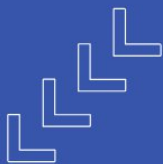


May 18-19, 2026



2026 PHD CONFERENCE

THESIS TO TOMORROW: SKILLS
BEYOND THE LAB

by DSA



Location
DJURÖNÄSET

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Naturvetarna

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Day 1

Programme

08:00 Departure from Cityterminalen 

09:00-09:45 Registration and Breakfast

Morning Session

09:45-10:00 **Welcome and Introduction**

10:00-10:20 **Ana Oliveira**
KI Career Service

10:20-11:00 **Maria Mecenero**
European Commission - European Competence Framework for Researchers (ResearchComp)
with introductory remarks and moderation by
Y. Vladimir Pabón-Martínez, Karolinska Institutet

11:00-11:30 Mingling and Bingo

11:30-12:00 **Presentation by Naturvetarna**

12:00-12:45 **Student presentations**

12:45-14:00 Lunch 

Afternoon Session

14:00-15:00 **Student presentations**

15:00-15:30 Bingo break and fika

15:30-16:00 **Frustration workshop**

16:00-16:30 Check-In  and hanging of posters

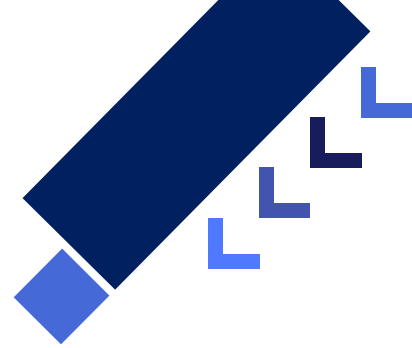
Evening Session

16:30-18:30 **Poster session**

18:30-20:30 Dinner 

Day 2

Programme



07:00-09:30

Breakfast and Check out 

Morning Session

09:30-10:00

Hela Galvis Bonilla

Switch to Sweden

10:00-10:30

Andreas Namslauer

Business Development Manager at Stockholm Science City

10:30-10:45

Presentation by SULF

10:45-11:00

Presentation by TdB Labs

11:00-11:30

Break

11:30-12:15

Mindfulness Session

with **Linda Kvastad**

12:15-12:45

Katarina Sternudd

KI Central Communications Office

12:45-14:00

Lunch 

Afternoon Session

14:00-14:30

Emannouil Tsakoumis

VR

14:30-15:00

Leo Hanke

KI

15:00-15:30

Bingo break and fika

15:30-16:30

Conclusions & Poster Prizes

17:00

Departures from Djurönäset 

Student oral presentation schedule

May 18th

25 presentations · 3 minutes each

Session 1: 12:00 – 12:45

1	12:00 – 12:03	Huy Dang	<i>Peripheral Lysosome Levels Dictate mTORC1 Inactivation even when Catabolically Impaired</i>
2	12:04 – 12:07	Taalke Maria Sitter	<i>Pharmacotherapy in Forensic Psychiatric Care in Sweden: Prevalence, Effectiveness, and Future Considerations</i>
3	12:08 – 12:11	Andrea Camilloni	<i>Development and Validation of a Multimodal AI Model to predict Biochemical Recurrence of Prostate Cancer after Primary Treatment</i>
4	12:12 – 12:15	Spyridon Pantelios	<i>From Metabolism to Mechanics: Targeting Filament-Forming Metabolic Enzymes in Cancer</i>
5	12:16 – 12:19	Emmy Erskine	<i>Profiling of Microglia in a Stem Cell and Murine Model of Anorexia Nervosa</i>
6	12:20 – 12:23	Daniela Skalt	<i>Is Prostate Cancer Screening Cost-Effective? A Health Economic Evaluation to Support Decision-Making in Sweden</i>
7	12:24 – 12:27	Sefanit Rezene	<i>ISG15-Dependent Immunometabolic Regulation during RNA Virus Infection and Viral Interference of Host Ubiquitylation and ISGylation Events</i>
8	12:28 – 12:31	Buse Esra Mercan	<i>Mapping Neuroinflammation in Corticobasal Degeneration Brains Using the TSPO PET Tracer ³H-ER176</i>
9	12:32 – 12:35	Kovi Rishya Shrung Govindarajan	<i>Pauci Cellular Proteomics of FACS-Sorted Cell Populations - Lymph Node Atlas</i>
10	12:36	Zhengan Lu	<i>Polygenic Overlap and Shared Genomic Loci between</i>

	– 12:39		<i>Anorexia Nervosa and Cardiometabolic Traits Suggest Shared Biological Mechanisms</i>
11	12:40 – 12:43	Emilia Lahtinen	<i>Rethinking BV Treatment: Community and Strain-Level Vaginal Microbiome Shifts After Treatment with pHyph</i>

Session 2: 14:00 – 15:00

12	14:00 – 14:03	Theodore Tianyi Miao	<i>Risk of Self-Harm Following Antidepressant Initiation Among Older Adults in Sweden: A Self-Controlled Case Series Study</i>
13	14:04 – 14:07	Lucille Margerie	<i>Identifying the Drivers of Mast Cell Neoplasia Using a Genome-Wide CRISPR Knockout Screen</i>
14	14:08 – 14:11	Julie Roux	<i>Effects of Intestinal Parasites on Immune Response to Pre-Existing Memory to Influenza A Virus</i>
15	14:12 – 14:15	Riccardo Lizzani	<i>An In Vivo Platform to Study the Crosstalk between the Exocrine and Endocrine Pancreas in Health and Disease</i>
16	14:16 – 14:19	Marlene Schüle	<i>Novel Approaches to Study Rheumatoid Arthritis-Associated Anti-Citrulline T Cell Reactivity</i>
17	14:20 – 14:23	Herbert Middleton	<i>Geometric Optimization of Coplanar Organic Electrochemical Transistors for High-Sensitivity IL-17 Detection</i>
18	14:24 – 14:27	Oromia Godanna Sero	<i>Reward, Social Learning, and Habit in Posting Choice on Social Media</i>
19	14:28 – 14:31	Liv Hog	<i>Associations between GLP-1RA Use and Lifetime Eating Disorders</i>

20	14:32 – 14:35	David Ziliang Hu	<i>How Malaria and Duffy-Null Spread in the World</i>
21	14:36 – 14:39	Cenk Gurdap	<i>Physics of Cells as New Biomarkers for Diseases</i>
22	14:40 – 14:43	Hala Habash	<i>Drugging the Undruggable Target: Cytarabine and Gemcitabine Kill Ewing Sarcoma Cells through SAMHD1 Inhibition and Ewing Sarcoma Fusion Protein Degradation</i>
23	14:44 – 14:47	Emma Zapel	<i>Therapist Behaviour in Psilocybin-Assisted Treatment for Depression: A Process-Oriented Analysis from the PSIPET Trial</i>
24	14:48 – 14:51	Annelien Hooijsma	<i>Deep Phenotyping of Joint Biopsies Implicates T and B Cell Crosstalk Already at Diagnosis of Rheumatoid Arthritis</i>
25	14:52 – 14:55	Stefan Bencina	<i>Human Placental Stem Cell–Mediated Immunomodulation Promotes Neuroprotection in the SOD1 G93A ALS Mouse Model</i>

Poster session order of posters

May 18th 16:30 – 18:30

Full abstracts in the next section

#	Full Name	Title
1	Aikaterini Papadimitropoulou	Establishment Of A Serum-Free Primary Cell-Based 3D Skeletal Muscle Model For Atrophy Research
2	Alessandra Muni	Uncovering The Role Of SAMHD1 For Immunotherapy Response In Melanoma
3	Ana Varas Sánchez	tTEscanR: An Advanced R-Based Package To Quantify And Visualize Translation Efficiency From Sequencing Data
4	Annelien Hooijsma	Deep Phenotyping Of Joint Biopsies Implicates T And B Cell Crosstalk Already At Diagnosis Of Rheumatoid Arthritis
5	Buse Esra Mercan	Mapping Neuroinflammation In Corticobasal Degeneration Brains Using The TSPO PET Tracer ³ H-ER176
6	Carlos Gallardo Dodd	Accelerating Large-Scale Analysis Of Omics Datasets With Osync
7	Cenk Gurdap	Physics Of Cells As New Biomarkers For Diseases
8	David Ziliang Hu	How Malaria And Duffy-Null Spread In The World
9	Delia Daniele	Harnessing Mesoporous Silica And Engineered Pore-Forming Toxins To Enhance Intracellular Genome-Editing Delivery
10	Emilia Lahtinen	Rethinking BV Treatment: Community And Strain-Level Vaginal Microbiome Shifts After Treatment With pHypH
11	Emmanouella Michaela Xanthopoulou	High-Fat Diet Exacerbates Ischemic Muscle Impairment In The FAL Murine Model Of Peripheral Artery Disease
12	Emmy Erskine	Profiling Of Microglia In A Stem Cell And Murine Model Of Anorexia Nervosa
13	Eva Meglic	Risk Of HPV-Related Cancers In Immunosuppressed Populations
14	Hager Saleh	Leveraging Pharmacovigilance Data To Detect Antibiotic Resistance And Inappropriate Use In LMICs
15	Heba Ali	Estrogen Receptor Mediated Neuroprotection In Models Of Alzheimers Disease
16	Jakob Sax	Bridging Bibliometrics And Mechanisms: A Framework For The Contextual Scoring And Biological Stratification Of Scalable MeSH Co-Occurrence

#	Full Name	Title
		Networks
17	Jia Qi Lee	Distinct Antiviral T Cell Immunity Patterns Against Common Viruses and its Correlation with SARS-CoV-2 Seroconversion
18	Joseph Baxendale	Serotonin And Serotonergic Inputs Modulate Cholinergic Interneurons In The Striatum On Different Timescales
19	Julia Zerebinski	Widespread Variants Of The Highly Polymorphic Plasmodium Falciparum Vaccine Candidate Antigen MSP2 Across Sub-Saharan Africa
20	Kovi Rishya Shrung Govindarajan	Pauci Cellular Proteomics Of FACS-Sorted Cell Populations - Lymph Node Atlas
21	Leon Heffinger	Identification Of An IDO-1 Inhibitor Reducing Growth Of Pancreatic Ductal Adenocarcinoma Cells, But With Little Effect On Surrounding Stromal Cells
22	Luana Xuan Liu	Automated Quantification Of Tumour Length In Digitised Prostate Core Needle Biopsies By Rule-Based Algorithm
23	Luca Verschure	The Annoying Orange: Dissociating The Roles Of Human Likeness And Eye Gaze Dynamics For Awareness Attribution
24	Magnus Tronstad	Cell Differentiation As A Superposition Of Dynamical Modes
25	María De Los Reyes Becerra Pérez	Metabolic Enzymes and their Epigenetic Roles in Acute Myeloid Leukaemia
26	Maria Tsiokou	Biophysical Remodeling Of Aging
27	Mariam Shahata	Impact Of Quorum Sensing On Human Skin Response To Staphylococcus Aureus
28	Marlene Schüle	Novel Approaches To Study Rheumatoid Arthritis-Associated Anti-Citrulline T Cell Reactivity
29	Navin Vincent	Validation Of Diagnostic Artificial Intelligence Models For Prostate Pathology In A Middle Eastern Cohort
30	Oromia Godanna Sero	Reward, Social Learning, And Habit In Posting Choice On Social Media
31	Rana Melisa Seren	Human Lung Tissue Exhibits Stimulus-Specific, Time-Dependent Activation Of Oxylinin Pathways
32	Riccardo Lizzani	An In Vivo Platform To Study The Crosstalk Between The Exocrine And Endocrine Pancreas In Health And Disease
33	Riccardo Mosca	Deciphering The Impact Of CAPRIN1 On Post-Transcriptional Regulation In

#	Full Name	Title
		Stress Response
34	Sefanit Rezene	ISG15-Dependent Immunometabolic Regulation During RNA Virus Infection And Viral Interference Of Host Ubiquitylation And ISGylation Events
35	Shen Tian	Semantic Knowledge Guides Innovation And Drives Cultural Evolution
36	Sofja Poznakovs	L-Tryptophan Suppresses HIV-1 Latency Reversal Through Metabolic Reprogramming In Pre-Monocytic Cells
37	Stan De Haan	Differentiated Myeloid Progenitors As A Model For Chimeric Antigen Receptor Neutrophil Function
38	Stefan Bencina	Human Placental Stem Cell-Mediated Immunomodulation Promotes Neuroprotection In The SOD1 G93A ALS Mouse Model
39	Thanh Hien Bui	Pain Is Associated With Disease Activity In Idiopathic Inflammatory Myopathies In A Longitudinal 10-Year Follow-Up Single-Centre Study
40	Tim Schäfer	Neuronal Cell Fate And Maturation Under Antidepressant Exposure: A Multi-Modal Single-Cell Investigation
41	Vera Danklmaier	Studies Of Adaptive NK Cells In Solid Tumors
42	Zhengan Lu	Polygenic Overlap And Shared Genomic Loci Between Anorexia Nervosa And Cardiometabolic Traits Suggest Shared Biological Mechanisms

Oral presentation abstracts

Development and Validation of a Multimodal AI Model to predict Biochemical Recurrence of Prostate Cancer after Primary Treatment

Name: Andrea Camilloni

Department: MEB

Abstract

Introduction

Biochemical recurrence (BCR) after primary treatment is a surrogate marker for aggressive prostate cancer and adverse outcomes, yet current prognostic tools remain imprecise. We developed and validated a multimodal AI model to predict BCR risk following radical prostatectomy (RP) and radiotherapy (RT).

Materials and Methods

This study utilized one biopsy cohort and three RP specimen cohorts. The biopsy cohort comprised patients from the STHLM3 trial undergoing either RP (development; n=676, BCR=183) or RT (validation; n=353, BCR=42). The external validation RP cohorts included LEOPARD (n=508, BCR=87), CHIMERA (n=95, BCR=27), and TCGA-PRAD (n=379, BCR=48). We employed foundation models and attention-based multiple instance learning to extract patient-level histopathological representations, integrated with clinical features (age, PSA, ISUP grade). Model performance was evaluated using Harrell's C-index and cumulative incidence risk stratification, with comparison against established clinical risk tools.

Results

The multimodal AI model achieved C-indices of 0.80 (95% CI: 0.65–0.93) in the STHLM3 RT validation set, 0.60 (0.53–0.67) in LEOPARD, 0.68 (0.54–0.80) in CHIMERA, and 0.69 (0.61–0.76) in TCGA-PRAD. The model stratified patients into clinically meaningful risk groups and provided prognostic value beyond EAU risk groups (RT cohort) and CAPRA-S scores (RP cohorts). Interpretability analyses identified cribriform patterns as key features associated with elevated BCR risk.

Conclusions

This multimodal AI model demonstrates robust BCR prediction across diverse populations, offering enhanced risk stratification beyond current standards with interpretable histological features, supporting its potential clinical utility in personalized prostate cancer management.

Deep phenotyping of joint biopsies implicates T and B cell crosstalk already at diagnosis of rheumatoid arthritis.

Name: Annelien Hooijsma

Department: Meds

Abstract

Rheumatoid arthritis (RA) is an autoimmune disease affecting peripheral joints in which breach of tolerance leads to autoantibodies (ACPA) targeting citrullinated proteins. Here we studied the cellular composition of joint biopsies captured at the time of diagnosis, i.e. before disease is biased by chronicity and immunomodulatory drugs. Single cell suspensions of joint biopsies from n= 10 patients were phenotyped using full spectral flow cytometry. We focused on activated and tissue resident memory (RM) phenotypes, the latter based on combinations of CD69, CD49a, and CD103. We find resident memory cells within CD4+, CD8+, $\gamma\delta$ T cells as well as B cells. PD1^{high}CXCR5- T peripheral helper cells, known for their B cell support, were also identified, implicating B cell crosstalk. Indeed, the presence of both activated naïve B cells (CD11c, CXCR5, CD69, and PD1), and plasmablasts (PB) further supporting B cell differentiation and T cell B cell crosstalk e.g. in extrafollicular reactions. Ectopic lymphoid structures have previously been observed in biopsies of patients with longstanding disease. In parallel activated Tregs were also prominent. In conclusion, our data implicates local immune responses potentially enhancing autoreactivity as well as efforts to counter regulate them already at diagnosis of RA and is hence not a result of chronicity.

Mapping Neuroinflammation in Corticobasal Degeneration Brains Using the TSPO PET Tracer ^3H -ER176

Name: Buse Esra Mercan

Department: NVS

Abstract

Background: Corticobasal degeneration (CBD) is a severe 4R tauopathy characterized by progressive motor and cognitive decline and neuroinflammation. However, there is currently no clinically established PET (positron emission tomography) tracer for neuroinflammation. ^3H -ER176, a promising brain imaging PET tracer targeting the microglial 18 kDa translocator protein (TSPO), which is upregulated during neuroinflammation, could fill this gap. Yet, its binding characteristics and relationship to CBD pathology remain insufficiently understood.

Methods: Using ^3H -ER176, radioligand binding assays and autoradiography were performed in brain tissue from CBD and cognitively normal (CN) cases. Saturation binding was conducted in frontal cortex homogenates, while regional binding assays were performed in caudate nucleus, globus pallidus, frontal cortex, and cerebellum. Autoradiography was performed on 20 μm frozen sections from the same regions, spanning early- to late-affected areas.

Results: Saturation binding confirmed a single binding site in CBD frontal cortex ($K_d=1.35$ nM, $B_{\text{max}}=0.11$ pmol/mg), consistent with specific TSPO engagement. Regional binding revealed significantly elevated ^3H -ER176 binding in CBD caudate nucleus relative to CN ($p<0.01$), with trends toward elevation in globus pallidus and frontal cortex. Cerebellar binding was unchanged. Autoradiography confirmed the regional distribution of binding.

Discussion: ^3H -ER176 detects region-specific neuroinflammation in CBD post-mortem brain, with the strongest signal in early affected basal ganglia structures, mapping onto the known staging of CBD tau pathology. The ongoing comparative immunostaining studies will further clarify these patterns and help validate ER176 as a potential marker of neuroinflammation in CBD.

Physics of cells as new biomarkers for diseases

Name: Cenk Gurdap

Department: KBH

Abstract

Cells undergo biophysical remodeling as a response to environmental changes, for survival and to execute their function. Changes in the biophysical properties of cells, such as membrane order, tension, and potential, are crucial to various diseases and have considerable potential as a diagnostic or prognostic marker. Over the years, numerous instruments have been developed to investigate the biophysical characteristics of cells. However, these technologies suffer from low throughput, which is a major obstacle to applying them to medical problems that require measuring thousands of cells. Moreover, low-parametric phenotyping lacks the power of integrating diverse biophysical properties and their underutilized correlations. Therefore, there is still a major gap in our understanding of how collective biophysical properties of the cells alter during both physiological and pathological processes. Here, we describe a high-throughput and multi-parametric platform with single cell resolution, which enables fast and correlative measurement of the biophysical properties of cells. We establish a unique pipeline to: 1) biophysically phenotype cells; 2) predicting health state of individuals from blood using biophysical remodeling and machine learning; 3) integrate biophysical phenotyping with multi-omics technologies; 4) explore drug treatments using biophysical measurements as readout. This method may aid the detection of different cellular pathogenic alterations directly from blood. Thus, our technique has the potential to be widely used in a variety of fields, where biophysical properties can be exploited as complementary to current protein or nucleic acid markers to diagnose and treat diseases.

Is prostate cancer screening cost-effective? A health economic evaluation to support decision-making in Sweden

Name: Daniela Skalt

Department: MEB

Abstract

How Malaria and Duffy-null spread in the world

Name: David Ziliang Hu

Department: FyFa

Abstract

The Duffy-null allele is in near fixation in sub-Saharan Africa. Previous studies suggested its presence in Oceania as a de novo mutation on a distinct genetic background. Within Africa, it has been suggested that it existed in multiple populations over 50,000 years ago before sweeping to fixation. This study aimed to clarify its spread within and beyond Africa. We show that increases in Duffy-null allele frequency in eastern and southern Africa occurred within the last 2,000 years and align with the Bantu expansion. The Oceanian mutation is likely to be a technical artifact.

Rethinking BV treatment: Community and strain-level vaginal microbiome shifts after treatment with pHyph

Name: Emilia Lahtinen

Department: MTC

Abstract

Bacterial vaginosis (BV) is the most common vaginal infection among reproductive-age women. Antibiotics are effective, yet up to 50% of women recur within a year. Repeated antibiotic exposure increases the load of antimicrobial resistance genes and disrupts the vaginal microbial balance. Therefore, there is a need for alternative therapies that support a beneficial microbiome while eradicating the infection. Here, we present results from a clinical trial evaluating pHyph, a novel, intravaginal, and antibiotic-free treatment for BV.

Vaginal swab samples were collected from 152 patients before and after treatment with either pHyph or a non-inert comparator. Samples were shotgun sequenced and annotated using the VIRGO2 gene catalog. Strain-level variation and its role in treatment outcomes were assessed with inStrain.

pHyph induced a shift in the vaginal microbiome towards *Lactobacillus*-dominated composition and promoted the growth of *Lactobacillus iners* and *Lactobacillus gasseri*. Among cured patients, pHyph decreased diversity and richness while decreasing the abundance of BV associated species, such as *Gardnerella vaginalis*, and *Megasphaera hutchinsonii*. Strain switching was common among pHyph-treated patients, occurring in 70% of the participants. Interestingly, all the strains identified were patient-specific, and if switching occurred, it involved a closely related strain.

These results showcase pHyph's potential as an alternative treatment for BV due to its ability to shape the vaginal microbiome towards a beneficial composition while providing BV symptom resolution. Future research will focus on building a machine learning model to identify variables associated with beneficial treatment outcome and studying the role of strain-switching in the long-term cure.

Therapist behaviour in psilocybin-assisted treatment for depression: A process-oriented analysis from the PSIPET trial

Name: Emma Zapel

Department: CNS (CPF)

Abstract

Background

As the search for more effective depression treatments continues, psilocybin has re-emerged as a promising intervention, with growing evidence of clinical benefits (Madsen et al., 2019). Psychological support as part of psilocybin treatments is widely regarded as essential for safety and tolerability

(Johnson et al., 2008), but despite its presumed importance, the psychotherapeutic component of psilocybin treatment remains both insufficiently described and understudied (Aday et al., 2024). Specific therapist behaviors, therapeutic stance, and treatment manuals are often not described, limiting replication, therapist training, and understanding of non-pharmacological effects. The PSIPET trial employs a non-directive, client-centered therapeutic manual along with audio-recordings of sessions, providing an opportunity to systematically examine specific therapist behaviors during treatment. The present study aims to characterize therapists' in-session behaviors and explore their potential associations with subsequent symptom change.

Methods

PSIPET is a Swedish double-blind, randomized, placebo-controlled phase II trial of psilocybin treatment for depression (n = 35). The preparatory and integration sessions were conducted by trained clinical psychologists, and the recordings were coded using a structured scheme informed by psychotherapy process frameworks and trial-specific behavioral categories (e.g. reflections and affirmations, advice). Descriptive analyses characterize the therapist in-session behaviors, followed by linear mixed models examining the associations between therapist behaviors, therapeutic alliance (WAI-S), and clinical outcomes (MADRS).

Implications and future directions

By empirically describing therapeutic processes in psilocybin-assisted treatment, this work aims to inform therapist training, treatment fidelity, and future mechanism-focused research in psychedelic therapy.

Profiling of Microglia in a Stem Cell and Murine Model of Anorexia Nervosa

Name: Emmy Erskine

Department: MMK

Abstract

Anorexia Nervosa (AN) is a psychiatric disorder characterized by restriction of energy intake, weight loss, and fear of weight gain, affecting around 1% of the population. The disorder has high mortality rates and there are currently no evidence based pharmacological treatments available for patients. Despite the presence of evolutionary mechanisms that should prevent elective starvation, AN patients maintain a negative energy balance for extended periods. Genome wide association studies (GWAS) have indicated dysregulation of metabolic signalling, and highlighted genetic variants associated with microglia. Using an anorectic murine model our lab has previously identified microglial activation in arcuate hypothalamus (ARC), alongside hypothalamic neuron degeneration. We therefore propose hypothalamic dysregulation involving microglia underpinning negative energy balance in AN.

To investigate the underpinnings of starvation in AN, we reprogrammed patient-derived fibroblasts to induced pluripotent stem cells (iPSCs) and differentiated microglia-like cells (iMGs) and hypothalamic and cortical neurons. We performed phagocytosis assays on iMGs by feeding them with synaptosomes from both neuronal populations, alongside characterizing cells with RNA-seq. In addition, we further explored the *anx/anx* anorectic mouse hypothalamus with spatial transcriptomics alongside immunofluorescence to assess synaptic pruning.

We identified a reduction in phagocytosis of hypothalamic synaptosomes in our AN-iMGs, but not cortical synaptosomes, indicating hypothalamic-specific aberrances in consumption. Additionally, we identified 81 differentially-expressed-genes (DEGs) including genes indicative of reduced response to peripheral appetite signaling. We identified several DEGs in hypothalamic microglia of the *anx/anx* mice, alongside IMARIS quantifications revealing altered synapse consumption in the hypothalamus. Taken together, this strengthens the metabo-psychiatric view on AN.

DRUGGING THE UNDRUGGABLE TARGET: CYTARABINE AND GEMCITABINE KILL EWING SARCOMA CELLS THROUGH SAMHD1 INHIBITION AND EWING SARCOMA FUSION PROTEIN DEGRADATION

Name: Hala Habash

Department: KBH

Abstract

Ewing sarcoma (ES) is the second-most frequent bone tumour in childhood and adolescence. Localised ES has a five-year relapse-free survival rate of around 70% which drops to 20-30% for metastatic ES. Survival has largely stagnated for the last decades despite efforts of treatment intensification. ES is driven by a fusion protein with aberrant transcription factor activity that reprogrammes the cellular transcriptome. Cytarabine, widely used for treatment of haematological malignancies, was identified as a drug that can induce fusion protein degradation and thereby reverse its transcriptomic effects. Its anti-tumour efficacy was confirmed in vivo. However, a phase-II trial with relapsed/refractory ES patients failed to demonstrate meaningful clinical efficacy of cytarabine. We hypothesize that the cytarabine resistance factor SAMHD1 may explain this discrepancy. Here, we demonstrated that SAMHD1 levels correlated with sensitivity to cytarabine in ES cell lines. In addition, we used immunoblotting to demonstrate the dose-dependent ability of cytarabine to deplete the ES fusion protein. More importantly, gemcitabine, previously described as a SAMHD1 inhibitor, sensitized ES cells to cytarabine in a SAMHD1-dependent manner and dramatically increased cytarabine-induced ES fusion protein depletion. We suggest a causal relationship between SAMHD1 and cytarabine/gemcitabine synergy through SAMHD1-knocked out cell lines. These findings were validated in a xenograft mouse model of ES, where combining cytarabine and gemcitabine significantly increased survival. This research promises to lay the ground for a novel treatment strategy of ES that targets its hitherto undruggable cancer-driving fusion protein which could quickly be translated into a clinical trial.

Geometric Optimization Of Coplanar Organic Electrochemical Transistors For High-Sensitivity IL-17 Detection

Name: Herbert Middleton

Department: MedS

Abstract

Early detection and continuous monitoring of Interleukin-17 (IL-17) are vital for managing psoriasis, yet traditional biopsies and blood draws remain invasive and impractical for frequent use. To address this, we developed a decentralized, painless biosensing platform using Organic Electrochemical Transistors (OECTs).

OECTs are ideal for epidermal integration due to their high transconductance and biocompatibility. However, detecting IL-17 in sweat requires extreme sensitivity, as concentrations often reside in the pg/mL range. This research, conducted at Karolinska Institutet, focuses on optimizing coplanar OECT architectures to maximize signal amplification.

Our 3D mesh data reveals that minimizing the distance between the coplanar gate and the channel significantly enhances ionic-electronic coupling. By establishing these precise geometric parameters, we have achieved the high-gain electrical baseline necessary for detecting low-abundance biomarkers.

This optimized platform provides the foundation for the next phase: integrating selective biorecognition elements. By enabling real-time, non-invasive monitoring of disease progression and therapeutic response, this wearable technology advances precision dermatology, allowing clinicians to manage chronic inflammatory cycles more effectively without patient distress.

Peripheral lysosome levels dictate mTORC1 inactivation even when catabolically impaired

Name: Huy Dang

Department: Laboratory Medicine

Abstract

The mechanistic target of rapamycin complex 1 (mTORC1) is a central driver of cell growth that is frequently hyperactivated in cancer. While mTORC1 is activated at the lysosomal surface in response

to growth factors and amino acids, the processes governing its inactivation are not fully understood. Here, we report that sustained mTORC1 suppression during leucine or arginine starvation requires the translocation of peripheral lysosomes to the perinuclear region. Our data suggest that a pool of mTOR remains active at peripheral lysosomes during starvation, and that increased spatial separation between lysosomes and the plasma membrane attenuates PI3K/Akt signaling—thereby reducing inputs that otherwise maintain mTORC1 activity. Consequently, preventing lysosome translocation and increasing peripheral lysosome levels sustains mTORC1 signaling during prolonged starvation in a PI3K/Akt-dependent manner independently of autophagy. Under these conditions, mTORC1 signaling persists even when lysosomal catabolism is perturbed by chloroquine or concanamycin A. Collectively, these data indicate that the peripheral lysosome pool, even when catabolically impaired, can sustain mTORC1 signaling under nutrient scarcity, by modulating PI3K/Akt signaling input to the pathway. These observations identify peripheral lysosome levels as a critical determinant of mTORC1 inactivation during nutrient stress and may have implications for diseases with aberrant mTORC1 signaling, including cancer.

Effects of intestinal parasites on immune response to pre-existing memory to influenza A virus

Name: Julie Roux Ciry

Department: MTC

Abstract

Helminth infections are highly prevalent in the world. While they do not cause a high pathogenicity, they can change the immune landscape of the body. It is not clear to what extent they might be beneficial or detrimental for the immune response to other infection. This study aims to address the effects of helminth infection on pre-existing immune memory to influenza and its effect on immune response to a challenge.

Pauci cellular proteomics of FACS-sorted cell populations - Lymph Node Atlas

Name: Kovi Rishya Shrung Govindarajan

Department: OnkPat

Abstract

We have separated reactive lymph node and tonsil samples into FACS cell compartments which were then analysed by low-cell number proteomics. Samples from 8 different donors yielded a total of 467 samples which comprised of 24 different immune cell types. The higher sensitivity of our analysis methodology allows to capture the proteome of rare cell populations. We plan to use this as a surrogate for a healthy base line against which the proteome of cancer cells can be compared to. This allows us to decipher the phenotype of the tumour cell type and its associated immune escape mechanisms.

Associations between GLP-1RA use and lifetime eating disorders

Name: Liv Hog

Department: MEB

Abstract

Identifying the drivers of mast cell neoplasia using a genome-wide CRISPR knockout screen

Name: Lucille Margerie

Department: MedS

Abstract

Novel approaches to study rheumatoid arthritis-associated anti-citrulline T cell reactivity

Name: Marlene Schüle

Department: MedS

Abstract

While autoreactive T cells recognizing citrullinated antigens have been implicated in rheumatoid arthritis (RA), they remain rare and difficult to study and are not reflected by current animal models. To accelerate the investigation of RA autoantigens we are exploring adeno-associated virus (AAV) mediated knock-in of patient-derived TCRs into murine T cells.

AAVs were used to knock-out the endogenous TCR β chain and knock-in a TCR of interest at the TCR α constant locus of CD4 $^{+}$ T cells isolated from Cas9-expressing mice. To allow investigation of several TCRs at once, AAVs were engineered to carry patient-derived TCR sequences followed by a unique triple peptide code (Flowcode), allowing identification of T cell clones by flow cytometry.

AAV-transduced murine CD4 $^{+}$ T cells respond to their cognate antigen in an HLA-restricted manner in vitro. After single peptide stimulation of CD4 $^{+}$ T cells transduced with a pool of AAVs carrying distinct TCRs, we observed clonal expansion of antigen-specific T cells. In addition, transfer of pooled AAV-transduced CD4 $^{+}$ T cells into HLA-DRB1*0401 recipients followed by immunization with relevant peptides was used to confirm antigen-specific T cell activation and expansion in vivo.

To summarize, AAV-mediated knock-in of patient-derived TCRs into murine CD4 $^{+}$ T cells generates functional and HLA-restricted antigen-specific T cells, and pooled TCR re-expression allows simultaneous study of distinct reactivities. This study constitutes the initial steps towards building a platform to explore patient-derived TCRs in a humanized murine setting, both in vitro and in vivo, while facilitating data translation from animal models into (pre)clinical settings.

Reward, Social Learning, and Habit in Posting Choice on Social Media

Name: Oromia Godanna Sero

Department: Clinical Neuroscience

Abstract

Social media has transformed how people create and share information at scale. Individuals repeatedly decide what to post while observing others' posts in their social network and receiving feedback in the form of engagement (likes, reposts, replies). Although a large body of work has examined population-level outcomes such as virality, misinformation, and polarization, less is known about the individual mechanisms that underlie these repeated posting choices. Here, we ask how feedback, social learning, and habit jointly shape what people choose to post over time.

To address this question, we analyze 3.8 million posts from 1,598 Bluesky users. We model each post's content using a transformer-based topic model, which yields a probability distribution over interpretable topics and allows us to track how users' topic choices shift over time. To capture social learning, we reconstruct each user's recent Following Feed on Bluesky's default chronological, non-ranked feed and derive topic-level social features, including how often topics appear, how much engagement they receive, and how popular their authors are.

We then compare computational models of posting behavior: an asocial reinforcement-learning model based on users' own past rewards, a social feature learning model that incorporates feed-derived social information, a habit model capturing topic repetition independent of reward, and hybrid models combining these mechanisms. Across users, a hybrid model combining social feature learning and habit provides the best overall account of posting behavior, indicating that no single mechanism alone sufficiently explains what people choose to post.

An in vivo platform to study the crosstalk between the exocrine and endocrine pancreas in health and disease

Name: Riccardo Lizzani

Department: MMK

Abstract

The endocrine and exocrine pancreas exert distinct functions despite cohabiting the same organ. For this reason, they have been long studied separately by different medical fields. Accumulating evidence shows that these two tissues strongly influence each other, also due to their vascular interconnection. However, longitudinal studies on the pancreas are limited by lack of valuable in vitro models, the fast loss of acinar phenotype upon isolation, and the optical inaccessibility of the organ in vivo.

In our work, we mimic the exocrine-endocrine crosstalk outside the pancreas by transplanting acinar-derived spheroids together with pancreatic islets into the anterior chamber of the mouse eye. By transplanting exocrine spheroids after 2 days in culture, they get vascularized, regain their acinar morphology, and can be non-invasively monitored overtime by confocal microscopy. Characterization performed on explanted grafts with immunofluorescence and transmission electron microscopy shows amylase expression, cell granularity and polarization, and presence of a common lumen in the acinus center. Blood is flowing in the graft, but only unidirectionally from the islet to the exocrine part.

Overall, this novel approach has the potential to overcome major limitations on pancreatic research by enabling longitudinal and non-invasive studies in an in vivo setup, refining animal usage and allowing for microvasculature and functionality studies by implementation of fluorescent probes. Additionally, morphological and functional changes may be detected upon administration of xenobiotics in toxicological studies or upon induction of pathological conditions in the experimental animal, i.e. diabetes or pancreatitis.

ISG15-Dependent Immunometabolic Regulation during RNA Virus Infection and Viral Interference of host ubiquitylation and ISGylation Events

Name: Sefanit Rezene

Department: LabMed

Abstract

The innate immune response is the first line of defense against pathogens and depends on precisely tuned signaling networks. Conjugation of ubiquitin (Ub) or Ub-like modifiers such as interferon-stimulated gene 15 (ISG15) regulates protein fate and antiviral signaling, while viral deubiquitinases (vDUBs) and deISGylases (vDISGs) counteract these modifications to suppress host defenses. Our work investigates ISG15's role in immunometabolic regulation and how viral proteases PLpro (SARS-CoV-2) and OTU-L (CCHFV) target Ub and Ub-like pathways, using quantitative and affinity-based proteomics approaches.

From Metabolism to Mechanics: Targeting Filament-Forming Metabolic Enzymes in Cancer

Name: Spyridon Pantelios

Department: LabMed

Abstract

Nucleotide biosynthesis is a central determinant of proliferative capacity and is often limited by fluctuating nutrient availability and metabolic stress. While metabolic enzymes are classically defined by their catalytic roles, their capacity to undergo higher-order assembly suggests additional functions that remain poorly understood. Here, we show that under nucleotide-limiting conditions, a metabolic enzyme undergoes a structural transition into filamentous assemblies that associate with the intermediate filament cytoskeleton. These filaments adopt a defined intracellular organization, aligning with cytokeratin and vimentin networks through non-covalent interactions. Disruption of filament formation does not impair enzymatic activity but alters cytoskeletal engagement and limits cell spreading under stress conditions. Notably, filament organization parallels cytoskeletal remodeling during adhesion, with increased association cytoskeletal structures. These findings identify a stress induced structural adaptation that links metabolic state to cytoskeletal organization, suggesting a

mechanism by which cancer cells coordinate metabolic constraints with mechanical properties required for growth and adaptation.

Human Placental Stem Cell–Mediated Immunomodulation Promotes Neuroprotection in the SOD1 G93A ALS mouse model

Name: Stefan Bencina

Department: CNS

Abstract

Amyotrophic Lateral Sclerosis (ALS) is a progressive, fatal neurodegenerative disorder defined by the selective loss of upper and lower motor neurons, leading to muscle atrophy and eventual paralysis. While neuronal death is the primary pathological feature, emerging evidence highlights the critical role of neuroinflammation in driving both the disease onset and progression, specifically regarding microglial activation and T-cell infiltration. These observations suggest that targeting specific brain immune cells is a promising therapeutic strategy for ALS. Specifically, human Amniotic Epithelial Stem Cell (hAEC) based immunotherapy has emerged as a potent approach to address neuroinflammation by shaping the immune landscape in favor of neuroprotection.

To investigate this approach, our group administered hAEC via cisterna magna injection directly into the cerebrospinal fluid of the SOD1 (G93A) mouse model. Stem cells were delivered before disease onset in both male and female cohorts. Our results demonstrated that hAEC injections significantly delayed disease onset and extended overall survival, with a notably more pronounced benefit observed in female mice. Flow cytometry analyses revealed an increase in protective immune cell populations, including immunoprotective Arginase-1 positive (Arg1⁺) macrophages in both brain and spinal cord, as well as the emergence of an inflammation-resolving population of myeloid-derived suppressor cells with eosinophilic features.

Together, these findings support stem cell-based immunotherapy delivered into the cerebrospinal fluid as a promising strategy to modulate neuroinflammation and modify disease progression in ALS, with potential sex-specific differences in therapeutic response.

Pharmacotherapy in forensic psychiatric care in Sweden: prevalence, effectiveness, and future considerations

Name: Taalke Maria Sitter

Department: MEB

Abstract

Background: Patients in forensic psychiatric care are commonly treated with a wide range of psychotropic medications. There is, however, a lack of understanding regarding how pharmacological treatments are used throughout care, and if they are effective in contributing to the goals of forensic psychiatry.

Aim: The presentation aims to give an overview of the field of pharmacotherapy in forensic psychiatric care, present the key take-aways of two conducted studies and give an outlook for the future of the field.

Methods: Swedish national registry data was utilized (1) to estimate prevalence of the use of major psychotropic medication in forensic psychiatric care in Sweden, and (2) to estimate the association of different psychotropic medications and the need for coercive measures and recidivism during forensic psychiatric care, using a within-individual design.

Key-Takeaways: Forensic psychiatric care is a setting with a high prevalence of psychotropic medication use. We observed that atypical antipsychotics, especially clozapine, are associated with a reduced risk of coercive measures and recidivism during care. While our results can help inform decision-making processes to some extent, there remains a significant need for more evidence to guide pharmacotherapy in forensic psychiatric care.

Risk of Self-Harm Following Antidepressant Initiation Among Older Adults in Sweden: A Self-Controlled Case Series Study

Name: Theodore Tianyi Miao

Department: MEB

Abstract

Background:

Older adults have a high risk of self-harm and suicide and are frequently exposed to antidepressants. However, the risk of self-harm and suicide may vary across treatment periods and antidepressant classes, and evidence in older adults remains limited.

Objective:

To examine the risk of self-harm and suicide in relation to antidepressant initiation among older adults in Sweden, and to compare this risk across antidepressant classes.

Methods:

We linked the Total Population Register, National Patient Register, Swedish Prescribed Drug Register, and Cause of Death Register using unique personal identification numbers. Individuals aged 65 years and older with at least one recorded self-harm event or suicide during follow-up were included. Antidepressants were classified as selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), and other antidepressants. A self-controlled case series design was applied, and conditional Poisson regression was used to estimate incidence rate ratios (IRRs) for self-harm and suicide across prespecified risk windows relative to antidepressant initiation. Age was adjusted for as a time-varying factor using 5-year age bands.

Results:

We identified 21,357 older adults aged 65 years or older between 2007 and 2022 who had self-harm event and initiated antidepressant treatment. 60% were women; 45% initiated SSRIs, 5% SNRIs, 15% TCAs, and 35% other antidepressants. Analyses of IRRs across treatment periods are ongoing.

Conclusions:

Our preliminary findings suggest that antidepressant initiation patterns differ across classes among older adults with self-harm records. Clarifying how risk varies across treatment periods may help identify high-risk periods and inform prevention strategies.

Polygenic overlap and shared genomic loci between anorexia nervosa and cardiometabolic traits suggest shared biological mechanisms

Name: Zhengan Lu

Department: Department of Medical Epidemiology and Biostatistics

Abstract

Anorexia nervosa (AN) is a serious psychiatric disorder with prominent metabolic features, but few studies have revealed the genetic mechanisms underlying its metabolic component. Based on genome-wide association studies, we examine the shared genetic architecture between AN and seven common cardiometabolic traits (body mass index, low-density lipoproteins, systolic blood pressure, diastolic blood pressure, type 2 diabetes, coronary artery disease, and metabolic syndrome). MiXeR and linkage-disequilibrium score regression were adopted to quantify the genetic overlap. A conditional/conjunctional FDR framework was employed to identify shared genomic loci. Gene-based enrichment analyses were performed to reveal overlapping biological mechanisms. Colocalization tests were performed to prioritize colocalized shared variants. We identified moderate to substantial polygenic overlap between AN and cardiometabolic traits and 43 unique shared loci. Genes mapped to the shared loci were enriched for biological processes relevant to brain cell growth and migration, cytoplasmic region, water transport, and muscle development. Furthermore, we identified eight colocalized shared variants, demonstrating genetic associations and potential interactions with drugs for somatic conditions including cardiometabolic and neuropsychiatric disorders. Overall, this study

reveals the biological underpinnings and clinical implications of the AN-metabolic component, providing novel insights into the etiology and gene-based treatment or prevention measures for AN.

Poster session abstracts

Establishment of a Serum-Free Primary Cell-Based 3D Skeletal Muscle Model for Atrophy Research

Name: Aikaterini Papadimitropoulou

Department: Labmed

Abstract

Skeletal muscle atrophy is a debilitating condition associated with disuse, aging, and disease, yet current in vitro models fail to recapitulate the complexity of native muscle tissue. Two-dimensional cultures using immortalized cell lines lack physiological relevance, while animal models present ethical and translational limitations. Here we describe the development of a three-dimensional skeletal muscle construct using primary isolated myoblasts cultured under serum-free conditions on a custom 3D printed scaffold.

Primary myoblasts were isolated, embedded in hydrogel, and dispensed onto a scaffold, then maintained in serum-free differentiation medium to promote myotube formation. This model offers a physiologically relevant, defined, and reproducible platform for the study of skeletal muscle atrophy in vitro. Future work will focus on inducing atrophic conditions to validate the model as a tool for investigating underlying mechanisms and potential countermeasures.

Uncovering the role of SAMHD1 for immunotherapy response in melanoma

Name: Alessandra Muni

Department: oncology-pathology

Abstract

Cutaneous melanoma (CM) is one of the most aggressive and deadly skin cancers, often associated with elevated tumor mutational burden and high immunogenicity. Even though treatment with immune checkpoint inhibitors (ICIs) has improved the survival of CM patients, nearly half do not achieve lasting benefits. Therefore, new combination therapies are needed to overcome immune resistance. SAMHD1, a deoxynucleoside triphosphate (dNTP) phosphohydrolase, plays a complex role in cancer development. We hypothesize that SAMHD1 loss in CM hyperactivates the cGAS–STING–TBK1 pathway, leading to upregulated expression of immunomodulatory molecules and induction of anergy. This highlights the therapeutic potential of STING pathway inhibition to enhance the anti tumor response to ICIs in SAMHD1 negative CM and frames the project's aim to investigate how SAMHD1 modulates immune activity in melanoma. Our data support the association between SAMHD1 loss and STING pathway hyperactivation in SAMHD1 wild type (wt) and knockout (KO) melanoma cell lines. Specifically, SAMHD1-KO cells showed increased expression of downstream target genes (ISG15, IFI16, CXCL10) and the immunomodulatory molecule PD-L1, which decreased upon STING inhibition. Furthermore, we demonstrated that SAMHD1-wt cells elicit stronger NK mediated killing in two and three dimensional cocultures. However, NK activation against SAMHD1-KO cells can be enhanced upon STING inhibition. Finally, we investigated the impact of SAMHD1 expression and STING pathway blockade on tumor progression and antitumor immune responses in vivo. Overall, these findings highlight the role of SAMHD1 in CM and its potential to guide novel therapeutic strategies.

tTEscanR: an advanced R-based package to quantify and visualize translation efficiency from sequencing data

Name: Ana Varas Sánchez

Department: MTC

Abstract

Protein translation unfolds in three stages: initiation, elongation and termination. Elongation is dependent on codon-anticodon interactions, with suitable nucleotide pairing being essential for efficient translation. To quantify translation efficiency, it is crucial to assess the availability of each mRNA codon and its corresponding tRNA anticodon. However, this process is challenging due to fluctuations in

mRNA and tRNA levels across tissues and cell types, which may introduce biases and hinder accuracy. Moreover, investigating tRNAs presents experimental difficulties.

In our previous work, we developed a computational pipeline to quantify and analyze mRNA codon usage relative to the availability of pairing tRNA anticodons as a proxy to determine its translation efficiency. Here, we extend its potential by introducing tTEscanR, a powerful and user-friendly R-based package designed to quantify translation efficiency from bulk and single-cell sequencing data. tTEscanR offers a comprehensive approach to quantify translation efficiency by integrating gene expression data and chromatin accessibility data. The modular design of tTEscanR ensures flexibility, allowing users to either run independent components or a complete pipeline. Its user-friendly R-based interface simplifies the analysis of complex data, even for researchers with minimal computational experience. Additionally, tTEscanR includes an advanced visualization module that generates high-quality plots, aiding in interpretation of results and enhancing the ability to communicate findings effectively. Applicable to both bulk and single-cell sequencing data, tTEscanR provides a versatile tool for a wide range of experimental setups and biological contexts, enabling deeper exploration of translation efficiency and its role in cellular processes, disease mechanisms, and therapeutic development.

Deep phenotyping of joint biopsies implicates T and B cell crosstalk already at diagnosis of rheumatoid arthritis.

Name: Annelien Hooijsma

Department: Meds

Abstract

Rheumatoid arthritis (RA) is an autoimmune disease affecting peripheral joints in which breach of tolerance leads to autoantibodies (ACPA) targeting citrullinated proteins. Here we studied the cellular composition of joint biopsies captured at the time of diagnosis, i.e. before disease is biased by chronicity and immunomodulatory drugs. Single cell suspensions of joint biopsies from n= 10 patients were phenotyped using full spectral flow cytometry. We focused on activated and tissue resident memory (RM) phenotypes, the latter based on combinations of CD69, CD49a, and CD103. We find resident memory cells within CD4+, CD8+, $\gamma\delta$ T cells as well as B cells. PD1^{high}CXCR5⁺ T peripheral helper cells, known for their B cell support, were also identified, implicating B cell crosstalk. Indeed, the presence of both activated naïve B cells (CD11c, CXCR5, CD69, and PD1), and plasmablasts (PB) further supporting B cell differentiation and T cell B cell crosstalk e.g. in extrafollicular reactions. Ectopic lymphoid structures have previously been observed in biopsies of patients with longstanding disease. In parallel activated Tregs were also prominent. In conclusion, our data implicates local immune responses potentially enhancing autoreactivity as well as efforts to counter regulate them already at diagnosis of RA and is hence not a result of chronicity.

Mapping Neuroinflammation in Corticobasal Degeneration Brains Using the TSPO PET Tracer ³H-ER176

Name: Buse Esra Mercan

Department: NVS

Abstract

Background: Corticobasal degeneration (CBD) is a severe 4R tauopathy characterized by progressive motor and cognitive decline and neuroinflammation. However, there is currently no clinically established PET (positron emission tomography) tracer for neuroinflammation. ³H-ER176, a promising brain imaging PET tracer targeting the microglial 18 kDa translocator protein (TSPO), which is upregulated during neuroinflammation, could fill this gap. Yet, its binding characteristics and relationship to CBD pathology remain insufficiently understood.

Methods: Using ³H-ER176, radioligand binding assays and autoradiography were performed in brain tissue from CBD and cognitively normal (CN) cases. Saturation binding was conducted in frontal cortex homogenates, while regional binding assays were performed in caudate nucleus, globus pallidus, frontal cortex, and cerebellum. Autoradiography was performed on 20 μ m frozen sections from the same regions, spanning early- to late-affected areas.

Results: Saturation binding confirmed a single binding site in CBD frontal cortex ($K_d=1.35$ nM, $B_{max}=0.11$ pmol/mg), consistent with specific TSPO engagement. Regional binding revealed significantly elevated ^3H -ER176 binding in CBD caudate nucleus relative to CN ($p<0.01$), with trends toward elevation in globus pallidus and frontal cortex. Cerebellar binding was unchanged. Autoradiography confirmed the regional distribution of binding.

Discussion: ^3H -ER176 detects region-specific neuroinflammation in CBD post-mortem brain, with the strongest signal in early affected basal ganglia structures, mapping onto the known staging of CBD tau pathology. The ongoing comparative immunostaining studies will further clarify these patterns and help validate ER176 as a potential marker of neuroinflammation in CBD.

Accelerating large-scale analysis of omics datasets with osync

Name: Carlos Gallardo Dodd

Department: MTC

Abstract

In the era of big data and data-driven research, it has become increasingly important to leverage large sequencing datasets to further our understanding of biology, human health and disease. Ensuring that the results of data processing and analysis workflows are reproducible and comparable remains a challenge, limiting the ability to effectively combine and integrate data. To address this, we introduce the osync framework, which aims to streamline the retrieval, processing, and analysis of high-throughput sequencing datasets, both publicly available and newly generated. Our implementation uses the snakemake workflow management system to efficiently process data locally or on a computer cluster, all while securing information relevant for execution and reproducibility in a configuration file. Together with a modular design, this enables osync to work with a variety of omics technologies, making it adaptable to diverse research needs, and capable of analyzing data in five steps or less. We demonstrate the broad applicability of osync on multiple datasets, underscoring the ease of use of its standardized workflows. Altogether, osync provides a powerful and reproducible execution environment, which makes it particularly suitable for multi-omics integration and large-scale meta-analysis projects. Importantly, it promotes transparency and provides a unified platform for biological discovery.

Physics of cells as new biomarkers for diseases

Name: Cenk Gurdap

Department: KBH

Abstract

Cells undergo biophysical remodeling as a response to environmental changes, for survival and to execute their function. Changes in the biophysical properties of cells, such as membrane order, tension, and potential, are crucial to various diseases and have considerable potential as a diagnostic or prognostic marker. Over the years, numerous instruments have been developed to investigate the biophysical characteristics of cells. However, these technologies suffer from low throughput, which is a major obstacle to applying them to medical problems that require measuring thousands of cells. Moreover, low-parametric phenotyping lacks the power of integrating diverse biophysical properties and their underutilized correlations. Therefore, there is still a major gap in our understanding of how collective biophysical properties of the cells alter during both physiological and pathological processes. Here, we describe a high-throughput and multi-parametric platform with single cell resolution, which enables fast and correlative measurement of the biophysical properties of cells. We establish a unique pipeline to: 1) biophysically phenotype cells; 2) predicting health state of individuals from blood using biophysical remodeling and machine learning; 3) integrate biophysical phenotyping with multi-omics technologies; 4) explore drug treatments using biophysical measurements as readout. This method may aid the detection of different cellular pathogenic alterations directly from blood. Thus, our technique has the potential to be widely used in a variety of fields, where biophysical properties can be exploited as complementary to current protein or nucleic acid markers to diagnose and treat diseases.

How Malaria and Duffy-null spread in the world

Name: David Ziliang Hu

Department: FyFa

Abstract

The Duffy-null allele is in near fixation in sub-Saharan Africa. Previous studies suggested its presence in Oceania as a de novo mutation on a distinct genetic background. Within Africa, it has been suggested that it existed in multiple populations over 50,000 years ago before sweeping to fixation. This study aimed to clarify its spread within and beyond Africa. We show that increases in Duffy-null allele frequency in eastern and southern Africa occurred within the last 2,000 years and align with the Bantu expansion. The Oceanian mutation is likely to be a technical artifact.

Harnessing Mesoporous Silica and Engineered Pore-Forming Toxins to Enhance Intracellular Genome-Editing Delivery

Name: Delia Daniele

Department: LabMed

Abstract

Efficient intracellular delivery remains a major barrier to the therapeutic use of gene-editing technologies, largely due to limited uptake, endosomal entrapment, and poor cytosolic access. To address these challenges, we developed a modular three-component platform integrating mesoporous silica nanoparticles (MSNs), engineered pore-forming bacterial toxins, and gene-editing cargoes. MSNs enhance cellular internalization and provide an exceptionally high-surface-area, tunable scaffold capable of complexing and protecting diverse biomolecules. Their chemically versatile surface allows for targeted or stability-enhancing modifications, while their fully biodegradable silica framework supports safe clearance and minimizes long-term accumulation. To overcome endosomal sequestration, we repurpose pore-forming bacterial toxins by redirecting their membrane-permeabilizing activity specifically to the endosomal membrane, enabling pore formation during endosomal maturation without compromising plasma membrane integrity. This coordinated system promotes efficient endosomal escape and robust cytosolic release of gene-editing tools, while maintaining biocompatibility and spatial control over membrane disruption. Together, these synergistic components establish a flexible and safe nanobiotechnology strategy capable of overcoming long-standing delivery bottlenecks and advancing the intracellular accessibility of genome-engineering therapeutics.

Rethinking BV treatment: Community and strain-level vaginal microbiome shifts after treatment with pHyph

Name: Emilia Lahtinen

Department: MTC

Abstract

Bacterial vaginosis (BV) is the most common vaginal infection among reproductive-age women. Antibiotics are effective, yet up to 50% of women recur within a year. Repeated antibiotic exposure increases the load of antimicrobial resistance genes and disrupts the vaginal microbial balance. Therefore, there is a need for alternative therapies that support a beneficial microbiome while eradicating the infection. Here, we present results from a clinical trial evaluating pHyph, a novel, intravaginal, and antibiotic-free treatment for BV.

Vaginal swab samples were collected from 152 patients before and after treatment with either pHyph or a non-inert comparator. Samples were shotgun sequenced and annotated using the VIRGO2 gene catalog. Strain-level variation and its role in treatment outcomes were assessed with inStrain.

pHyph induced a shift in the vaginal microbiome towards *Lactobacillus*-dominated composition and promoted the growth of *Lactobacillus iners* and *Lactobacillus gasseri*. Among cured patients, pHyph decreased diversity and richness while decreasing the abundance of BV associated species, such as *Gardnerella vaginalis*, and *Megasphaera hutchinsonii*. Strain switching was common among pHyph-treated patients, occurring in 70% of the participants. Interestingly, all the strains identified were patient-specific, and if switching occurred, it involved a closely related strain.

These results showcase pHyph's potential as an alternative treatment for BV due to its ability to shape the vaginal microbiome towards a beneficial composition while providing BV symptom resolution. Future research will focus on building a machine learning model to identify variables associated with beneficial treatment outcome and studying the role of strain-switching in the long-term cure.

Therapist behaviour in psilocybin-assisted treatment for depression: A process-oriented analysis from the PSIPET trial

Name: Emma Zapel

Department: CNS (CPF)

Abstract

Background

As the search for more effective depression treatments continues, psilocybin has re-emerged as a promising intervention, with growing evidence of clinical benefits (Madsen et al., 2019). Psychological support as part of psilocybin treatments is widely regarded as essential for safety and tolerability (Johnson et al., 2008), but despite its presumed importance, the psychotherapeutic component of psilocybin treatment remains both insufficiently described and understudied (Aday et al., 2024). Specific therapist behaviors, therapeutic stance, and treatment manuals are often not described, limiting replication, therapist training, and understanding of non-pharmacological effects. The PSIPET trial employs a non-directive, client-centered therapeutic manual along with audio-recordings of sessions, providing an opportunity to systematically examine specific therapist behaviors during treatment. The present study aims to characterize therapists' in-session behaviors and explore their potential associations with subsequent symptom change.

Methods

PSIPET is a Swedish double-blind, randomized, placebo-controlled phase II trial of psilocybin treatment for depression (n = 35). The preparatory and integration sessions were conducted by trained clinical psychologists, and the recordings were coded using a structured scheme informed by psychotherapy process frameworks and trial-specific behavioral categories (e.g. reflections and affirmations, advice). Descriptive analyses characterize the therapist in-session behaviors, followed by linear mixed models examining the associations between therapist behaviors, therapeutic alliance (WAI-S), and clinical outcomes (MADRS).

Implications and future directions

By empirically describing therapeutic processes in psilocybin-assisted treatment, this work aims to inform therapist training, treatment fidelity, and future mechanism-focused research in psychedelic therapy.

High-fat diet exacerbates ischemic muscle impairment in the FAL murine model of Peripheral Artery Disease

Name: Emmanouella Michaela Xanthopoulou

Department: Physiology and Pharmacology

Abstract

Peripheral artery disease (PAD) affects over 200 million people worldwide and often co-occurs with type 2 diabetes. PAD arises from reduced limb perfusion causing ischemia and progressive skeletal muscle impairment, further aggravated by diabetes-associated metabolic stress. Current treatments aim to restore perfusion but do not fully recover muscle function, highlighting the need to better understand mechanisms driving PAD related myopathy. The femoral artery ligation (FAL) mouse model is widely used to induce ischemia, yet its muscle phenotype under diabetic-like metabolic conditions remains uncharacterized.

We examined skeletal muscle responses to FAL in mice on a normal diet (ND) or high fat diet (HFD), the latter modelling diabetes-related metabolic stress. ND mice showed substantial recovery of muscle force by 30 days post FAL, whereas HFD mice displayed persistent deficits. Mitochondrial respiration was markedly reduced in HFD FAL muscles, indicating impaired oxidative capacity. Histology revealed smaller myofibers, increased lipid accumulation and elevated macrophage infiltration post FAL, all

worsened by HFD. These findings show that ischemia combined with metabolic stress reproduces key features of PAD myopathy in the FAL mouse model.

Ongoing bulk-RNA-sequencing analysis of muscles at 3 days, 1, 2 & 4 weeks after FAL in ND and HFD mice aims to define transcriptional programs underlying divergent recovery. Analyses examine time and diet dependent gene trajectories and pathways controlling, among others, mitochondrial function, inflammation and adipogenic signaling.

Profiling of Microglia in a Stem Cell and Murine Model of Anorexia Nervosa

Name: Emmy Erskine

Department: MMK

Abstract

Anorexia Nervosa (AN) is a psychiatric disorder characterized by restriction of energy intake, weight loss, and fear of weight gain, affecting around 1% of the population. The disorder has high mortality rates and there are currently no evidence based pharmacological treatments available for patients. Despite the presence of evolutionary mechanisms that should prevent elective starvation, AN patients maintain a negative energy balance for extended periods. Genome wide association studies (GWAS) have indicated dysregulation of metabolic signalling, and highlighted genetic variants associated with microglia. Using an anorectic murine model our lab has previously identified microglial activation in arcuate hypothalamus (ARC), alongside hypothalamic neuron degeneration. We therefore propose hypothalamic dysregulation involving microglia underpinning negative energy balance in AN.

To investigate the underpinnings of starvation in AN, we reprogrammed patient-derived fibroblasts to induced pluripotent stem cells (iPSCs) and differentiated microglia-like cells (iMGs) and hypothalamic and cortical neurons. We performed phagocytosis assays on iMGs by feeding them with synaptosomes from both neuronal populations, alongside characterizing cells with RNA-seq. In addition, we further explored the anx/anx anorectic mouse hypothalamus with spatial transcriptomics alongside immunofluorescence to assess synaptic pruning.

We identified a reduction in phagocytosis of hypothalamic synaptosomes in our AN-iMGs, but not cortical synaptosomes, indicating hypothalamic-specific aberrances in consumption. Additionally, we identified 81 differentially-expressed-genes (DEGs) including genes indicative of reduced response to peripheral appetite signaling. We identified several DEGs in hypothalamic microglia of the anx/anx mice, alongside IMARIS quantifications revealing altered synapse consumption in the hypothalamus. Taken together, this strengthens the metabo-psychiatric view on AN.

Risk of HPV-related cancers in immunosuppressed populations

Name: Eva Meglic

Department: MEB

Abstract

Introduction:

Human Papillomavirus (HPV)-related cancers contribute substantially to morbidity and mortality. People with HIV (PWH) and solid organ transplant recipients (SOTr) are at elevated risk due to immunosuppression, but direct comparisons within the same population are limited. Understanding relative risk and contributing factors is crucial for targeted prevention and screening.

Methods:

We conducted a nested case-control study using incidence density sampling within the Swedish population from 1983 to 2024. HPV-related cancer cases were matched 1:10 with controls on sex, birth year, and region of birth. The study included 353,023 individuals born 1940–2000 and resident in Sweden during the study period. Exposure was defined as HIV infection or history of SOT. HPV-related cancers were identified via ICD codes in the Swedish Cancer Registry. Adjusted odds ratios (aORs) were estimated for overall and site-specific cancers, accounting for clinical and sociodemographic factors.

Results:

Both PWH and SOTr had elevated risk compared with the general population: aOR 4.50 (95% CI 3.46–5.84) for PWH and 1.74 (95% CI 1.49–2.03) for SOTr. Among PWH, anal (aOR 56.37) and penile

cancers (aOR 8.10) were highest. Among SOTr, vulvar (aOR 4.79) and penile cancers (aOR 3.61) were most elevated. Risk varied by organ type, time since transplant, CD4 counts, viral suppression, and sociodemographic factors.

Conclusions:

HPV-related cancer risk is increased in immunosuppressed populations, particularly PWH. These findings highlight the need for enhanced prevention, including HPV vaccination, screening, and optimized immunosuppressive management, to reduce cancer burden.

Leveraging Pharmacovigilance Data to Detect Antibiotic Resistance and Inappropriate Use in LMICs

Name: Hager Saleh

Department: GPH

Abstract

Background

Pharmacovigilance (PV) has traditionally focused on monitoring adverse drug reactions (ADRs), but its role in identifying antibiotic resistance and inappropriate use is increasingly recognized. Global PV databases, such as Vigibase, contain reports that include resistance-related terms, offering valuable real-world evidence. This information can support antimicrobial stewardship and inform public health strategies, particularly in low- and middle-income countries (LMICs), where surveillance systems are often limited.

Objectives

To explore the utility of pharmacovigilance databases in identifying potential antibiotic resistance and inappropriate antibiotic use in low- and middle-income countries (LMICs).

Methods

A retrospective observational study was conducted using data extracted from Vigibase, the WHO global database of individual case safety reports (ICSRs), maintained by the Uppsala Monitoring Centre (UMC). The study focused on ICSRs involving systemic antibiotics originating from LMICs, submitted up to January 2024. Reports were screened using MedDRA preferred terms that reflect resistance and inappropriate use. Descriptive statistics were applied to summarize reports by MedDRA coding, drug class, and country. Where relevant, statistical tests were employed. All analyses were conducted using R software.

Results

65 MedDRA PTs related to resistance, ineffectiveness, off-label use, and error of use were included. A total of 1,614 unique cases, representing 3,014 individual reports, were analyzed.

Conclusions

Pharmacovigilance databases such as Vigibase can provide valuable insights into antibiotic resistance and inappropriate use beyond traditional ADR monitoring. The identified reports highlight patterns of therapeutic ineffectiveness and off-label antibiotic use, suggesting possible of resistance and misuse.

Estrogen receptor mediated neuroprotection in models of Alzheimers disease

Name: Heba Ali

Department: Neurobiology, Care science and society

Abstract

Background:

Alzheimer's disease (AD) exhibits strong sex differences, yet the molecular mechanisms underlying this dimorphism remain unclear. Estrogen receptor beta (ER β ; Esr2) has been implicated in neuroprotection, but its role in modulating sex-specific amyloid pathology and cellular responses in the AD brain is not fully understood. Using the AppNL-G-F knock-in mouse model of AD, this study investigates how Esr2 loss affects hippocampal cellular processes in males and females.

Methods:

Male and female AppNL-G-F and AppNL-G-F/Esr2KO mice were assessed at six months. Behavioral testing included Y maze, elevated plus maze, and fear conditioning. Pathology was evaluated using immunostaining, cytokine assays, and RT-qPCR. Single-cell RNA sequencing enabled cell-type annotation, ligand–receptor inference, and sex-stratified analyses.

Results:

Loss of Esr2 impaired associative memory in males but not females. Male Esr2-deficient mice showed increased hippocampal A β burden and higher insoluble A β 42/A β 40 ratios, while females remained largely unaffected. Single-cell analysis revealed disrupted endothelium-centered communication, particularly in males, with a shift toward the APP and PSAP pathways. Astrocytes and vascular cells showed both shared and sex-specific responses. Transthyretin (Ttr) was the most strongly sex-modulated gene, with reduced expression in male Esr2-deficient mice.

Conclusions:

ER β protects the male hippocampus by maintaining microglial, astrocytic, and vascular functions and may support TTR-mediated A β clearance. Females show resilience to Esr2 loss, possibly via ER α compensation. These findings highlight ER β –TTR signaling as a sex-specific neuroprotective axis in AD.

Bridging Bibliometrics and Mechanisms: A Framework for the Contextual Scoring and Biological Stratification of Scalable MeSH Co-occurrence Networks

Name: Jakob Sax

Department: IMM

Abstract

Systematic literature review of biomedical articles is often limited by the rigidity of search strings, potentially leading to inadequately designed queries that fail to identify non-obvious but highly relevant linked topics. While standard ontologies such as the MEDLINE database's Medical Subject Headings (MeSH) help facilitate the review process, relationships between terms and their relevance to the hypothesis of interest is not often explicitly stated. We present here a MeSH term extraction and networking technique based on an initial query of the disease Allergic Contact Dermatitis to form a “themed” network of terms. This is accomplished by constructing a co-occurrence network and applying an unbiased consensus pruning strategy through combining Simulated Annealing and Global Likelihood Filters to isolate a significant core subgraph. Furthermore, a novel hybrid scoring system consisting of Article Relevance Scores (ARS) and Contextual Relevance Scores (CRS) is introduced to evaluate a node's topical importance to the final subgraph's central theme within the context of the entire literature corpus. The final graph revealed distinct community themes and hierarchies. When terms were stratified by biological levels resembling those within Adverse Outcome Pathways (AOP), Molecular and Cellular groupings exhibited higher baseline relevance or boost by association compared to other strata. We demonstrate an unbiased, dynamic data-driven approach to quantitatively assess associated MeSH terminology for its relevancy to a queried network, further assisting biomedical literature review and hypothesis evaluation. Our results show this technique effectively identifies biologically relevant concepts and key relationships directly associated to an initial hypothesis.

Distinct antiviral T cell immunity patterns against common viruses and its correlation with SARS-CoV-2 seroconversion

Name: Jia Qi Lee

Department: Laboratory medicine (LabMed)

Abstract

The importance of the cell-mediated immunity for protection against severe disease was emphasised during the COVID-19 pandemic. In addition to their antiviral functions, T cells promote IgG seroconversion, whose link to infection clearance is well known. Yet, the interplay between SARS-CoV-2-specific T cells and seroconversion is not well established. Thus, the aim of this study is to characterise antigen-specific memory (m) CD4⁺ T cells against SARS-CoV-2 and other common viruses in healthy young adults (n=80; 24-27 years old) in relation to SARS-CoV-2 seroconversion status.

Serotonin and serotonergic inputs modulate cholinergic interneurons in the striatum on different timescales

Name: Joseph Baxendale

Department: Neuro

Abstract

The striatum, the major input hub of the basal ganglia, integrates converging glutamatergic and GABAergic inputs from cortical and subcortical regions, along with modulatory dopaminergic signals from the midbrain that are critical for motor initiation, learning, and reward. In addition, approximately one-third of serotonergic neurons in the dorsal raphe nucleus project to the striatum, yet the influence of serotonin on striatal circuits remains less well understood. Here, we examined how serotonin and serotonergic inputs affect striatal cholinergic interneurons (ChINs). ChINs regulate action selection and reinforcement signalling by exerting inhibitory control over medium spiny neurons and are interconnected through polysynaptic pathways, enabling widespread coordination across the striatum. Using paired whole-cell recordings combined with pharmacological manipulations, we found that serotonin modulates ChIN intrinsic excitability and suppresses polysynaptic inhibitory interactions between them via 5-HT₂ receptors. Furthermore, optogenetic activation of striatal serotonergic fibres revealed a fast, monosynaptic glutamatergic input onto ChINs. Together, these findings identify previously unrecognized mechanisms by which serotonin and serotonergic projections modulate ChIN networks, highlighting the intricate interplay between acetylcholine, dopamine, and serotonin in shaping striatal function. Given the broad influence of ChIN activity, serotonergic modulation likely has widespread consequences for striatal circuits and may provide insight into the mechanisms underlying non-motor symptoms of Parkinson's disease.

Widespread variants of the highly polymorphic Plasmodium falciparum vaccine candidate antigen MSP2 across Sub-Saharan Africa

Name: Julia Zerebinski

Department: MedS

Abstract

A multicomponent vaccine is increasingly recognized as a necessary tool to control and eliminate malaria globally. However, genetic diversity in *Plasmodium falciparum* poses a significant challenge, particularly for blood-stage antigens associated with protective immunity. Individuals in endemic regions acquire clinical immunity without exposure to all antigenic variants, suggesting that a deeper understanding of antigen diversity could inform more effective vaccine strategies. We explored the genetic diversity of the polymorphic antigen merozoite surface protein 2 (MSP2), in 2761 *P. falciparum* isolates collected across Sub-Saharan Africa. Notably, several size variants were consistently overrepresented across geographical regions, transmission intensities, and time points. These variants comprised multiple unique sequences, of which several were geographically and temporally widespread. Similarities in sequence composition and gene length of this highly polymorphic antigen across Africa underscores the potential of newly identified common MSP2 variants as targets for next-generation, multicomponent malaria vaccines.

Pauci cellular proteomics of FACS-sorted cell populations - Lymph Node Atlas

Name: Kovi Rishya Shrung Govindarajan

Department: OnkPat

Abstract

We have separated reactive lymph node and tonsil samples into FACS cell compartments which were then analysed by low-cell number proteomics. Samples from 8 different donors yielded a total of 467 samples which comprised of 24 different immune cell types. The higher sensitivity of our analysis methodology allows to capture the proteome of rare cell populations. We plan to use this as a surrogate for a healthy base line against which the proteome of cancer cells can be compared to. This allows us to decipher the phenotype of the tumour cell type and its associated immune escape mechanisms.

Identification of an IDO-1 inhibitor reducing growth of pancreatic ductal adenocarcinoma cells, but with little effect on surrounding stromal cells

Name: Leon Heffinger

Department: LabMed

Abstract

Pancreatic ductal adenocarcinoma (PDAC) remains an unmanaged disease with only small improvements in overall and median survival times in the past decades. One problem is the small selection of recognized therapies for PDAC and a second is the density of the tumor, making drug delivery more difficult than in well vascularized tumors. Thus, we carried out a high throughput drug screen (HTS) to identify auxiliary treatments for PDAC and applied a 3D cell culture model which incorporates with pancreatic stellate cells/cancer associated fibroblasts a major aspect of the dense stroma prevalent in this disease.

The HTS was carried out with a 3D cell co-culture model, consisting of Panc1 and human pancreatic stellate cells (hPSC) to form heterospheroids. We developed an automated-image-based digital viability assay, which was further refined to also identify phenotypical changes upon treatment. Additionally, this digital assay showed to be robust against pan-assay interference compounds (PAINS).

We identified an inhibitor of indoleamine 2,3-dioxygenase 1, (iIDO-1) to exert a significant growth inhibitory effect on PDAC cells (Panc1, MiaPaCa-2), while sparing the stromal component of the heterospheroid. It will be interesting to see if this iIDO-1 can synergize with commonly used chemotherapeutics to more specifically attack the cancer cells and reduce the systemic toxicity at the same time.

We used an image-based high throughput screen to identify an IDO-1 inhibitor that has a growth inhibitory effect on pancreatic cancer cells with little effect on surrounding stromal cells.

Automated Quantification of Tumour Length in Digitised Prostate Core Needle Biopsies by Rule-Based Algorithm

Name: Luana Xuan Liu

Department: MEB

Abstract

Accurate assessment of tumour length in prostate biopsy cores is essential for treatment decisions, particularly when selecting patients for active surveillance. However, no standardized measurement protocol exists, and pathologists often apply different approaches—such as bridging or excluding benign gaps—leading to substantial inter-observer variability. Combined with increasing biopsy workloads and a shortage of specialists, this underscores the need for automated and standardized solutions.

In this study, we developed an automated method to quantify tumour length in digitized prostate core needle biopsies. Tumour probability maps were generated using a previously developed AI model for prostate cancer detection and grading. These maps were processed using a rule-based algorithm incorporating skeletonisation, which estimates tumour length by thresholding and extracting medial axes within tumour regions. As a comparison, an XGBoost model was retrained using aggregated tumour probability features.

The rule-based method demonstrated stable performance across development, internal, and external validation cohorts, achieving mean absolute errors (MAE) of 1.08 mm, 1.41 mm, and 1.57 mm, respectively, with Pearson correlation coefficients above 0.86. This outperformed the XGBoost baseline and approached the lower bound of variability reported among human observers. Outlier analysis revealed that most discrepancies were due to boundary artefacts at tissue edges.

In conclusion, the proposed rule-based algorithm provides accurate, consistent, and reproducible tumour length measurements, offering a clinically meaningful and standardized tool to reduce variability in prostate cancer assessment.

The Annoying Orange: Dissociating the Roles of HumanLikeness and Eye Gaze Dynamics for Awareness Attribution

Name: Luca Verschure

Department: CNS

Abstract

Although consciousness is often conceptualized as individual, its etymology (conscientia; “to know with”) highlights its inherently social dimension. Humans appear to have evolved mechanisms that tailor behaviour toward agents perceived as conscious. Attention Schema Theory (AST) proposes that the brain constructs a model of its own attention that is used to predict and attribute awareness to others. One of the most important cues for inferring others’ awareness is gaze (Calder et al., 2002; Frischen et al., 2007; Ziman et al., 2023). Preliminary results from our lab indicate high sensitivity to real versus artificially shuffled gaze dynamics.

However, we hypothesise that this sensitivity depends on socially meaningful context: the face must still resemble a human. To test this, we manipulate human-likeness while preserving the properties of natural and shuffled gaze videos. Stimuli vary along a continuum from fully human faces to increasingly orange-like forms, progressively removing social salience while maintaining gaze dynamics.

We are collecting data from a neurotypical cohort (N = 40) and an autism cohort (N = 120). We predict that as avatars become more orange-like, accuracy and confidence in distinguishing real from shuffled gaze will decline. We further predict that autistic participants will perform relatively better with orange-like stimuli than neurotypicals, possibly because reduced social cues lessen constraints typically associated with human faces. By dissociating human-likeness from gaze dynamics, this study aims to clarify how perceived awareness emerges from visual input and how social context shapes it. These findings may refine models of social perception and awareness attribution.

Cell differentiation as a superposition of dynamical modes

Name: Magnus Tronstad

Department: MedS

Abstract

Cell differentiation is an essential biological process that enables a rich diversity of specialized cell types. Single-cell RNA-sequencing enables the capture of a snapshot of a cell differentiation process at single-cell resolution. This has revealed complex differentiation landscapes by sequencing cells from all stages of development in a single snapshot. However, we still lack a detailed description of how genes are expressed and co-expressed across development, and many differentiation trajectories remain largely unknown at the transcriptional level. Here, we develop a mathematical framework for estimating gene regulatory networks across complex cell differentiation processes captured in a single cell snapshot. We approximate the complex, nonlinear, cell differentiation dynamics by formulating it as a superposition of multiple, much simpler, dynamical systems. This approach provides a highly expressive - yet interpretable and explainable - model of gene expression dynamics and enables us to study how gene regulatory networks change across the entire differentiation process. We apply our framework to snapshot data from hematopoiesis, demonstrating its ability to learn lineage-specific gene expression trajectories in a complex branching system. Our approach also provides a generative framework for simulating trajectories in silico from initial conditions, and to infer difference-making genes involved in fate decision.

Biophysical remodeling of aging

Name: Maria Tsiokou

Department: CMB

Abstract

Immunosenescence is characterized by functional decline and altered cellular phenotypes that collectively impair host defense during aging. Although molecular and transcriptional alterations in senescent immune cells have been extensively studied, the contribution of biophysical properties—such as membrane fluidity—to immune aging remains poorly understood. We hypothesized that immune cells undergo biophysical remodeling as they transition to a senescent state, and that these changes contribute to age-associated immune dysfunction.

To test this hypothesis, we employed organelle-specific probes to assess membrane fluidity and mitochondrial membrane potential, combined with high-throughput spectral flow cytometry for quantitative single-cell analysis of T cells. In parallel, we utilized a molecular pixelation approach to characterize age-related alterations in the cell surface protein interactome, including protein abundance, clustering, and colocalization patterns.

Methodological validation comparing immune cells from young and older donors revealed distinct age-associated shifts in membrane order. We identified subpopulations exhibiting altered membrane fluidity during aging and functionally characterized these subsets. Notably, T cells with higher membrane fluidity displayed a more inflammatory phenotype. Furthermore, molecular pixelation analysis uncovered unique patterns of surface marker colocalization in aged immune cells compared to those from young donors.

Collectively, our findings suggest that biophysical remodeling is a conserved feature of immune cell senescence and may contribute to immune frailty during aging. Ongoing studies aim to elucidate the mechanistic links between altered membrane dynamics and functional decline, with the ultimate goal of identifying strategies to restore immune function in aging populations.

Challenges for general practitioners in post-stroke follow-up within a fragmented healthcare system – a qualitative study

Name: Maria Wolf

Department: NVS

Abstract

Background: Secondary medical prevention after stroke is effective and well evidenced making long-term follow-up crucial. This follow-up is mainly made by general practitioners (GPs) in Sweden. A study from 2022 described low target achievement and an up to fourfold practice variation in dispensation of secondary preventive drugs between different primary care units in Region Stockholm. Although several factors at individual practices have been observed to be associated with insufficient target achievements, the underlying reasons for this variation are unclear.

Objectives: To explore the perspectives of GPs concerning secondary preventive practices after stroke to shed light on areas of improvement

Methods: This qualitative study was based on eight focus group discussions with 49 GPs in Region Stockholm. They were strategically invited in relation to target achievement, and the interviews were performed using a semi-structured interview guide. The interviews were transcribed and analysed using qualitative content analysis.

Results: The overall theme that emerged was “Difficult mission for GPs following up stroke”. The theme was underpinned by two sub-themes: “Multifaceted mission in an insufficiently organized healthcare system” and “The complexity of adherence”. There were six main categories that encompassed shortcomings in the areas of: sufficient time for the patients, the overarching structure of the healthcare system, the internal structure of follow-ups, medical adherence, the responsibility for renewals of medication and tools for adherence.

Conclusion: The perspectives of GPs revealed structural problems at different levels in the health care system as well as difficulties in handling medication adherence indicating a need for improvement.

Impact of Quorum Sensing on Human Skin Response to Staphylococcus aureus

Name: Mariam Shahata

Department: MedS

Abstract

Antibiotic-resistant infections are increasing globally, yet effective alternatives to antibiotics remain limited, posing a major public health challenge. Methicillin-resistant Staphylococcus aureus (MRSA) is a leading cause of resistant infections. Although S. aureus commonly colonizes human skin without causing disease, it can also cause severe and invasive infections. Virulence in S. aureus is regulated by auto-inducing peptides (AIPs) that signal through a quorum sensing (QS) pathway, primarily the accessory gene regulator (agr) system. Murine skin infection models show that agr becomes activated during infection and that interference with this signaling using inhibitory AIPs can suppress agr activity and prevent skin infections. However, the mechanisms that trigger initial agr activation upon contact

with human skin remain unclear. Here, we investigate how QS signaling is initiated during early *S. aureus* colonization using an ex vivo human skin model. Skin samples were infected with *S. aureus* and analyzed at 6, 24, and 48 hours post-infection. Microscopy localized agr-active bacteria within the skin tissue, while quantitative PCR quantified agr gene expression. Host immune responses were assessed by measuring IL-1 β and IL-8 secretion using ELISA. Preliminary results indicate that agr is activated during early colonization and changes dynamically over time, while IL-8 secretion increased as infection progressed. Ongoing work will evaluate AIP inhibitors from *Staphylococcus* species and other skin commensals to determine their ability to suppress agr signaling during colonization.

Novel approaches to study rheumatoid arthritis-associated anti-citrulline T cell reactivity

Name: Marlene Schüle

Department: MedS

Abstract

While autoreactive T cells recognizing citrullinated antigens have been implicated in rheumatoid arthritis (RA), they remain rare and difficult to study and are not reflected by current animal models. To accelerate the investigation of RA autoantigens we are exploring adeno-associated virus (AAV) mediated knock-in of patient-derived TCRs into murine T cells.

AAVs were used to knock-out the endogenous TCR β chain and knock-in a TCR of interest at the TCR α constant locus of CD4 $^{+}$ T cells isolated from Cas9-expressing mice. To allow investigation of several TCRs at once, AAVs were engineered to carry patient-derived TCR sequences followed by a unique triple peptide code (Flowcode), allowing identification of T cell clones by flow cytometry.

AAV-transduced murine CD4 $^{+}$ T cells respond to their cognate antigen in an HLA-restricted manner in vitro. After single peptide stimulation of CD4 $^{+}$ T cells transduced with a pool of AAVs carrying distinct TCRs, we observed clonal expansion of antigen-specific T cells. In addition, transfer of pooled AAV-transduced CD4 $^{+}$ T cells into HLA-DRB1*0401 recipients followed by immunization with relevant peptides was used to confirm antigen-specific T cell activation and expansion in vivo.

To summarize, AAV-mediated knock-in of patient-derived TCRs into murine CD4 $^{+}$ T cells generates functional and HLA-restricted antigen-specific T cells, and pooled TCR re-expression allows simultaneous study of distinct reactivities. This study constitutes the initial steps towards building a platform to explore patient-derived TCRs in a humanized murine setting, both in vitro and in vivo, while facilitating data translation from animal models into (pre)clinical settings.

[Title not provided in submitted data]

Name: María de los Reyes Becerra Pérez

Department: MedH

Abstract

Acute myeloid leukemia (AML) is a heterogeneous disease on both the molecular- and phenotypic level, caused by malignant transformation of hematopoietic progenitor cells during clonal hematopoiesis.

During preleukemic evolution and disease progression, affected hematopoietic cells gradually accumulate a range of molecular alterations, including somatic mutations, cytogenetic abnormalities, epigenetic alterations, and transcriptomic changes. Epigenetic regulators are known to be dysregulated at an early stage of leukemogenesis and are an important source for potential therapies.

To date, substantial progress has been made in the understanding of AML pathogenesis with respect to genomic or proteomic abnormalities, but our knowledge about the metabolic behaviour of leukaemia is far from satisfactory. Understanding how different metabolic pathway alterations could result in cellular abnormalities could bring new insights into finding novel biomarkers in AML.

Given that metabolic reprogramming is generally regarded as a hallmark of cancer cells, studies are now aiming to report on the link between serum metabolites and cytogenetic abnormalities and treatment response in AML. In the Andreas Lennartsson lab, my PhD project explores how metabolic enzymes influence gene regulation in AML through epigenetic mechanisms. Focusing on their non-canonical "moonlighting" roles in the nucleus, we seek to understand how these enzymes are recruited to chromatin, potentially through long non-coding RNAs and transcription factors. Further, we aim to

characterise novel metabolism-linked histone modifications, which may drive or suppress leukemogenesis. Ultimately, the work aims to uncover how these processes drive leukemia progression and lineage switching, identifying potential therapeutic targets.

Validation of Diagnostic Artificial Intelligence Models for Prostate Pathology in a Middle Eastern Cohort

Name: Navin Vincent

Department: MEB

Abstract

Artificial intelligence (AI) for pathology is accelerating cancer diagnostics. For global adoption, studies in currently under-represented populations – where the potential gains from AI may also be greatest – are needed. We present the first external validation study in a Middle Eastern setting, focusing on diagnosis and Gleason grading of prostate cancer. We digitised 339 prostate biopsies from Kurdistan, Iraq, representing a consecutive series of 185 patients from 2013-2024. Task-specific and foundation AI models demonstrated pathologist-level performance with AI-pathologist grading concordance similar to pathologist-pathologist concordance (Cohen's quadratically weighted kappa 0.801 vs. 0.799, $p=0.9824$). Cross-scanner concordance was high (kappa > 0.90) for all AI models across three scanners. Demonstrated robust performance on a low-cost compact scanner could enable validation studies in non-digitalised settings and cost-effective AI adoption in laboratories with limited sample volumes. The publicly shared dataset supports further research to accelerate globally equitable uptake of AI pathology.

Reward, Social Learning, and Habit in Posting Choice on Social Media

Name: Oromia Godanna Sero

Department: Clinical Neuroscience

Abstract

Social media has transformed how people create and share information at scale. Individuals repeatedly decide what to post while observing others' posts in their social network and receiving feedback in the form of engagement (likes, reposts, replies). Although a large body of work has examined population-level outcomes such as virality, misinformation, and polarization, less is known about the individual mechanisms that underlie these repeated posting choices. Here, we ask how feedback, social learning, and habit jointly shape what people choose to post over time.

To address this question, we analyze 3.8 million posts from 1,598 Bluesky users. We model each post's content using a transformer-based topic model, which yields a probability distribution over interpretable topics and allows us to track how users' topic choices shift over time. To capture social learning, we reconstruct each user's recent Following Feed on Bluesky's default chronological, non-ranked feed and derive topic-level social features, including how often topics appear, how much engagement they receive, and how popular their authors are.

We then compare computational models of posting behavior: an asocial reinforcement-learning model based on users' own past rewards, a social feature learning model that incorporates feed-derived social information, a habit model capturing topic repetition independent of reward, and hybrid models combining these mechanisms. Across users, a hybrid model combining social feature learning and habit provides the best overall account of posting behavior, indicating that no single mechanism alone sufficiently explains what people choose to post.

Human lung tissue exhibits stimulus-specific, time-dependent activation of oxylipin pathways

Name: Rana Melisa Seren

Department: IMM

Abstract

Introduction: Oxylipins are lipid mediators that can regulate inflammatory responses in the human lung; however, stimulus-specific kinetics are poorly defined.

Aim: To determine the influence of inflammatory stimuli on the magnitude and kinetics of oxylipin formation in human lung tissue.

Methods: Isolated human lung tissue (N=5-7) was stimulated with 50 µg/mL anti-human IgE antibody (anti IgE), 10 µM calcium ionophore (A23187), a type 1 cytokine mix of each 100 ng/mL IL-1β, TNFα, IL-6 and 200 ng/mL IL-6R (T1), or a type 2 cytokine mix of each 100 ng/mL IL-5, IL-13, IL-25, IL-33, TSLP (T2) for 5, 15, or 60 min. Oxylipins were quantified from tissue homogenates using mass spectrometry.

Results: Of 110 oxylipins screened, 45 were detected in isolated human lung tissue across all treatments and time points. Anti-IgE triggered a rapid, early increase dominated by cyclooxygenase-derived metabolites, peaking at 5–15 min ($p \leq 0.05$). In contrast, calcium ionophore elicited a delayed, lipoxygenase skewed increase, that was most prominent at 60 min ($p \leq 0.05$). The T1 cytokine mix caused a suppression of oxylipin levels relative to control tissue ($p \leq 0.05$), whereas T2 cytokines produced no significant change.

Conclusion: Intact human lung tissue exhibits stimulus-specific, time-dependent oxylipin responses. These distinct kinetic fingerprints highlight endotype-relevant lipid mediator pathways that may exert a role in inflammatory airway diseases, demonstrating that each stimulation need to be evaluated on an individual basis.

An in vivo platform to study the crosstalk between the exocrine and endocrine pancreas in health and disease

Name: Riccardo Lizzani

Department: MMK

Abstract

The endocrine and exocrine pancreas exert distinct functions despite cohabiting the same organ. For this reason, they have been long studied separately by different medical fields. Accumulating evidence shows that these two tissues strongly influence each other, also due to their vascular interconnection. However, longitudinal studies on the pancreas are limited by lack of valuable in vitro models, the fast loss of acinar phenotype upon isolation, and the optical inaccessibility of the organ in vivo.

In our work, we mimic the exocrine-endocrine crosstalk outside the pancreas by transplanting acinar-derived spheroids together with pancreatic islets into the anterior chamber of the mouse eye. By transplanting exocrine spheroids after 2 days in culture, they get vascularized, regain their acinar morphology, and can be non-invasively monitored overtime by confocal microscopy. Characterization performed on explanted grafts with immunofluorescence and transmission electron microscopy shows amylase expression, cell granularity and polarization, and presence of a common lumen in the acinus center. Blood is flowing in the graft, but only unidirectionally from the islet to the exocrine part.

Overall, this novel approach has the potential to overcome major limitations on pancreatic research by enabling longitudinal and non-invasive studies in an in vivo setup, refining animal usage and allowing for microvasculature and functionality studies by implementation of fluorescent probes. Additionally, morphological and functional changes may be detected upon administration of xenobiotics in toxicological studies or upon induction of pathological conditions in the experimental animal, i.e. diabetes or pancreatitis.

Deciphering the impact of CAPRIN1 on post-transcriptional regulation in stress response.

Name: Riccardo Mosca

Department: MTC

Abstract

Hepatocellular carcinoma (HCC) remains difficult to treat due to high recurrence and limited response to existing therapies. Our work investigates how RNA regulation influences drug response in HCC, particularly under treatment with Sorafenib, a first-line tyrosine kinase inhibitor targeting cell cycle and stress-response pathways.

RNA regulation occurs at both transcriptional and post-transcriptional levels. RNA-binding proteins (RBPs) are key post-transcriptional regulators that interact with RNA to control cellular processes. We

have shown that Sorafenib induces the formation of stress granules (SGs) in liver cancer cells, which may contribute to drug resistance. Notably, we identified CAPRIN1 as a critical factor in SG maturation. CAPRIN1 is reactivated in HCC and appears to support cancer cell adaptation to drug-induced stress.

To understand CAPRIN1 function, we developed RAPseq, an in vitro RBP-centric method that identifies and quantifies RBP binding sites across transcriptomes. Using RAPseq, we found that CAPRIN1 preferentially binds RNAs involved in cell cycle and stress responses.

To complement this, we are applying APEX-seq in living cells under Sorafenib treatment to map CAPRIN1-associated RNA proximity in situ. Integrating RAPseq (direct binding) with APEX-seq (cellular context) will reveal how CAPRIN1 redistributes RNAs during stress.

We hypothesize that CAPRIN1 sequesters key transcripts into SGs to transiently repress translation, promoting tolerance to therapy. These findings suggest CAPRIN1-dependent RNA networks as biomarkers of treatment response and potential targets for combination therapies to overcome resistance.

ISG15-Dependent Immunometabolic Regulation during RNA Virus Infection and Viral Interference of host ubiquitylation and ISGylation Events

Name: Sefanit Rezene

Department: LabMed

Abstract

The innate immune response is the first line of defense against pathogens and depends on precisely tuned signaling networks. Conjugation of ubiquitin (Ub) or Ub-like modifiers such as interferon-stimulated gene 15 (ISG15) regulates protein fate and antiviral signaling, while viral deubiquitinases (vDUBs) and deISGylases (vDISGs) counteract these modifications to suppress host defenses. Our work investigates ISG15's role in immunometabolic regulation and how viral proteases PLpro (SARS-CoV-2) and OTU-L (CCHFV) target Ub and Ub-like pathways, using quantitative and affinity-based proteomics approaches.

TMT-labeled mass spectrometry in Huh7 wild-type and ISG15-knockout cells revealed broad induction of interferon-stimulated genes (ISGs) in the absence of ISG15, supporting its role as a negative regulator of antiviral signaling. The antiviral enzyme viperin (RSAD2), which produces the chain-terminating metabolite ddhCTP, was strongly upregulated in ISG15-deficient cells. This regulation occurs at the transcriptional level, and increased viperin expression enhanced resistance to both SARS-CoV-2 and CCHFV. HPLC analysis confirmed elevated ddhCTP levels in ISG15-knockout cells, while viperin knockdown reversed these effects, demonstrating that ISG15 modulates antiviral restriction through viperin control.

To define viral interference of host ubiquitylation and ISGylation, we performed affinity-based mass spectrometry to identify cellular targets of PLpro and OTU-L under resting and infection-like conditions. PLpro substrates were identified in the RIG-I signaling pathway, and PLpro overexpression disrupted K63-linked ubiquitination of RIG-I and MAVS, dampening type I interferon responses. Collectively, these findings position ISG15 as a critical regulator linking antiviral defense and metabolism, while revealing how viral protease exploit these host networks for immune evasion.

Semantic knowledge guides innovation and drives cultural evolution

Name: Shen Tian

Department: CNS

Abstract

Cultural evolution allows ideas and technologies to accumulate across generations, reaching their most complex and open-ended form in humans. While social learning enables the transmission of such innovations, the cognitive processes that generate them remain poorly understood. Classical theories typically treat innovation as random variation, a simplification insufficient for explaining the complexity of human cultural evolution. We propose that semantic knowledge—the associations linking concepts to their properties and functions—guides human innovation and drives cumulative culture. To test this, we combined an agent-based model, which examines how semantic knowledge shapes cultural evolutionary dynamics, with a large-scale behavioral experiment (N = 1,243) testing its role in human innovation. Across both approaches, we found that semantic knowledge directed exploration toward

meaningful solutions, enhanced innovation success, and enabled generalization from prior discoveries. Moreover, semantic knowledge interacted synergistically with social learning to amplify innovation and accelerate cumulative cultural change. In contrast, experimental participants lacking access to semantic knowledge performed no better than chance, even when social learning was possible, and relied on shallow exploration strategies for innovation. Together, these findings suggest that semantic knowledge is a key cognitive process underpinning human cumulative culture.

L-tryptophan suppresses HIV-1 latency reversal through metabolic reprogramming in pre-monocytic cells

Name: Sofja Poznakovs

Department: LabMed

Abstract

Despite advancements in antiviral therapy, human immunodeficiency virus 1 (HIV-1) remains a significant global health concern. Viral reservoirs represent the primary challenge in achieving a functional cure. While myeloid cells may contribute to HIV-1 latency, the mechanisms remain poorly understood. Emerging evidence suggests that cellular metabolism plays an important role in regulating HIV-1 latency and reactivation. Based on this, we investigated whether specific amino acids influence HIV-1 reactivation in myeloid cells. To address this, we treated the pre-monocytic U1 cell line with seven amino acids and assessed their effects on HIV-1 latency reversal following stimulation with phorbol 12-myristate 13-acetate (PMA). Reactivation from latency was evaluated using flow cytometry. From this initial screen, L-tryptophan was selected for further investigation due to its pronounced modulatory effect. To examine the durability of this response, L-tryptophan-treated cells were incubated in fresh media for 48 hours prior to PMA stimulation and analyzed by flow cytometry and quantitative real-time PCR. Here, we show that L-tryptophan treatment significantly reduces HIV-1 reactivation following PMA stimulation and that this inhibitory effect is maintained for up to 48 hours post-treatment. These findings indicate that metabolic pathways associated with L-tryptophan play an important role in regulating HIV-1 latency. Our results highlight L-tryptophan metabolism as a potential target for modulating viral reactivation and support further investigation of metabolic interventions as part of HIV-1 cure strategies.

From Metabolism to Mechanics: Targeting Filament-Forming Metabolic Enzymes in Cancer

Name: Spyridon Pantelios

Department: LabMed

Abstract

Nucleotide biosynthesis is a central determinant of proliferative capacity and is often limited by fluctuating nutrient availability and metabolic stress. While metabolic enzymes are classically defined by their catalytic roles, their capacity to undergo higher-order assembly suggests additional functions that remain poorly understood. Here, we show that under nucleotide-limiting conditions, a metabolic enzyme undergoes a structural transition into filamentous assemblies that associate with the intermediate filament cytoskeleton. These filaments adopt a defined intracellular organization, aligning with cytokeratin and vimentin networks through non-covalent interactions. Disruption of filament formation does not impair enzymatic activity but alters cytoskeletal engagement and limits cell spreading under stress conditions. Notably, filament organization parallels cytoskeletal remodeling during adhesion, with increased association cytoskeletal structures. These findings identify a stress induced structural adaptation that links metabolic state to cytoskeletal organization, suggesting a mechanism by which cancer cells coordinate metabolic constraints with mechanical properties required for growth and adaptation.

Differentiated Myeloid Progenitors as a Model for Chimeric Antigen Receptor Neutrophil Function

Name: Stan de Haan

Department: MedH/HERM

Abstract

Neutrophils are the most abundant leukocytes in the body and constitute a large fraction of immune cell infiltrate across cancer types, including “cold” tumours that secrete chemokines such as CXCL8/IL-8 to recruit CXCR1/2-expressing neutrophils. This makes them attractive candidates for anti-cancer immunotherapy. However, neutrophils display pro- and anti-tumour plasticity in the tumour microenvironment, and modifying their behaviour is difficult and transient due to their short lifespan.

To overcome this, we generated an inducible mouse myeloid progenitor model by expressing an oestrogen receptor (ER)-HoxB8 fusion in bone marrow-derived progenitors. This enables long-term expansion in the presence of oestrogen and controlled differentiation upon its withdrawal. Upon culture with G-CSF and AM580, ER-HoxB8 cells differentiate into neutrophil-like cells upregulating mature markers Ly6G (>60%) and CXCR2 (>80%), while the progenitor marker c-kit is reduced to <10%. Moreover, they display key effector functions with phagocytosis comparable to primary neutrophils and >4-fold higher ROS production upon stimulation than undifferentiated progenitors. This establishes the HoxB8-ER system as a controllable neutrophil platform suitable for genetic engineering.

We will exploit this platform to systematically evaluate a panel of novel chimeric antigen receptor (CAR) constructs incorporating different immunoreceptor tyrosine-based activation motif (ITAM) configurations and co-stimulatory domains. These will be introduced at the progenitor stage and functionally assessed after neutrophil differentiation. Our goal is to identify CAR designs that impose anti-tumour programs on neutrophils and enhance antigen-specific phagocytosis, ROS production and tumour cell killing in neutrophil-like cells, and to utilise these for subsequent validation in mouse models of solid tumours.

Human Placental Stem Cell–Mediated Immunomodulation Promotes Neuroprotection in the SOD1 G93A ALS mouse model

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Abstract

Amyotrophic Lateral Sclerosis (ALS) is a progressive, fatal neurodegenerative disorder defined by the selective loss of upper and lower motor neurons, leading to muscle atrophy and eventual paralysis. While neuronal death is the primary pathological feature, emerging evidence highlights the critical role of neuroinflammation in driving both the disease onset and progression, specifically regarding microglial activation and T-cell infiltration. These observations suggest that targeting specific brain immune cells is a promising therapeutic strategy for ALS. Specifically, human Amniotic Epithelial Stem Cell (hAEC) based immunotherapy has emerged as a potent approach to address neuroinflammation by shaping the immune landscape in favor of neuroprotection.

To investigate this approach, our group administered hAEC via cisterna magna injection directly into the cerebrospinal fluid of the SOD1 (G93A) mouse model. Stem cells were delivered before disease onset in both male and female cohorts. Our results demonstrated that hAEC injections significantly delayed disease onset and extended overall survival, with a notably more pronounced benefit observed in female mice. Flow cytometry analyses revealed an increase in protective immune cell populations, including immunoprotective Arginase-1 positive (Arg1⁺) macrophages in both brain and spinal cord, as well as the emergence of an inflammation-resolving population of myeloid-derived suppressor cells with eosinophilic features.

Together, these findings support stem cell-based immunotherapy delivered into the cerebrospinal fluid as a promising strategy to modulate neuroinflammation and modify disease progression in ALS, with potential sex-specific differences in therapeutic response.

Pain is associated with disease activity in idiopathic inflammatory myopathies in a longitudinal 10-year follow-up single-centre study

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Abstract

Background: Idiopathic inflammatory myopathies (IIM) constitute a group of rare autoimmune diseases with high morbidity and mortality. Pain is a prominent and persistent symptom, ranked as one of the most important symptoms by patients with IIM. However, the longitudinal association between pain and disease activity in IIM remains unclear.

Aim: To investigate the longitudinal association between pain and disease activity over 10 years after diagnosis in adult patients with IIM.

Methods: A dataset of all patients in the Karolinska Myositis Cohort was extracted from SweMyoNet, the module for IIM from the Swedish national registry for patients with rheumatic diseases, on June 2, 2025 (n=755). Patients with missing baseline data and those belonging to diagnostic subgroups with fewer than 21 individuals were excluded. From the remaining cohort, patients with assessment at baseline, and with available longitudinal visit data up to 10 years of follow-up were included. Patients were classified according to the EULAR/ACR 2017 criteria for IIM. Pain was assessed using a Visual Analogue Scale (VAS) (0–100 mm), where 0 indicates no pain. Pain severity was determined as mild (0–30), moderate (>30 – 70), or severe (>70–100). Disease activity was measured by the Physician Global Assessment (VAS) and the Myositis Disease Activity Assessment Tool (MDAAT). Within MDAAT, we also considered separately six organ-specific VAS scores, the composite score MYOACT, muscle disease activity, and global disease activity. Muscle weakness and muscle inflammation were also assessed using the manual muscle test 8 (MMT8) and creatine kinase (CK) level, respectively. Associations were analysed using linear mixed-effects models, adjusted for age and stratified by sex.

Results: A total of 632 patients were included (61.6% women). Compared to men, women were younger at symptom onset (53.20 ± 15.61 vs 58.45 ± 15.92 , $p < 0.001$), at diagnosis (54.92 ± 15.38 vs 59.92 ± 15.38 , $p < 0.01$), and reported significantly higher levels of pain at first visit (median 29 vs 14, $p < 0.001$). Pain severity varied across diagnostic subgroups. Pairwise comparison showed that patients with inclusion body myositis had lower pain at baseline (median = 8) than patients with dermatomyositis (median = 29, $p < 0.01$), polymyositis (median = 23, $p = 0.03$), and overlap myositis (median = 29, $p < 0.001$).

Over the following 10 years after patients' inclusion in SweMyoNet, pain was associated with disease activity, both when measured by physician global disease activity ($\beta = 0.14$ men; $\beta = 0.19$ women, $p < 0.001$) and MYOACT ($\beta = 0.0003$ men; $\beta = 0.0004$ women, $p < 0.001$). Analysis of the separate items in MDAAT showed that pain was significantly associated with constitutional, cutaneous, and skeletal disease activity in both sexes (all $p < 0.05$). Pulmonary involvement was associated with pain only in women ($p = 0.010$), while gastrointestinal and cardiovascular domains showed no significant associations. Global disease activity and muscle activity domains were strongly correlated with pain in both sexes ($p < 0.001$).

Pain was associated with muscle inflammation (CK: $\beta = 0.27$ men; $\beta = 0.08$ women, $p < 0.01$) and muscle weakness (MMT8: $\beta = -0.04$ men; $\beta = -0.05$ women, $p < 0.001$). Subgroup analysis showed significant associations between pain and physician global disease activity in all diagnostic subgroups except inclusion body myositis. In immune-mediated necrotising myopathy, the association was found only in women ($\beta = 0.13$, $p = 0.02$).

Conclusions: Pain in idiopathic inflammatory myopathies was more pronounced in women and varied across diagnostic subgroups. Longitudinal analyses over 10 years demonstrated that pain was consistently associated with overall disease activity, muscle weakness, and systemic features. These findings show that pain is an important marker of disease burden. We recommend pain to be included in standardised outcome measures, treatment evaluation, and clinical care of patients with IIM.

Key words

Idiopathic inflammatory myopathies, myositis, pain, patient-reported outcome measures

Risk of Self-Harm Following Antidepressant Initiation Among Older Adults in Sweden: A Self-Controlled Case Series Study

Name: Theodore Tianyi Miao

Department: MEB

Abstract

Background:

Older adults have a high risk of self-harm and suicide and are frequently exposed to antidepressants. However, the risk of self-harm and suicide may vary across treatment periods and antidepressant classes, and evidence in older adults remains limited.

Objective:

To examine the risk of self-harm and suicide in relation to antidepressant initiation among older adults in Sweden, and to compare this risk across antidepressant classes.

Methods:

We linked the Total Population Register, National Patient Register, Swedish Prescribed Drug Register, and Cause of Death Register using unique personal identification numbers. Individuals aged 65 years and older with at least one recorded self-harm event or suicide during follow-up were included. Antidepressants were classified as selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), and other antidepressants. A self-controlled case series design was applied, and conditional Poisson regression was used to estimate incidence rate ratios (IRRs) for self-harm and suicide across prespecified risk windows relative to antidepressant initiation. Age was adjusted for as a time-varying factor using 5-year age bands.

Results:

We identified 21,357 older adults aged 65 years or older between 2007 and 2022 who had self-harm event and initiated antidepressant treatment. 60% were women; 45% initiated SSRIs, 5% SNRIs, 15% TCAs, and 35% other antidepressants. Analyses of IRRs across treatment periods are ongoing.

Conclusions:

Our preliminary findings suggest that antidepressant initiation patterns differ across classes among older adults with self-harm records. Clarifying how risk varies across treatment periods may help identify high-risk periods and inform prevention strategies.

Neuronal cell fate and maturation under antidepressant exposure: a multi-modal single-cell investigation

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Department: FyFa

Abstract

Prenatal exposure to antidepressants is increasingly common as rising rates of perinatal depression drive clinical need. Yet, despite widespread use of conventional selective serotonin reuptake inhibitors (SSRIs) and growing interest in rapid acting psychedelic therapeutics such as psilocybin, their impact on early human brain development remains poorly understood. This project investigates how traditional and rapid acting antidepressants influence neuronal cell fate, maturation, and multicellular interactions during critical periods of cortical development.

Using human derived cerebral organoids and fetal brain-derived organoids (FeBOs), we establish a developmental exposure paradigm to define physiologically relevant windows of vulnerability. We then employ single cell multi omic profiling (RNA seq, ATAC seq, nano Cut&Tag) to quantify lasting cell type specific transcriptomic and epigenomic alterations following chronic sertraline or acute psilocin exposure. Lineage tracing with viral barcoding allows us to map how these exposures shape human specific cell differentiation trajectories, identifying altered clonal dynamics or disruptions in neuronal fate commitment. In parallel, forebrain patterned organoid fusion models with fluorescent lineage reporters enable high content imaging of excitatory and inhibitory neuronal migration, complemented by functional readouts through calcium imaging and electrophysiology.

Together, this multimodal framework integrates molecular, spatial, and functional datasets to uncover mechanisms by which antidepressants reshape early brain development. By elucidating exposure

driven changes in differentiation, migration, and epigenetic regulation, this work provides foundational evidence to guide safer pharmacological strategies during pregnancy. These insights are essential for balancing maternal mental health needs with long term neurodevelopmental outcomes in exposed offspring.

Studies of adaptive NK cells in solid tumors

Name: Vera Danklmaier

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Abstract

The tumor microenvironment (TME) plays a central role in shaping cancer progression and response to immunotherapy by either suppressing or supporting anti-tumor immunity. Natural killer (NK) cells are key mediators of tumor surveillance; however, conventional NK (cNK) cells are often dysfunctional in solid tumors due to immunosuppressive conditions. In contrast, adaptive NK (aNK) cells show enhanced persistence, metabolic flexibility, and memory-like responses, yet their role in human solid tumors remains poorly understood. Evidence suggests that local immune niches, particularly tertiary lymphoid structures (TLS), may provide critical sites for immune cell priming. Within these niches, B cells can act as antigen-presenting cells and modulators of immune responses, raising the possibility that B-NK cell interactions contribute to aNK cell function. My PhD project aims to investigate how aNK cells interact with the TME, with focus on infiltration, functional adaptation, and crosstalk with B cells. To address this, we employ advanced in vitro 3D tumor models that recapitulate key architectural and immune features of ovarian cancer. Using multi-omics approaches, including immunofluorescence and spatial transcriptomics, we map the spatial organization of tumor and immune cells and identify key ligand-receptor interactions. Preliminary data indicate that aNK cells exhibit enhanced tumor infiltration and functional activity, supporting tumor surveillance. Ongoing work focuses on defining mechanisms underlying aNK cell persistence and memory-like responses, as well as their modulation through therapeutic interventions.

Overall, this project seeks to uncover fundamental principles of NK cell biology in solid tumors and explore the potential of aNK cells as a next-generation immunotherapeutic strategy.

Polygenic overlap and shared genomic loci between anorexia nervosa and cardiometabolic traits suggest shared biological mechanisms

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Abstract

Anorexia nervosa (AN) is a serious psychiatric disorder with prominent metabolic features, but few studies have revealed the genetic mechanisms underlying its metabolic component. Based on genome-wide association studies, we examine the shared genetic architecture between AN and seven common cardiometabolic traits (body mass index, low-density lipoproteins, systolic blood pressure, diastolic blood pressure, type 2 diabetes, coronary artery disease, and metabolic syndrome). MiXeR and linkage-disequilibrium score regression were adopted to quantify the genetic overlap. A conditional/conjunctive FDR framework was employed to identify shared genomic loci. Gene-based enrichment analyses were performed to reveal overlapping biological mechanisms. Colocalization tests were performed to prioritize colocalized shared variants. We identified moderate to substantial polygenic overlap between AN and cardiometabolic traits and 43 unique shared loci. Genes mapped to the shared loci were enriched for biological processes relevant to brain cell growth and migration, cytoplasmic region, water transport, and muscle development. Furthermore, we identified eight colocalized shared variants, demonstrating genetic associations and potential interactions with drugs for somatic conditions including cardiometabolic and neuropsychiatric disorders. Overall, this study reveals the biological underpinnings and clinical implications of the AN-metabolic component, providing novel insights into the etiology and gene-based treatment or prevention measures for AN.