and genome assembly, easier to perform. Furthermore, all recent long-read technologies can detect methylation without any changes to a standard sequencing run. Therefore, long reads are a prime target for adoption in large-scale human sequencing projects and certain clinical applications, such as rare diseases, where complete and high-resolution genomic information is essential.

However, one major hurdle towards widespread adoption of long reads is the lack of a universal, ready-to-use pipeline. While several long-read pipelines exist, many are platform-specific and only run in certain environments. A platform-agnostic analysis pipeline for long reads which works seamlessly across environments could facilitate the transition to long-reads in research and the clinic.

Here, we introduce Genomic-Medicine-Sweden/Nallo, a Nextflow-based pipeline for human long-read sequencing analysis, which covers all steps from alignment to variant calling and annotation, assembly, phasing and methylation analysis. Nallo integrates widely used tools into a single workflow that is simple to set up and runs natively on various computing environments. It supports both major long-read technologies and is designed with clinical and population-scale projects in mind. Through the application of reuseable nf-core modules and infrastructure, Nallo facilitates collaboration across teams and environments as well as reproducibility.

OP17: Women with knee osteoarthritis: the role of progesterone in a post-menopausal age window

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Objective:
Post-menopausal women represent a significant proportion of knee osteoarthritis patients, suggesting potential hormonal influences on disease prevalence and progression. In our study, we sought to clarify the associations between gonadal hormones and osteoarthritis onset and severity by investigating sex-based differences in pain perception, radiological score, and synovial protein signature.
Methods:
Blood and synovial membrane samples were collected from 40 male and 34 female patients at the time of total knee replacement arthroplasty. Patient information was collected via self-reported questionnaires. Plasma levels of gonadal hormones and sex hormones binding globulin (SHBG) were measured using commercial ELISA kits. Sex-based differences in the activation of molecular pathways within the synovial membrane and isolated fibroblast-like synoviocytes (FLS) were assessed through proteomic analysis. De novo protein synthesis was evaluated with a commercial click-reaction-based kit.
Results:
The patients involved in the study were similar in age, average BMI, radiographic scores, and reported pain intensity. When stratifying by age, pain intensity differed between sexes: females aged 49–60 years reported higher pain intensity than males in the same age group. Additionally, in the overall female cohort, correlations were found between progesterone, estradiol, SHBG, and radiographic scores. The synovial tissues of the female patients show an upregulation of pathways involved in the protein synthesis machinery. In isolated FLS, pro-fibrotic and pro-inflammatory pathways were altered in female patients compared to men. In vitro studies performed to define the role of progesterone in de novo protein synthesis indicate that progesterone inhibits protein synthesis in FLS isolated from patients of both sexes.
Conclusion:
Sex differences in pain perception among patients with established knee osteoarthritis (OA) are most pronounced in the period shortly after menopause. Pain intensity might be associated with a higher concentration of progesterone as a result of an increased release of the hormone by the adrenal gland due to stress related to pain and reduced mobility.

PP01: Mito-gatk: A pipeline for comprehensive mitochondrial short-variant discovery

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We have developed a Snakemake workflow, Mito-gatk, engineered for the detection and annotation of short genetic variants within the mitochondrial genome across both human and mouse models. This workflow adheres to the GATK Best Practices, ensuring high standards of accuracy and reliability in variant calling. Mito-GATK has a mapping strategy tailored for species with extensive nuclear mitochondrial DNA (NuMT) regions, such as mouse, allowing for enhanced coverage uniformity and improved variant detection. While many existing mitochondrial variant calling pipelines and annotation tools are predominantly designed for human genomic data, our pipeline addresses the critical need for a comparable workflow suited for other model organisms. This capability is essential given the prevalence of e.g. mouse models in genetic research and the corresponding requirement for accurate mitochondrial variant analysis in these organisms.

PP02: Characterization of biological nanoparticles using Dual-Angle Interferometric Scattering microscopY (DAISY).

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Multiple challenges remain in characterizing colloidal particles of low optical contrast in their native liquid environment. One important challenge is to distinguish between different types of biological submicron and nanoparticles in a heterogeneous sample. This can be especially difficult when the particles to be characterized are surrounded by a high concentration of smaller nanoparticles or large molecules.

We present a method which enables powerful particle characterization in a broad size range from nanoparticles to microparticles. The method is based on particle tracking and a combination of holographic and interferometric scattering microscopy which use two opposing illumination angles.

We demonstrate characterization of heterogeneous particle dispersions in the size range 50-500nm, where hydrodynamic size as well as quantitative optical properties of individual particles is determined. The combination of hydrodynamic and optical parameters enables differentiation of particles based on their refractive index, which in the case of biological particles is indicative of their density. Further, for particles in the submicron range, combination of quantitative optical data from opposing illumination angles enables to estimate the distribution of mass between the center and periphery of a particle or to estimate particle size from purely optical data.
Finally, we demonstrate the possibility to use holographic microscopy in combination with gold nanoparticle labeling to detect specific EV or virus, and discuss the potential advantages compared to fluorescent labeling.
To conclude, particle tracking using holographic/interferometric microscopy enables powerful optical characterization of biological submicron- and nanoparticles.

PP03: The effects of iodixanol density solution on cellular morphology and viability

Camilla Locatelli, Emma Symonds, Roger Olofsson Bagge, Rossella Crescitelli

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Introduction:
Extracellular vesicles (EVs) are bilayer membrane particles involved in cell-to-cell communication and released by all cell types. An increasing number of studies focus on the role of EVs in biology. One of the crucial points in the field is EV isolation. The most common EV isolation method includes density gradient centrifugation using iodixanol (Optiprep™), a sucrose-based solution that separates EVs from contaminants by density. The EVs are then resuspended in the iodixanol solution after the isolation. This study aims to investigate the effects of the iodixanol solution on cell function and viability.

Methods:
The breast cancer cells MCF7 were treated with increasing concentrations of iodixanol (0.03% – 0.1% – 0.3% – 1% – 3% – 10% – 30%), followed by cell viability and morphology analysis. The effects of iodixanol on the recipient cells were analysed at three different time points: 24, 48 and 72h. At each time point, the cells were visualized by microscopy (morphology analysis) followed by viability assay using CCK8 kit.

Results:
Preliminary data showed no significant effects on morphology and viability (86-100%) when the cells were treated with iodixanol concentrations between 0.03% and 3%. At higher concentrations (10% and 30%), the cells were detached and dead; indeed, the viability was lower compared to the other concentrations at each time point (62-73% in 10% Optiprep™, 27-41% in 30% Optiprep™).

Conclusions:
Although iodixanol is widely used to isolate EVs, these preliminary data show that it is not completely inactive or inert. Possible side effects of iodixanol should be kept in consideration in EV studies.

PP04: Rapid Griess Assay (RGA): A Chairside Test for Ex Vivo Semi-Quantitative Oral Nitrite Measurement and In Vitro Assessment of Nitrite Production by Oral Bacteria

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Abstract:

Background and aims:

Specific oral bacteria produce nitrite (NO2-) through reduction of nitrate (NO3-), contributing to cardiovascular health, and possibly also to oral health, according to new studies. Current NO2- quantitation methods are complex and unsuitable for chairside use. We primarily aimed to develop the Rapid Griess Assay (RGA), a chairside method for NO2- measurement, and evaluate oral NO2- production in healthy individuals. Further, we verified the NO2- generating capacity in a number of oral and non-oral bacterial species.

Materials and Methods:

Samples from 12 healthy individuals were collected weekly from the tongue, saliva, and plaque across four weeks. NO2- levels were measured using the RGA. In vitro NO2- production capacities were evaluated with RGA on selected bacterial species.

Results:

The RGA provided reproducible results, with tongue samples showing most stable and highest NO2- levels. The oral bacteria Actinomyces spp. (including Schaalia odontolytica), Veillonella parvula and Rothia spp. showed high and medium NO2- production.

Conclusions:

The RGA is a reliable chairside method for oral NO2- semi-quantitation, revealing consistent, elevated NO2- levels in tongue samples among healthy individuals. NO2- production in various bacterial species was confirmed In vitro, demonstrating the potential for clinical and research applications of RGA.

PP05: Pre-clinical models of osteoarthritis: effect of ovaries removal on the joint of aged mice.

Lindsay Zentveld, Sofia Wustenhagen, Loise Råberg, Francesco Longo, Anders Nguyen, Julia Scheffler, Alexandra Stubelius, Mattias Svensson, Ulrika Islander, Carmen Corciulo

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Osteoarthritis is a common disease affecting 500 million people worldwide, marked by cartilage degradation, bone alterations, and inflammation, all of which contribute to chronic pain and reduced mobility. Post-menopausal women constitute a significant proportion of knee osteoarthritis (OA) patients, indicating potential hormonal influences on disease symptoms and progression.

OA primarily affects older adults, yet many preclinical studies examining the role of gonadal hormones in OA use young animals in ovariectomy models, overlooking the aging context in which OA commonly develops. Although mice do not undergo menopause, they experience a gradual decline in fertility and mild hormonal changes beginning around 7 months of age. This differs significantly from the pronounced hormonal shifts seen in women, where estradiol and progesterone levels fluctuate in pre-menopause before stabilizing at low levels in the post-menopause phase.

Our study aims to explore the combined effects of ovariectomy and aging on joint health in adult female mice. Adult mice were ovariectomized (n=15) or subjected to sham surgery (n=15), and their motor ability and pain sensitivity were assessed every 3 months until they reached 18 months of age. Cartilage and bone integrity in the knee joints were also evaluated to determine spontaneous OA development by histological analysis and micro-computed tomography.

The motor ability did not differ in the ovariectomized mice compared to the control group. The pain sensitivity was greater in the ovariectomized mice in a short age window (between 13 and 16 months of age). The histological analysis reveals alteration of the cartilage in both groups with loss of proteoglycans and cartilage damage being more pronounced in the ovariectomized animals.

PP06: Determinants affecting fractional exhaled nitric oxide in a population-representative adult sample in western Sweden

Reshed Abohalaka, Selin Ercan, Lauri Lehtimäki, Saliha Selin Ozuygur Ermis, Daniil Lisik, Muwada Bashir Awad Bashir, Radhika Jadhav, Linda Ekerljung, Jan Lötvall, Helena Backman, Madeleine Rådinger, Bright I. Nwaru, Hannu Kankaanranta

Internal Medicine and Clinical Nutrition , Institute of Medicine

Background:
Fractional exhaled nitric oxide (FeNO) is used to differentiate asthma inflammatory phenotypes and guide its management. However, data on FeNO reference values in a representative adult population is limited. Thus, we aim to derive reference values for FeNO in a representative adult population.

Methods:
The West Sweden Asthma Study is a clinical-epidemiological population-representative study of randomly selected adults in Western Sweden. From this cohort, 943 subjects participated in comprehensive clinical investigations, including skin prick testing (SPT), specific immunoglobulin E (sIgE) analysis, and FeNO measurement. Clinical allergy was defined as co-occurrence of atopy (positivity to SPT or sIgE) and self-reported allergic symptoms to the same allergen family. FeNO levels were analysed in relation to the presence or absence of clinical allergy, asthma, and other factors.

Results:
The 95th percentile of FeNO ranged from 34 to 52 parts per billion (ppb) in the entire sample (N=943), and from 26 to 37 ppb among individuals without clinical allergy, asthma, or chronic obstructive pulmonary disease (COPD) (n=587), depending on age.

Conclusion:
The 95th percentile for FeNO ranges, depending on age, from 26 to 37 ppb in healthy population devoid of clinical allergy, asthma, or COPD. These findings provide a guide for interpreting FeNO in the general population and in asthma and COPD clinics.

PP07: Optimizing for Vitamin d Intake and Low-Carbon Emissions in Diets among Swedish Adolescents

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Internal Medicine and Clinical Nutrition, Medicine

Background:
In the Nordic countries, key dietary sources of vitamin D include milk, yoghurt, fat spreads (all vitamin D fortified in Sweden by law) and fatty fish. Previous studies indicate that Swedish adolescents consume less vitamin D than recommended. Additionally, global climate change initiatives could lead to decreased consumption of vitamin D-rich foods with high climate impact. Our aim was to assess dietary changes required among Swedish adolescents to achieve both adequate vitamin D intake and targets for dietary greenhouse gas emissions (GHGEs).

Methods:
We developed a linear optimization model using data from the national food survey Riksmaten Adolescents 2016-17 (n = 3,099). Dietary data was collected via two web-based 24-hour recalls and linked to the Swedish Food Agency's food composition database, updated with current vitamin D fortification levels. Climate impact estimates per food item were obtained from the Research Institutes of Sweden's (RISE) Food Climate Database. The model was programmed to minimize changes from the original diet, reach the recommended vitamin D intake (10 µg/day) and keep dietary GHGEs below 1.6 kg CO2-equivalents per person, per day. Intake of other essential nutrients could not be worse than the original diet.

Results:
The optimized diet eliminated fatty fish (mainly salmon) entirely, favoring more vitamin D-rich sources with lower GHGEs: milk and yoghurt (+24%), dishes with milk (+79%) and fat spreads (+80%). Together with a substantial increase in egg consumption (+174%), these foods accounted for 84% of total vitamin D intake. The diet also favored plant-based foods (potatoes, bread, pasta, grains excluding rice) over meat and meat products, resulting in a 57% reduction in dietary GHGEs. However, seven nutrients did not meet recommended intakes: saturated and polyunsaturated fats, vitamin C, iron, zinc, selenium and sodium.

Conclusions:
Our results suggest Swedish adolescents can achieve recommended vitamin D intakes and simultaneously limit carbon footprint while deviating minimally from current consumption. This is achievable through increases in vitamin D-rich foods, especially fortified products. While these findings offer valuable insights regarding vitamin D, addressing all essential nutrients is necessary to plan nutritionally adequate diets with lower climate impact for this demographic.

PP08: Prospective Comparison of Temporal Changes in Myocardial Function in Women with Takotsubo versus Women with Anterior STEMI

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Background:
Takotsubo syndrome (TS) and ST-elevation myocardial infarction (STEMI) with prompt reperfusion both lead to a unique form of acute myocardial dysfunction known as myocardial stunning. Although this condition is typically reversible, the precise course of cardiac function recovery remains poorly defined, especially when comparing the distinctly different mechanisms of TS, often triggered by emotional or physical stress, and STEMI, which is caused by coronary artery blockage. Since TS primarily affects women, this study focused exclusively on women in both groups, enabling a direct comparison of recovery patterns between women with TS and those with anterior STEMI.

Methods:
The Stunning in Takotsubo versus Acute Myocardial Infarction (STAMI) study prospectively enrolled 53 women with TS and 36 women with anterior STEMI. Echocardiography and blood sampling were conducted within 4 hours of admission and repeated at 1, 2, 3, 7, 14, and 30 days to capture a detailed recovery timeline. The primary outcome measured was the proportion of reversible left ventricular akinesia (from baseline to 30 days) resolved by 72 hours. Secondary outcomes included left ventricular ejection fraction (LVEF), global longitudinal strain (GLS), and tricuspid annular plane systolic excursion (TAPSE). Mixed effects linear regression and tobit models with random intercepts were used to analyze changes in echocardiographic parameters over time.

Results:
At 72 hours, recovery of reversible akinesia was observed in 57.9% (95% CI 47.8-68.4) of TS patients and 53.5% (95% CI 36.7-70.5) of STEMI patients, indicating comparable early-phase recovery (difference 4.4%, 95% CI -15.7-24.4). LVEF and GLS showed similar recovery trajectories in both groups, while TAPSE was initially reduced in TS but remained normal in STEMI, recovering in parallel with left ventricular indices. Significant functional recovery continued beyond 7 days in both groups, suggesting ongoing cardiac repair.

Conclusions:
Despite their differing triggers and presentations, the trajectory of cardiac function recovery in TS closely parallels that in STEMI.

PP09: Pre-pregnancy BMI and BMI Change as Predictors of Breastfeeding Duration: Findings from the Swedish CArdioPulmonary bioImage Study (SCAPIS)

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Internal Medicine and Clinical Nutrition, Medicine

Background:
Overweight and obesity are increasing globally, and young adult women are gaining weight at increasing rates. Maternal overweight pre-pregnancy negatively affects breastfeeding duration. Understanding factors influencing breastfeeding is crucial due to its benefits for both mother and infant.
Aim:
To determine the effect of pre-pregnancy BMI (preBMI), and the novel exposure preBMI change, on breastfeeding duration of the first child.
Methods:
Data from the Umeå sub-cohort of the Swedish Cardiopulmonary Bioimage Study (SCAPIS) was obtained. We included parous women aged 50-64 who retrospectively reported their duration of exclusive (EBF) and any breastfeeding (ABF). PreBMIs were calculated from height at inclusion and self-reported weights at age 20 and before first pregnancy. PreBMI change was the BMI difference between those two points. Relationships between preBMI or preBMI change, and breastfeeding duration were explored using multivariable logistic regression analysis, adjusted for age at first delivery, education, and smoking. Breastfeeding duration was categorized as >4 months vs. ≤4 months (reference).
Results:
Among 943 women, the mean (SD) duration of EBF was 4.8 (2.8) months, and ABF was 8.5 (5.3) months. Each unit increase in preBMI decreased the likelihood of EBF >4 months by 7% (OR = 0.93, 95% CI: 0.88, 0.98). No significant association was found between preBMI and duration of ABF. No relationship between preBMI change and EBF or ABF was found among women across all preBMI categories and preBMI changes. However, in a subsample of women with preBMI gain within the normal BMI range, the likelihood of sustaining ABF > 4 months decreased by 26% (OR = 0.74, 95% CI: 0.58, 0.94) for each unit increase in preBMI.
Conclusion:
Our results suggest that both preBMI and preBMI change can negatively affect duration of breastfeeding. Women of reproductive age should receive support to achieve and maintain a healthy weight before pregnancy.

PP10: Diabetes and diabetes-related complications are associated with periodontitis. Population data from Sweden.

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Odontology Section (Dept Periodontology), Odontology

Background:
Previous evidence suggests that periodontitis is associated with type 2 diabetes (T2D) and may contribute to diabetes-related complications. Corresponding data on type 1 diabetes (T1D) and periodontitis are limited.
Aim:
To evaluate the association between type 1 diabetes (T1D)/type 2 diabetes (T2D) and periodontitis and assess the influence of periodontitis on diabetes-related complications.
Material and methods:
This observational study was based on data from multiple Swedish registries. We identified two groups of individuals with diabetes (T1D: 28801; T2D: 251645) and two groups without diabetes (non-T1D: 57839; non-T2D: 539805), matched for age, gender and county of residence. Data on glycemic control, periodontitis and diabetes-related complications were obtained for a 10-year period (2010-2020). We used regression models adjusted for age, gender, education and income.
Results:
Periodontitis was more common among T2D (22%) than non-T2D (17%). Differences were larger in younger age groups (adjusted RR at age 30-39 years 1.92; 95%CI 1.81 to 2.03) and exacerbated by poor glycemic control. Periodontitis prevalence was 13% in T1D and 11% in non-T1D; only the subgroup with poor glycemic control was at higher risk for periodontitis. Periodontitis was associated with a higher incidence of retinopathy (T1D HR 1.08, 95%CI 1.02 to 1.14; T2D HR 1.08, 95%CI 1.06 to 1.10) and albuminuria (T1D HR 1.14, 95%CI 1.06 to 1.23; T2D HR 1.09, 95%CI 1.07 to 1.11). Periodontitis was not associated with a higher risk for stroke, cardiovascular disease, or higher mortality.
Conclusion:
The association between T2D and periodontitis was strong and exacerbated by poor glycaemic control. For T1D, the association to periodontitis was limited to subgroups with poor glycaemic control. Periodontitis contributed to an increased risk for retinopathy and albuminuria in T1D and T2D.

PP11: Identification of allergy-like mucosal immune responses mounted against local injection of dietary antigens in IBS patients

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Irritable bowel syndrome (IBS) is a quality-of-life impairing disorder of gut-brain interaction (DGBI) which manifest itself as recurrent abdominal pain and disordered bowel habits in predisposed individuals. Although the causes behind disturbed gut function and gut-brain interaction remain largely unknown, changes in gut microenvironment (e.g., gut microbiota alterations, dysregulated immune response) seem to be involved IBS symptom generation. Furthermore, food is an important trigger of symptoms for majority of IBS patients. In this study, we aim to determine the immune consequences of local injection of food antigens in IBS patients. Therefore, IBS patients with local allergy-like reaction to food antigens will be identified through local injection of dietary antigens into the duodenum by making use of an endoscopic technique called confocal laser endomicroscopy (CLE). Tissue biopsies before and after CLE will be obtained and examined through ELISA, immunohistochemistry, and polymerase chain reaction (PCR) to assess for mast cell and immune cell activation. Fecal samples will also be collected and analyzed for allergy markers (e.g., eosinophil derived neurotoxin, tryptase/histamine, total IgE). We expect more than 50% of the IBS patients with food associated symptoms to have a positive response to at least one of the tested food antigens during the endoscopic food challenge tests, as also shown in earlier studies. Furthermore, we expect to identify clinically relevant immunologic factors that differentiate IBS patients with intestinal allergy-like reactions from IBS patients with no local reaction to food antigens. We hope that this study will lead to better understanding of IBS pathophysiology and more effective and evidence based dietary recommendations for patients with IBS.

PP12: BAP-1 deletion disrupts IFNγ signaling and sensitizies cancer cells to NK cell cytotoxicity

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Medical Biochemistry and Cell Biology , Biomedicine

Natural Killer (NK) cell recognition and killing of malignant cells involves multiple structures expressed by NK cells and target cells. Here, we used genome-wide CRISPR screens to identify genes of importance for K562 cell susceptibility and resistance to NK cell cytotoxicity. A recurrent top hit in our screens was the BRCA1-associated protein 1 (BAP1) gene that was found to protect K562 cells from NK cell cytotoxicity. BAP1 is a tumor suppressor gene that encodes a deubiquitinating enzyme that modulates multiple cellular processes. Germline BAP1 mutations are associated with a tumor predisposition syndrome and somatic loss of function mutations have been frequently associated with various tumors. To determine how BAP1 affected K562 susceptibility to NK cells, we generated BAP1 knock-out cells. In agreement with the screen, these BAP1-KO cells triggered increased NK cell degranulation and were more sensitive towards NK cell killing. Interestingly, in the presence of IFNγ, BAP1-deficient cells failed to upregulate HLA class I expression that otherwise inhibit NK cell cytotoxicity. Further experiments revealed that these cells displayed reduced expression of the IFNγ receptor. In phosphoflow experiments, IFNγ stimulation thus triggered less phosphorylation of STAT1 in deficient cells, leading to reduced up-regulation of multiple IFNγ-regulated proteins.
This study provides further insight into biological consequences of BAP1 mutations in cancer, and suggests a rationale for NK cell-based therapies in malignancies with BAP1 mutations.

PP13: The Swedish vitamin D fortification policy may benefit most pregnant women, but not equally

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Internal Medicine and Clinicial Nutrition , Medicine

Vitamin D fortification of dairy and margarine is mandatory in Sweden due to limited natural food sources of vitamin D. In 2018, the fortification policy was extended, but its impact has yet to be evaluated. Did changes in levels and choice of foods target those most in need? We aimed to investigate whether the potential effect among pregnant women of the extended Swedish fortification policy on vitamin D intake depends on continent of origin. Data collection for the population-representative GraviD cohort were carried out during routine antenatal care in southwest Sweden between 2013 and 2014. In the third trimester of pregnancy participants (N=1761) completed a short food frequency questionnaire with focus on fortified foods to estimate vitamin D intake. Reported vitamin D intake pre-expansion in 2013-2014 was compared to simulated vitamin D intake post-expansion following the 2018 vitamin D fortification policy. Between pre-expansion and post-expansion, medians of vitamin D intakes from fortified foods increased differently depending on continent of origin; from 2.4 to 6.3 µg/day (Northern Europe), 2.0 to 5.5 µg/day (Continental Europe), 1.6 to 5.0 µg/day (Asia), and 2.0 to 5.0 µg/day (Africa). The largest simulated change in vitamin D intake between pre- and post-expansion was among those of European origin, while the smallest change was among those from Asia and Africa. Non-consumers of milk and margarine were more common among those of Asian origin, whereas non-consumers of fermented milk were more common among those of African origin. Although the expanded fortification policy in Sweden had a positive potential impact on vitamin D intake during pregnancy for all consumers of fortified foods, the results imply that the impact may be smallest for those from Asia and Africa. Thus, the current Swedish fortification policy may be most beneficial for individuals of European origin, indicating a challenge for health equity.

PP14: Construction of a gene panel for liquid biopsy-based diagnostics of gynecologic cancer

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Background:
Ovarian carcinoma (OC) is the leading cause of death from gynecologic cancers mainly due to late detection, where most patients are diagnosed at advanced stages (51% in stage III; 29% in stage IV). Despite an overall more favorable prognosis, endometrial carcinoma (EC) is the most common gynecologic cancer, with an increasing incidence and where some subtypes are accompanied by a poor prognosis. Identification of DNA mutations from early-stage OC and EC would allow for earlier intervention. Previous studies have shown that tumor-derived mutations can be detected in samples collected from the gynecologic tract. Herein, we aimed to construct a diagnostic gene panel corresponding to common mutation profiles of OC and EC to detect early-stage malignancy through a non-invasive approach.
Methods:
A gene panel targeting mutations in OC and EC-associated genes was constructed using the NGS-method, Simple multiplexed PCR-based barcoding of DNA for sensitive mutation detection using sequencing (SiMSen-Seq). Hotspots were identified using the Catalogue of Somatic Mutations in Cancer (COSMIC) database and assays were designed for amplification of short DNA fragments. Included assays were validated in multiple steps using qPCR and fragment analysis.
Results:
The two constructed multiplexes, together composed of 125 single assays targeting genomic regions in 34 EC and OC-associated genes, displayed good performance at low DNA input (10 ng). Validation of individual assays showed high specificity and efficient amplification where >80% of assays displayed a sequencing coverage >500 UMI counts at a consensus depth of 3. Patient coverage calculations of COSMIC data suggested comparable coverage as similar published approaches.
Conclusion:
The results suggest that the constructed gene panel has great potential to detect mutations in liquid biopsies, with low tumor DNA levels. Validation of the two multiplexes by fragment analysis and sequencing showed high performance, hence, prospective for the approaching sequencing of liquid biopsies.

PP15: Novel CSF astrocyte-related biomarkers for Alzheimer's disease

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Background:
Astrocytes are highly involved in Alzheimer's disease (AD) pathophysiology. GFAP, an astrocyte-enriched protein, increases in response to amyloid (Aβ) pathology, but it does not fully reflect the astrocytic dynamics in response to the disease. Thus, we aimed to identify novel astrocyte biomarkers in CSF that contribute to the understanding of pathological changes in AD.

Method:
We selected 424 astrocyte-enriched and enhanced genes in Human Protein Atlas and SEA-AD single cell and nuclei transcriptomics datasets. The list of astrocyte-enriched and enhanced genes was contrasted with the available CSF proteomic data (SomaLogic) from ADNI (n=663) and Emory Discovery (n=296) cohorts. Linear regression models evaluated the differential protein expression between designated groups. Then, in the ADNI cohort, the differentially expressed proteins were clustered based on their pseudo-progression in cognitively unimpaired (CU) and impaired (CI) individuals who were also categorized according to their Aβ status (ptau181/Aβ42 ratio cut-off=0.028). Voxelwise models assessed associations between the protein clusters' average quantification and [18F]AV45-PET in a subset of the individuals. Models also included age and sex, and RFT was used for multiple comparisons correction in the imaging analyses.

Results:
Analysis of the ADNI dataset revealed 8 upregulated and 10 downregulated proteins in CI individuals relative to CU, while 31 proteins were elevated and 9 were reduced in Aβ+ individuals. In the Emory dataset, AD individuals exhibited 20 increased and 5 decreased proteins compared to controls. Clustering analysis categorized the proteins into four distinct groups, and their average levels were associated with [18F]AV45-PET imaging. Clusters 1, 2 and 3 presented no associations with [18F]AV45-PET, while cluster 4 (composed of 24 proteins) displayed a widespread association, especially in cortical gray matter.

Conclusion:
This study identified 56 astrocyte-related proteins altered across the AD continuum and highlighted their association with brain Aβ deposition. Further validation will be performed in external cohorts.

PP16: Consequences of environmental noise and noise masking for sleep fragmentation and metabolic function

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Epidemiological studies show associations between chronic noise exposure and disease, but the biological pathways remain poorly understood. Here we aim to investigate the mechanisms that may link sleep disruption by environmental noise with the development of disease, and the efficacy of a non-pharmacological intervention to mitigate these effects.

N=12 young, healthy individuals slept for five consecutive nights in acoustically isolated bedrooms. Following a familiarisation period, nights included the following, in a randomised order: one quiet baseline night; one night with nocturnal traffic noise of different types (road, rail and air) and noise levels (45-65 dB LAS,max); one night with continuous 45 dB broadband pink noise; and one night with both traffic noise and pink noise. Sleep was measured with polysomnography and assessed using the Odds Ratio Product (ORP), a novel measure of continuous sleep depth and stability. Perceived sleep quality and recouperation were measured with morning questionnaires. Blood samples were collected each morning for metabolomics analysis.

Discrete traffic noise events induced elevations of ORP (z-score +0.19; $p<.001$ relative to baseline, averaged over all traffic types and levels), indicating acute sleep fragmentation, even while total sleep time and overall sleep macrostructure were preserved. The traffic noise night was further associated with significant elevations in concentrations of leucine, lactic acid, and acetone relative to quiet control. Sleep and metabolic disturbances by traffic noise were attenuated when pink noise was played continuously throughout the night (averaged ORP z-score +0.06; $p=.11$ re: baseline).

Noise-induced sleep fragmentation induced changes in metabolic processes that in the long-term may be precursors for cardiometabolic disorders. Masking of traffic noise by continuous, neutral sound can mitigate acute physiological sleep disturbance and downstream metabolic effects. These results need to be interpreted cautiously however, given the limited sample size and subject homogeneity.

PP17: The microglial receptor AXL is involved in the antiviral defense against HSV-1 infection.

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Background:
Herpes simplex virus type 1 (HSV1) is a very common virus and known for causing cold sores. In rare cases, HSV1 may enter the brain to cause a severe herpes simplex encephalitis (HSE). As the innate immune cells of the brain, microglia protect against viral infections through sensing the virus and release of the antiviral type I interferons (IFN-Is). IFN-Is induce a wide range of interferon-stimulated genes (ISGs) which act in concert to exert antiviral effects. One such ISG is the microglial receptor AXL which a phagocytic receptor known to play important roles in innate immune processes. The role of AXL in the antiviral defense in response to HSV-1 infection is, however, unknown.

Aims:
Immunological control of viral infection in the brain is essential for immediate protection, but also for long-term maintenance of brain integrity. The aim of this study was to investigate in detail the role of the microglial receptor AXL during herpesvirus infection.

Methods:
Here, we used human induced pluripotent stem cell (iPSC)-derived microglia and neurons. CRISPR-Cas9 technology was employed to create AXL knockout (KO) iPSCs.

Results:
AXL KO microglia differentiated normally, morphology and marker expression were indistinguishable from controls. AXL is strongly induced in control microglia upon stimulation with IFNβ alone and by HSV-1 infection. Since HSV-1 primarily replicates in neurons, we investigated viral replication in neuron-microglia co-cultures. We found significantly increased viral replication when neurons were co-cultured with AXL KO microglia suggesting impaired antiviral responses. In AXL KO microglia, we observed decreased viral uptake, decreased viral sensing, and consequently impaired induction of IFNb and key ISGs.

Conclusion:
Our findings suggest that AXL is an important mediator of the microglial response to HSV-1 infection, contributing to viral uptake, sensing, and subsequent activation of antiviral pathways.

PP18: Nicotine-induced neuroplasticity in prelimbic cortex may drive the increased risk of alcohol misuse

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Pharmacology, Neuroscience and Physiology

Nicotine use is a major risk factor for alcohol misuse, independent of the nicotine product used. While genetical, environmental and social aspects may partially explain the connection, neurobiological underpinnings may also drive the association. In fact, experimental studies in rodent demonstrate that the rewarding properties of alcohol are regulated by nicotinic acetylcholine receptors (nAChRs), and repeated exposure to nicotine is associated with an increase in alcohol consumption, implicating a causal relationship between nicotine exposure and alcohol use. Although the neurobiological mechanisms underlying alcohol use disorder (AUD) have not been fully established, we have previously demonstrated that an AUD-like behavioral phenotype is associated with specific neurophysiological signatures in the prelimbic cortex (PL) of Wistar rats. This brain area plays a key role in decision-making and drug-seeking behaviour, making it a valuable target for further investigation. Thus, the aim of this study was to define if nicotine exposure could promote alcohol use by producing neuroplasticity in the PL. To this end, we combined voluntary alcohol consumption, nicotine injections, and ex-vivo electrophysiology in the PL to investigate the mechanisms behind nicotine-induced escalation of alcohol intake. Additionally, we examined the mechanisms underlying the acute effects by ethanol on neurotransmission in the PL. Our data demonstrate that nicotine selectively enhances alcohol intake in rats that are not high consumers at baseline, and that hightened sensitivity to nAChR signalling might underlie the separation between the two groups. Furthermore, alcohol-naïve rats exposed to nicotine demonstrated an enhanced neurophysiological responsiveness to alcohol, which appeared to be driven by an increased GABAergic tone. In conclusion, our data suggest that nicotine enhances the responsiveness to alcohol through mechanisms that involves neuroplasticity in GABAergic neurotransmission, which in turn may further impair decision making and increase the risk of alcohol misuse.

PP19: Preanalytical errors in liquid biopsies.

Christoffer D. Petersson, Åsa Torinsson Nalaui

Clinical Genetics, Biomedicine

Introduction:
This poster presents the results that builds on the analysis from the PREAN-1 study to investigate the effects of time and temperature on the expression of genes in plasma preparation tubes. These findings do compare with previous results and have been investigated with advanced regression methods. The samples have also been subject to RNA-seq. In this poster the aim is to further describe the changes to gene expression with more extensive gene expression

Method:
Healthy volunteers were recruited to the PREAN-1 study and samples where incubated at 4C, 25C and 37C. these samples were stored during 10min (control) 1,5 hours, 2,5hours and 3,5hours
The samples where sequenced by Sahlgrenska Clinical Genetics /Gothenburg University Core facility. Then the samples were analysed by different statistical methods including principal component regression to further illuminate and confirm the changes in gene expression. The RNA-seq data was analysed with EnrichR and HMDB.

Results:
It can be concluded that the genes that are changed by temperature are largely consistent with ETS1, OAS2 and RPL6 being by far being the most consistent genes that have changed expression because of temperature. This agreed with Principal component regression having OAS2, IPO8 and ETS1 as the genes that is explain the 43,10% of the variation of the data. The RNA-seq data points to the GIMAP family as the main contributor to the metabolites that are changed because of changes in temperature but also rRNA processing as the main biological process being involved in stress response to temperature.

Conclusion:
This study validated previous results by RNA sequencing and more robust statistical analysis of the data. Showing that there is a connection between ribosomal processing and stress responses to temperature but also a change in N1-acetylspermine and GIMAP family and cold shock.

PP20: A clinical guide to a Nordic adaptation of the Crohn's Disease Exclusion Diet

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Abstract

In this clinical guide on how to adapt the Crohn's' Disease Exclusion Diet (CDED) to a Nordic setting, we argue that the translation of CDED diet into practical recommendations should be tailored to the local food culture. Such modification may increase the dietary adherence which is a common challenge in advanced nutritional therapy. The adaptation aims to guide the dietitian to individualise the Nordic CDED to the patient ´s age, lifestyle, and preferences, which in turn could improve adherence and quality of life. This can also help to preserve cultural diversity and, since environmental preservation and sustainability is a rising public health challenge, environmental sustainability will also be considered. To successfully achieve the dietary changes that CDED demands, population-specific barriers should be identified, and strategies sought to overcome them to support adequate nutritional intake, including key food availability, regulation of food additives used in the food industry, and food processing. Such an approach is likely to promote long-term adherence to CDED, thus having an impact on this patient group.

The objective of this paper is to present an adaptation of the CDED to a Nordic diet, while preserving its basic health-promoting principles and nutritional composition. The adaptation is presented in practical terms, including a description of the theoretical basis for including or excluding specific foods. We present substitutions to the original whole food list in line with the Nordic diet, enteral nutrition formulas with demonstrated similar effect, and how to support the patient's nutritional intake according to the Nordic Nutritional Recommendations 2023.

PP21: Light-based footprinting of a complete eukaryotic genome

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Identification of protein-bound sites is key to understanding genome function and regulation, but protein-DNA interactions are difficult to study in living, unperturbed cells. UV footprinting has been used to study such interactions in vivo by detecting changes in DNA photoproduct formation in the presence of bound proteins, but so far only at a limited scale. Here we describe whole-genome deamination sequencing (Deam-seq), wherein pyrimidine dimers induced by high-dose UV irradiation manifest as easily detectable C>T mutations, enabling generation of a quantitative photofootprint of the yeast Saccharomyces Cerevisiae at ultra-deep (>7,000×) coverage. By comparing cellular and naked DNA, we find that this approach can resolve protein occupancy at high resolution, with differential signals commonly overlapping with DNase I footprints, ChIP peaks and predicted regulatory sites. Our results showcase Deam-seq as a complement to current protein-DNA mapping methods and provide proof of concept for the study of protein-DNA interaction using light and sequencing at genome scale.

PP22: Finding new mechanisms of schizophrenia using a novel postnatal stem-cell based neuronal model

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Schizophrenia (SCZ) is a complex, heterogeneous syndrome which is thought to originate from neurodevelopmental disruptions caused by genetic and environmental factors. It imposes a profound burden for both individual families and society. The onset of SCZ typically occurs during adolescence or early adulthood suggesting a critical time window in postnatal developmental stage for pathogenesis as well as an opportunity for early diagnosis and intervention. However, postnatal neurodevelopment remains understudied in both physiological and pathological conditions due to the major limitations in neuronal maturation of current human pluripotent stem cell (hPSC)-derived models. Thus, the objective of this project is to establish a neuron/glia co-culture model combined with optogenetic stimulation in order to study the function of SCZ-risk genes in postnatal neurodevelopment. The overall goal is to elucidate the molecular mechanisms of SCZ pathogenesis and shed the light on new therapy development.

PP23: Synaptic plasticity, synapse loss, and proteinopathy in mild neurocognitive disorder: Study design

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Abstract: Alzheimer's disease (AD) is a significant public health challenge, yet the precise etiology of AD-related dementia, especially the hypothesized sequence of events, remains debated. There is consensus, however, that cognitive symptoms in AD are likely a consequence of synaptic plasticity loss and reduction of synaptic density. This study proposes a comprehensive investigation into the physiology of early cognitive impairment, by integrating measurements of synaptic density in the living human brain, assessments of learning-related synaptic plasticity, and evaluations of proteinopathy in older adults with mild neurocognitive disorder (mild NCD). We will employ repeated measures [18F]SynVest-1 positron emission tomography (PET) neuroimaging to estimate synaptic density pre- and post- learning intervention, in combination with magnetic resonance imaging (MRI), clinical and neuropsychological assessments, evaluation of cognitive performance, and blood biomarkers for A and tau proteinopathy. The main purpose of this study is to clarify the physiology of the early phases of cognitive impairment in older age and pave the way for future larger-scale research honing in on clinical applications, such as early diagnosis of AD and related treatment. The novel assessment of learning-related synaptic plasticity is a key feature of the study that will be of groundbreaking importance not only for the understanding of the early etiology of major NCD/dementia, but also for basic cognitive neuroscience of learning and memory. We aim to establish learning-related plasticity of synaptic density in humans, which is likely to be a core neural correlate of learning and memory in both healthy aging and AD, and we may study whether learning-related changes in synaptic density are related to Ab and tau pathology.

PP24: Chemical Biology and Fragment based screens using solution NMR

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Chemical biology comprises interdisciplinary efforts to understand and characterize interactions between biological targets and natural or synthetically produced molecules and to develop these findings in a biological context. NMR spectroscopy is well suited to studies of transient or strong interactions between specific protein targets and low molecular weight molecules such as natural products or lipids, or synthetically produced fragments, drug candidates or approved drugs. Fragment based drug discovery approaches are used for the design and development of novel lead compounds and NMR spectroscopy has emerged as a powerful method to study non-covalent protein-ligand complexes using ligand-observed techniques. Complementary, high resolution NMR spectroscopy studies of protein – ligand complexes can be made with protein target observed methodologies, for both low- and high-affinity complexes.

Fragment based screens (FBS) using NMR spectroscopy enables joint testing of a large number of fragments with low molecular weight (typically < 500 Da) against a target protein molecule or molecular complex. The Swedish NMR Centre is equipped with high field spectrometers (600-800 MHz) with cryogenically cooled probes optimized for either 1H or 19F-detection and SampleJet sample changers as well as liquid handling systems for sample preparations for FBS campaigns. With this setup, libraries of 1.000 fragments can be screened against a target protein molecule within days.

PP25: BaTwa populations from Zambia retain ancestry of past hunter-gatherer groups

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Core Facilities (Bdc), Core Facilities

Sub-equatorial Africa is today inhabited predominantly by Bantu-speaking groups of Western African descent. Their ancestors brought agriculture to the region some thousand years ago; in particular, agriculture was initiated in the Luangwa valley in eastern Zambia ~2000 years ago. Before the arrival of Bantu-speaking agriculturalists, the area was inhabited by hunter-gatherers, who in many cases were subsequently replaced, displaced or assimilated. In Zambia, we know little about the genetic affinities of these hunter-gatherers. We examined the ancestry of two isolated communities in Zambia, known as BaTwa and possible descendants of recent hunter-gatherers. We genotyped over two million genome-wide SNPs from two BaTwa populations (total of 80 individuals) and from three comparative farming populations to: (i) determine if the BaTwa carry genetic links to past hunter-gatherer-groups, and (ii) characterise the genetic affinities of past Zambian hunter-gatherer-groups. We combined the newly generated data to genotypes from modern and ancient comparative samples and described the genetic diversity of the Zambian populations using various population genetics methods. We then investigated the admixture history of the Zambian populations and contrasted the inferred admixture dates with evidence from the archaeological literature. We found that the BaTwa populations do harbour a hunter-gatherer-like genetic ancestry and Western African ancestry. The hunter-gatherer component is a unique local signature, intermediate between current-day Khoe-San ancestry from southern Africa and central African rainforest hunter-gatherer ancestry. This work contributes to a wider understanding of the history of south-central Africa.

PP26: Coronary atherosclerosis and oral status – a case control study

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Background and aim:
While many studies have explored links between oral diseases and coronary events, i.e. Myocardial infarction (MI), fewer have investigated how oral status relates to MI risk. Considering that coronary artery atherosclerosis (CA) is a known predictor of future coronary events, this study aimed to examine the association between CA and oral status.

Methods:
From SCAPIS, 400 participants assessed for coronary atherosclerosis (CA) using coronary computed tomography angiography, were selected for this study. The sample comprised 200 individuals diagnosed with CA (defined as a Segment Involvement Score (SIS) ≥ 3) and 200 without CA (SIS = 0). Analyses excluded those with current tobacco use, diabetes, or a history of myocardial infarction. Oral status was assessed using clinical and radiographic examinations, producing an oral score (OS) based on missing teeth, caries and dental restorations (DFT), root fillings, apical lesions, and marginal bone loss.

Results:
Those with CA exhibited higher OS (adjusted mean difference: 2.9; 95%CI 1.4/4.5), driven by more missing teeth, higher DFT, and more marginal bone loss, with differences most pronounced in females (adjusted mean difference: 5.3; 95%CI 2.2/8.4). A history of smoking correlated negatively with OS (adjusted mean difference: 2.2; 95%CI 1.0/3.4).

Conclusion:
The present data suggest an association between CA and oral status.

PP27: Causal association between body mass index and risk of rheumatic joint disorders: A systematic review and meta-analysis of Mendelian randomization studies

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Background:
Increasing evidence suggests that body mass index (BMI) may play a causal role in the development of rheumatic joint disorders [1-3], yet the extent and specificity of this association remain unclear. Mendelian randomization (MR) offers a powerful approach to infer causality by using genetic variants as proxies for an exposure (BMI in this case), reducing the impact of confounding and reverse causation common in observational studies [4].

Aim:
This study was aimed to systematically review and summarise the evidence from MR studies to appraise the causal role of BMI in a wide range of rheumatic joint disorders.

Methods:
A comprehensive literature search was conducted across PubMed, Embase, Web of Science, and MEDLINE databases up to the 17th of June 2024. Identifying MR studies that explored BMI as an exposure for a range of rheumatic joint disorders: osteoarthritis (hand, hip, knee), rheumatoid arthritis, gout, spondylitis arthritis, and psoriatic arthritis. Eligible studies were screened, and data on study design, population characteristics, genetic instruments, and outcomes were extracted. Pooled causal effect estimates were calculated for each disorder, using random-effects meta-analysis to account for study heterogeneity. All analyses were conducted using the 'metafor' package in R v4.4.1.

Results:
Of 1662 total studies searched in online databases, 24 were included in the systematic review, while the meta-analysis included eight (for 12 outcomes) MR studies. Higher genetically predicted BMI was significantly associated with an increased risk of rheumatic joint disorders [inverse-variance weighted OR (95% CI) = 1.45 (1.31 to 1.61) $p < 0.0001$, $phet < 0.001$]. Consistent results were obtained when the data on sensitivity analyses were summarized in meta-analysis [weighted-median OR (95% CI) = 1.46 (1.36 to 1.58), $p < 0.0001$; MR-Egger OR (95% CI) = 1.25 (1.07 to 1.45), $p = 0.004$], confirming the robustness of the findings in primary analysis.

Conclusions:
This systematic review and meta-analysis provided robust evidence supporting a causal link between elevated BMI and an increased risk of certain rheumatic joint disorders. These findings underscore the importance of BMI management in preventing and potentially alleviating the burden of these disorders. Future MR studies with larger sample sizes and diverse populations are warranted to further clarify the role of BMI in these and other less studied joint disorders.

References:
[1] T. Karlsson, F. Hadizadeh, M. Rask□Andersen, Å. Johansson, and W. E. Ek, "Body mass index and the risk of rheumatic disease: linear and nonlinear mendelian randomization analyses," Arthritis & Rheumatology, vol. 75, no. 11, pp. 2027-2035, Nov 2023, doi: 10.1002/art.42613.
[2] X. Li et al., "The causal effect of obesity on the risk of 15 autoimmune diseases: A Mendelian randomization study," Obesity Facts, vol. 16, no. 6, pp. 598-605, 2023, doi: 10.1159/000534468.
[3] C. He et al., "Novel insights into the consequences of obesity: a phenotype-wide Mendelian randomization study," European Journal of Human Genetics, vol. 30, no. 5, pp. 540-546, 2022.

[4] P. Sekula, M. Fabiola Del Greco, C. Pattaro, and A. Köttgen, “Mendelian randomization as an approach to assess causality using observational data,” Journal of the American Society of Nephrology, vol. 27, no. 11, pp. 3253-3265, 2016.

PP28: Physical training and senolytic interventions reduce cellular senescence in skeletal muscle

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Cellular senescence (CS) is a hallmark of aging characterized by irreversible cell cycle arrest, functional alterations, and the secretion of pro-inflammatory factors known as the senescence-associated secretory phenotype (SASP). Accumulation of senescent cells contributes to tissue dysfunction, chronic inflammation, and impaired regeneration. In skeletal muscle (SkM), CS is linked to sarcopenia—the age-related decline in muscle mass and strength—posing significant health challenges for the aging population.

Physical exercise is a well-documented strategy for improving metabolic health and delaying age-related diseases. Emerging evidence suggests that exercise may also mitigate senescence, as seen in reductions of senescence biomarkers in the colon and circulation. However, its effects on cellular senescence within skeletal muscle remain poorly understood.

To address this, we analyzed muscle biopsies from the vastus lateralis of 55 individuals (lean and obese) to examine the relationship between obesity and SkM senescence. Obese individuals exhibited significantly elevated senescence markers, reduced expression of GLUT4 and lower levels of the satellite cell marker PAX7. Physical intervention improved these parameters, with lean individuals showing benefits after one month and obese individuals after six months of exercise. These improvements included reductions in cellular senescence markers, enhanced metabolic profiles, and activation of satellite cell responses.

Complementary in vitro studies revealed that cellular senescence impairs satellite cell function, downregulating regulatory genes and reducing insulin signaling activity.

In conclusion, exercise is a potent modulator of skeletal muscle health, effectively reducing cellular senescence and restoring satellite cell functionality, thereby supporting healthy aging and metabolic resilience.

PP29: Metabolomics and lipidomics in juvenile localized scleroderma

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Background:
Juvenile localized scleroderma (jLS) is a rare disease in children characterized by inflammation and fibrosis in the skin. Omics technologies have been used to identify biomarkers in different diseases. Among the different omics technologies, metabolomics and lipidomics provide snapshots of the metabolic network.

Aim:
We aim to identify biomarkers and treatment targets for jLS using metabolomics and lipidomics.

Methods:
and materials
Children with jLS and age-matched controls were recruited. Plasma samples from 9 controls and 12 patients with jLS (before treatment initiation and 17 months after treatment) were sent to Swedish Metabolomics Center, where liquid- and gas-chromatography – mass spectrometry was performed. Peak intensities were recorded, and data analysis was performed using Metaboanalyst5.0. Mann-Whitney test was used to compare healthy control and baseline patient groups, and Wilcoxon test was used to compare differences between baseline and treated patients.

Results:
In total, 250 metabolites and 194 lipids were annotated. Patients at baseline had significantly lower peak intensities of lenticin, 3-hydroxybutyrylcarnitine, 1-dodecanoyllysophosphatidylcholine, phosphatidylcholine 38:6 and 40:9, and phosphatidylserine 38:1 as well as significantly higher peak intensities of L-tyrosine, phenylpyruvicacid, (3-hydroxyphenyl)hydracrylate, and cortisol compared to controls.
After treatment, peak intensities of adenosinemonophosphate, hypoxanthine, 3-phosphoglyceric acid, lysophosphatidylcholine (18:2), Cholesteryloctanoate (8:0), and 2-Hydroxylauroylcarnitine (12:0) were decreased, whereas peak intensities of L-octanoylcarnitine and eleven molecular species of triacylglycerols were increased compared to baseline patients.

Conclusion:
Children with jLS show a distinct metabolic profile compared to healthy children, especially in tyrosine-related pathways. Compared to baseline levels, the metabolism of several amino acids was altered after treatment, and the energy storage function might be modified as eleven molecular species of triacylglycerols were found decreased.

PP30: Cytokine Stimulation of Airway Mucins

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Invärtesmedicin Och Klinisk Nutrition , Medicin

Background:
Cytokines activate airway epithelial cells in T2-high asthma and are associated with accumulation of mucin-producing cells that play a major role in airway mucus plugging. MUC5AC and MUC5B are the predominant gel-forming mucins in human airways and are dysregulated in asthma. Although, the mechanisms modifying their expression are unclear. The aim of this study was to identify transcriptional programs in lung epithelial cells that contribute to aberrant mucin responses in T2-high asthma.
Methods:
Integrated analysis was performed using five different datasets: 1) genes that correlate with MUC5AC and/or MUC5B expression in airway epithelial cells, and 2) gene clusters defined by pseudotime trajectory analysis of airway mucus secretory cell development by scRNA-seq. 3 and 4) gene expression in human bronchial epithelial cells (HBECs) cultured at air-liquid-interface with inflammatory cytokines (IL-13, IL-17) by bulk RNA-seq and scRNA-seq, and 5) gene expression in airway brushings from T2-high asthmatics and healthy controls assessed by gene array.
Results:
More than half of the genes expressed during mucus secretory cell development in human airways were regulated by IL-13 and/or IL-17 in HBECs cultures. IL-17 stimulation upregulated expression of both mucins, whereas IL-13 induced MUC5AC and T2-high signature genes, and repressed MUC5B. Transcription factors correlating with MUC5B single-expressing cells were reduced in T2-high asthma epithelium, and as expected, transcriptional programs promoting MUC5AC (single or co-expressing cells) were increased. IL-13 stimulated HBECs demonstrated a similar shift in transcriptional regulators associated with MUC5AC versus MUC5B expression. Interestingly, transcription factors promoting MUC5B were distributed throughout the mucus secretory cell lineage, whereas MUC5AC-associated factors appeared late during terminal mucus secretory cell development.
Conclusions:
IL-13 not only upregulates MUC5AC but ensures MUC5AC predominance by effectively repressing MUC5B transcriptional programs. Modulation of gene networks affecting selective mucin expression has potential to restrain pathological mucus responses in asthma without compromising basal mucus defense.

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