May 22-23, 2025

2025 PHD CONFERENCE

BEYOND THE DEFENCE: UNLOCKING THE POTENTIAL OF A PHD

by DSA

Location
DJURÖNÄSET

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Day 1

Programme

07:30	Departure from Cityterminalen 
08:30-10:00	Registration and Breakfast

Morning Session

10:00-10:15	**Welcome and Introduction**
10:15-11:00	**Bob Harris** Academic Vice President for Doctoral Education
11:00-11:30	**Andreas Lundquist** KI Innovations
11:30-12:00	Break
12:00-12:45	**Richard Cowburn** Head of External Engagement Office – KI
12:45-14:00	Lunch 

Afternoon Session

14:00-14:30	**3MT Flash Talks by Doctoral Students**
14:30-14:45	**Sponsor Spotlight: Merck**
14:45-15:15	**Elena Hoffer** CEO – Alma.me
15:15-16:00	Check-In  , Bingo and Fika Break

Evening Session

16:00-16:30	**Jessica Gracias Lekander** Miltenyi Biotec
16:30-17:00	**Joanne Bakker** Technical Writer - Cytiva
17:00-18:15	**Fireside Chat with Speakers**
18:15-20:00	Dinner 
20:00-22:00	**Poster Session**

Day 2

Programme

07:30-08:45	Breakfast and Check out
09:00-9:10	**Introduction**
09:10-9:45	**Yoga and Mindfulness Session** with **Ina Schuppe Koistinen**
9:45-10:15	**Photo Session**

Morning Session

10:15-10:45	**Ina Schuppe Koistinen** Associate Professor – KI / Microbiome Expert / Entrepreneur / Artist
10:45-11:15	**Samer Yammine** Serial Entrepreneur – Stockholm School of Entrepreneurship
11:15-11:45	Bingo and Fika Break
11:45-12:15	**Armando Cázares-Körner** Head of Community – The Park
12:15-12:45	**Mark Smith** Prof. Emeritus – KTH / Co-founder and Director – Autotelics AB
12:45-14:00	Lunch & Mingle

Afternoon Session

14:00-14:40	**3MT Flash Talks by Doctoral Students**
14:40-15:00	**Sponsor Spotlight: ABC Labs**
15:00-15:30	**Alfredo Gimenez-Cassina** Senior Editor – Nature Metabolism & Springer Nature
15:30-16:15	**Maja Neiman** Science Director – SwedenBIO
16:15-16:45	Fika Break
16:45-17:30	**Panel Discussion: Beyond the Defence!**
17:30-18:00	**Conclusions & Poster Prizes**
18:15	Departures from Djurönäset

3MT ORAL PITCHES

Implementation of remote monitoring for patients with chronic diseases in the Swedish primary health care – a qualitative and quantitative process evaluation

Name: Alex Jaranka

Abstract:

Introduction: Remote patient monitoring (RPM) of chronic patients has the potential to reduce in-clinic visits and promote proactive care in primary care settings. However, managing the vast data from RPM platforms has led to inefficiencies and project closures. A research project launched at a primary care centre in Stockholm Region, in collaboration with Karolinska Institutet, investigated the piloting of a virtual care team to monitor chronic patients via an RPM platform. This study explores patient perceptions and understanding of sharing vitals and interacting with a virtual care team outside their primary centre. Methods: The project was conducted between October 2018 and April 2019 with 395 patients at a Stockholm primary care centre. In-depth interviews with 22 patients were performed and qualitatively analyzed. Results: Interviews revealed a positive attitude towards RPM, with a key theme of Team-based remote monitoring that is accessible, secure, and stringent. Participants highlighted enhanced accessibility, security, care competence, stringent monitoring, and communication challenges between the virtual care team and the clinical staff at the primary care centre. Conclusions: The patient-centred experience was enhanced by increased interactions and shared vital signs with the virtual care team. Further research is needed to understand factors impacting the patients´ perception on virtual care team in the primary care settings. Discussion: Facilitating micro-consultations and frequent interactions through remote monitoring can improve care management. Effective communication and data integration between virtual care teams and primary care clinicians are crucial for successful remote care delivery in the primary care settings.

The Mechanisms of Psychedelic Drugs for Treatment of Major Depressive Disorder

Name: Daniel Doyon

Abstract:

Major Depressive Disorder (MDD) is the most common psychiatric disorder and a major source of disability worldwide. Depression pathophysiology is best understood as a combination of genetic and environmental factors which determine disease manifestation in susceptible individuals. Frontline treatment for depression, in addition to psychotherapy and healthy lifestyle, is pharmacological intervention, usually in the form of selective serotonin reuptake inhibitors (SSRIs). These drugs are widely prescribed, but are ineffective in a large number of individuals. In addition, they present many unwanted side-effects and have a delayed onset of action, taking weeks or even months to begin any therapeutic action. There is a need for better antidepressants, and in recent years psychedelic drugs, such as ketamine and psilocybin, have shown enormous promise as effective, safe and fast-acting treatments against even severe depression cases. The mechanisms of action for these drugs remain poorly understood, and more research about them is needed if they are to come into mainstream psychiatric medical practice. The aim of my PhD project is to investigate, both clinically and preclinically, the effects of psychedelic drugs on the treatment of depression in order to gain insights into the mechanisms of action of these drugs. On the clinical side, I am following a cohort of MDD patients who are undergoing psilocybin treatment in a clinical trial. I am analyzing their blood and cerebrospinal fluid, checking for inflammatory and neuroplasticity markers. This data will be plotted in combination with MADRS depression evaluation scores and PET-scan data measuring synaptic density in brain regions associated with mood regulation. Preclinically, I am working with mouse models of depression. These mice are followed through a series of behavioral tests evaluating anxiety and depression phenotype, and are treated with psychedelic drugs to assess their impacts on behavior. Changes in proteome and transcriptome are also evaluated.

Translation termination in mammalian mitochondria

Name: Daria Kovalchuk

Abstract:

Mitochondrial translation relies on specialized mitoribosomes and dedicated release factors (RFs) to ensure accurate synthesis and proper termination of 13 proteins involved in oxidative phosphorylation (OXPHOS). While sharing features with both prokaryotic and eukaryotic systems, mitochondrial translation is uniquely adapted to accommodate deviations from the standard genetic code, including the use of non-canonical stop codons AGA and AGG. In human mitochondria, the RF mtRF1a is known to recognize canonical stop codons (UAA/UAG), whereas mtRF1 has recently been elucidated to decode non-canonical stop codons AGA and AGG present in the open-reading frames (ORFs) of COX1 and ND6, respectively. However, the presence of mtRF1 in mammalian species lacking AGA/AGG stop codons like in mouse or rat raises questions regarding its conserved function. Herein, we performed comparative analyses of human and murine mitochondrial translation by combining biochemical assays, mitoribosome profiling, and siRNA screening. Our results reveal species-specific adaptations: in murine mitochondria, mtRF1 mediates an alternative mechanism for COX1 termination, whereas in human mitochondria, the absence of mtRF1 leads to COX1 degradation via the mitochondrial degradosome, while ND6 translation is rescued by mtRF1a through a stalling-induced read-through that leads mitoribosomes to encounter a downstream canonical stop codon. Furthermore, our deep mitoribosome profiling analysis of RF-deficient models reveals widespread mitoribosome stalling on unprocessed mt-transcripts. Together, our findings uncover evolutionarily tailored release mechanisms in mammalian mitochondria that ensure the fidelity of OXPHOS protein synthesis and maintain mitochondrial function.

The cellular thermal proteome during Semliki Forest virus Infection

Name: David Mentrup

Abstract:

Alphaviruses are ssRNA (+) viruses, that adeptly manipulate host cells within a very brief timeframe. Employing Mass Spectrometry coupled with Cellular Thermal Shift Assay (MSCETSA), we assessed alterations in the thermal stability of the cellular proteome at 2 and 6 hours post-infection with Semliki Forest virus (SFV) or SFV-Y369F, a mutant inducing significantly diminished hyperactivation of the AKT pathway and distinct localization of the replication complex. Given that alphaviruses induce translational arrest followed by rapid pathogenesis, both virus-induced host modulation and host response primarily depend on changes in the existing proteome. Profiling the proteome-wide thermal proteome during an in situ infection offers valuable insights into global shifts in protein interaction states, enabling the identification of known and novel host factors, along with modulated pathways. Already at 2 hours post-infection (p.i.), we observed changes in thermal protein stability, particularly in RNA binding proteins and metabolic enzymes expressing thermal stability. While the quantitative proteome remains stable, the thermal proteome undergoes comprehensive changes at 6 hours after SFV infection, involving numerous known host factors such as G3BP, DHX9, and IMPDH, as well as other promising host factor candidates. In comparison to SFV-WT, the SFV-Y369F mutant displayed distinctive thermal protein shifts.

Impact of HPV vaccination on the incidence of high-grade cervical lesions or worse in unvaccinated individuals: A Swedish register study

Name: Eva Meglic

Abstract:

Background HPV vaccination has significantly reduced the incidence of cervical lesions among vaccinated individuals, but understanding the burden of HPV-related conditions in unvaccinated populations remains critical for evaluating the indirect protection from vaccination programs. This study aimed to assess the herd effect of HPV vaccination by examining the incidence of high-grade cervical lesions among unvaccinated women in Sweden. Methods We conducted a register-based cohort study using nationwide Swedish registries. The study population consisted of 857,168 women born between 1985 and 2000, who were unvaccinated and free from high-grade cervical lesions at baseline. Participants were followed from age 10 or 1 January 2006, whichever came later, until their first HPV vaccination, diagnosis of high-grade cervical lesions, emigration, death, their 35th birthday, or December 31, 2022. We used Kaplan-Meier survival analysis and Poisson regression to evaluate the association between birth cohorts and high-grade cervical lesions incidence. Results A total of 42,274 cases of high-grade cervical lesions were identified among unvaccinated women. Kaplan-Meier analysis showed significant differences in cumulative incidence across birth cohorts. Age-specific incidence rate ratios (IRRs) revealed a consistent reduction in risk across cohorts. The subsidized cohort's IRR decreased from 1.34 (95% CI: 0.98–1.85) at age 15 to 0.96 (95% CI: 0.90–1.02) at age 35. The catch-up cohorts IRR decreased from 1.12 (95% CI: 0.75–1.69) at age 15 to 0.87 (95% CI: 0.79–0.96) at age 29. The school-based cohort showed the largest reduction, with an IRR of 0.67 (95% CI: 0.15–3.04) at age 15, dropping to 0.51 (95% CI: 0.38–0.69) by age 23. Conclusion The incidence of high-grade cervical lesions in unvaccinated women declined significantly in cohorts vaccinated through catch-up and school-based programs. The most substantial reduction was observed in the school-based cohort, emphasizing the strong herd effect of HPV vaccination.

Proteomic-based classification of NSCLC patients and personalised medicine stratification

Name: George Field

Abstract:

Lung cancer is the most common type of cancer worldwide with 2.1 million new cases each year. Most cases are diagnosed when the cancer has already metastasized and surgical resection is no longer an option, resulting in a dismal overall 5-year survival rate in stage 4 disease. Targeted therapies and immunotherapy present a major opportunity, but the impact on survival so far is blunted by a lack of biomarkers for therapy selection and limited knowledge of how therapies should be combined. Current treatment stratification for targeted therapy in cancer is based on DNA analysis. This *genome driven medicine* has revolutionized cancer treatment and improved survival, but less than 15% of all cancer patients are eligible and only 11% that receive genome-informed therapy show significant response. Response prediction and treatment stratification for immunotherapy is currently underdeveloped and rely on estimation of the tumor mutational burden of each cancer, or the protein level assessment of inhibitory ligands (PD-L1). Neither of the two approaches provide accurate response prediction resulting in poor response rates. Recent improvements in MS-based proteomics have enabled a direct analysis of the cancer molecular phenotype providing new insight of the functional consequences of genetic aberrations. Integration of proteome level information into clinical trials and patient care thus provide an excellent opportunity to improve the current precision medicine and increase the patient benefit. The *in-depth* MS-methods used for describing the proteogenomics landscapes has been previously used to identify 6 proteomic subtypes in NSCLC, unique to those currently used for categorisation by histology. These each subtype had specific enrichments in targetable mutations and variations in immune infiltration, providing a clear insight into how we could better stratify patient treatment. Here we will explore the possibility of creating a machine learning model to predict patient subtype in a prospective clinical trial, create a useable output for clinicians to be able make informed decisions on patient treatment and assess the integration of this workflow into clinical routine.

Genetic diversity of Plasmodium falciparum vaccine candidate merozoite surface protein 2 across sub-Saharan Africa

Name: Julia Zerebinski

Abstract:

Genetic diversity in the malaria parasite Plasmodium falciparum is a significant hurdle to the development of efficacious vaccines. We investigated the genetic diversity of the highly polymorphic blood stage antigen MSP2 in 2761 P. falciparum isolates from across sub-Saharan Africa where malaria is endemic. Using PCR-based genotyping and high-fidelity long-read sequencing, we found that some msp2 variants were more prevalent than others even across geographical, transmission intensity, and temporal groups. We determined that msp2 variants were made up of multiple sequence variants, although dominant sequences were usually detected. Our findings suggest the true diversity of msp2 is much more extensive than shown with previous genotyping tools. Our findings also indicate some biological advantage of size variants, and of specific sequence variants, to the parasite.

Modelling the time-varying effect of hormonal treatment on time to detection of distant metastases among oestrogen receptor-positive breast cancer patients - a natural history modelling approach

Name: Letizia Orsini

Abstract:

Breast cancer treatment depends on tumour subtypes. In particular, patients with oestrogen receptor-positive (ER+) tumours are treated with hormonal therapy. In Sweden, the recommended treatment duration has been five years, with current guidelines advising an additional five years for women at high risk of recurrence, as some studies have linked prolonged endocrine therapy to improved disease-free survival. However, the impact of extended therapy on metastatic progression has not been thoroughly quantified at the population level. In this article, we use a modelling approach to estimate the time-varying effect of hormonal treatment on the time to metastasis diagnosis. We then use it to compare 5-year and 10-year treatment for different-sized tumours. We incorporated the effect of endocrine therapy in a biologically inspired natural history model of breast cancer. Individual tumour growth was modelled as exponential, with an inverse growth rate following a gamma distribution. We model the metastatic seeding with a non-homogeneous Poisson process dependent on tumour size. We incorporate the treatment effect as a multiplicative factor of the inverse growth rate of metastases, allowing us to quantify its impact on tumour dynamics. We fitted our model using a likelihood-based approach to an incident cases cohort of 9716 patients diagnosed with invasive ER+ breast cancer between 2005-2020. 299 metastatic events occurred during follow-up. Based on our model estimates, for a symptomatic patient with a 20mm tumour we estimate that the 10-year metastasis-free survival would improve from 92.8% to 96.1% with ten years instead of five years of hormonal treatment. Our natural history model quantifies the impact of prolonged hormonal treatment on metastatic events in ER+ breast cancer patients. Results suggest a significant reduction in metastatic tumour growth rates during treatment, supporting the extension of endocrine therapy to 10 years for people with large tumours.

Scattering and absorption free confocal imaging of 3D samples

Name: Louise Gsell

Abstract:

3D samples, such as organoids and spheroids, have emerged as essential tools in biology, designed to replicate organ and tissue physiology while enabling rapid, reproducible experiments. The transition from traditional 2D cell cultures and animal models to these advanced 3D systems is accelerating in biomedical research. However, a major challenge remains in imaging these cultures due to their size, opacity, and structural complexity, limiting standard microscopy techniques effectiveness. Confocal microscopy, the current gold standard for imaging 3D cell cultures, often faces issues with light attenuation caused by absorption and scattering, making it difficult to obtain accurate, quantitative data across the entire sample. To address this, we have developed a novel approach to quantify light attenuation by leveraging the properties of fluorescent molecules. Our method integrates an imaging protocol with post-processing adjustments to correct for light attenuation, allowing for precise, quantitative analysis using conventional confocal microscopes. With this method, we aim to achieve robust quantitative imaging in 3D cell cultures, paving the way for more accurate experimental comparisons in biomedical research.

Beyond HER2: A Multi-Omics Perspective on the Need for Additional Biomarkers in HER2-Positive Breast Cancer

Name: Luca Gaessler

Abstract:

Breast cancer (BC) is the most prevalent malignancy among women worldwide. The overexpression of human epidermal growth factor receptor 2 (HER2) drives an especially aggressive BC subtype. HER2-targeted therapies exploit this dependency and have significantly improved the survival of HER2-positive BC patients over the last three decades. However, HER2 remains the sole biomarker to guide clinicians in selecting among the available HER2-targeted treatment options. This highlights the need for additional biomarkers to personalize therapy, thus optimizing treatment response while minimizing unnecessary toxicity. To address this, we analyzed multi-omics data from pre-treatment tumor biopsies in the neoadjuvant PREDIX trial, which compared two antibody-based therapies for early-stage HER2-positive BC. We found an inverse relationship between ERBB2 and ESR1 expression and could show that an ERBB2-high/ESR1-low expression profile correlated with pathological complete response (pCR). This suggests that estrogen signaling plays a key role in resistance to HER2-directed therapy. Mass-spectrometry-based proteomics data identified a subset of “pseudo-HER2-positive” patients associated with residual disease and reduced HER2 signaling. This finding indicates that proteomics can improve the clinical assessment of HER2-directed therapy eligibility. Immune profiling revealed that the immune response varied between treatment arms. Patients achieving pCR in the DHP (docetaxel, trastuzumab, and pertuzumab) arm exhibited higher levels of immune-related proteins. In contrast, pCR to T-DM1 (trastuzumab-emtansine) was associated with reduced levels of immune-related pathways, highlighting the complex and treatment-specific mechanisms of treatment efficacy.

A Frozen Future: Investigating the impact of clinically applied cryopreservation methods on embryo development

Name: Mariana Barroso

Abstract:

Cryopreservation and warming of human embryos have become standardized procedures in medically assisted reproduction worldwide. The ability to freeze and subsequently warm embryos has enhanced the efficacy of in vitro fertilization (IVF) treatments, allowing surplus embryos to be stored for future use. Although embryo cryopreservation has been clinically applied for over four decades and is generally considered safe, its full impact on embryo development is not yet fully understood. Epidemiological studies involving large datasets have raised concerns about differences in birth weight and size between newborns born after fresh versus cryopreserved embryo transfer, as well as potential long-term health implications. In this study, we used mouse embryos to investigate the impact of vitrification and warming protocols by following their developmental kinetics, and examining mitochondrial structure and function, and the integrity of cytoplasmic lattices. Using time-lapse imaging, a significant developmental delay was evident in vitrified embryos across all preimplantation stages (from the 4-cell to the blastocyst stage) compared to fresh embryos. Additionally, mitochondrial distribution patterns, volume, and function exhibited signs of impairment following vitrification/warming. To further investigate the structural consequences, we employed Transmission Electron Microscopy (TEM), a high-resolution imaging technique, to examine the ultrastructural changes during early embryonic development. TEM analysis revealed mitochondrial membrane rupture and disruption of cytoplasmic lattices during the first cell divisions. In vitrified blastocysts, we observed poorly developed mitochondrial cristae and a reduction or absence of cytoplasmic lattices. We hypothesize that cryopreservation through vitrification disrupts mitochondrial activity and destabilizes cytoplasmic lattices, ultimately leading to developmental delays in preimplantation embryos.

Social Perception of Other People's Covert Attention—A Mind Reading Study

Name: Martha Paskin

Abstract:

Covert attention is the act of orienting one's attention to a stimulus, without moving one's eyes. In the absence of other overt bodily or environmental cues indicating an attention shift, the reorienting of one's covert attention is considered, almost by definition, undetectable by outside observers. Social perception of others' covert attention is a largely unexplored subject, perhaps due to the aforementioned reasons. Here we tested the hypothesis that people implicitly perceive the direction of another person's covert attention, possibly by processing that person's involuntary miniature eye movements or subtle bodily cues associated with reorienting covert attention. We tested 34 participants each for a visual and an auditory covert attention task. We analyzed the behavioral and gaze data, as well as subtle facial movements of the participants as they covertly attended to the left or right side while keeping their eyes fixated. Results reveal that humans perform better than chance at decoding others' direction of covert attention in both visual and auditory domains. A machine learning model trained on facial data out-performs human subjects. Although including miniature eye movement data does not improve model performance, we found that subtle facial movements might hold information on our direction of covert attention. Our results have the potential to impact research in the fields of social attention, brain-computer interfaces and consciousness.

A new mouse model of thrombopoietin deficiency arising from a spontaneous single base pair mutation

Name: Nan Sophia Han

Abstract:

Thrombopoietin (TPO) is the principal regulator of bone marrow platelet production and performs an important role in maintaining hematopoietic stem and progenitor cells. Predominantly produced in the liver, circulating TPO levels are thought to be primarily modulated by receptor-mediated clearance of TPO by target cells such as platelets. However, there is an additional component of TPO regulation at the transcriptional level, which may be affected in the setting of platelet-associated diseases. Current TPO knockout mouse models partially limit the study of transcriptional regulation because of disruption of the TPO genomic locus. Here we describe a novel mouse model of TPO-deficiency arising from a spontaneous mutation in a single base pair within exon 5 of the thrombopoietin gene. The resulting amino acid change (leucine to histidine) predicts a dramatic alteration in protein structure, and ultimately results in a >95% decrease of circulating TPO. The hematological phenotype of this new C57Bl/6(IMPC)J-TPOL121H strain mimics that of other TPO knockout mice, but the genomic locus is intact and therefore preserves normal TPO transcriptional regulation. We characterize the hematological phenotype of this new strain and discuss its applications as a model of transcriptional TPO regulation and clinical thrombocytopenia. Our findings highlight the theoretical possibility that TPO protein destabilizing mutations may explain rare cases of patient thrombocytopenia.

Discovery of plasma protein signatures for diagnosis of non-small cell lung cancer (NSCLC) using in-depth proteomics and machine learning

Name: Noora Sissala

Abstract:

Lung cancer remains the leading cause of cancer-related death worldwide, largely due to late-stage diagnosis and lack of methods for early detection. In this study, we aimed to identify plasma protein biomarkers for diagnosis of non-small cell lung cancer (NSCLC) by analyzing pre-diagnostic plasma samples from two retrospective cohorts of non-small cell lung cancer (NSCLC) patients and non-cancer controls using two complementary proteomics platforms: global mass-spectrometry based proteomics (HiRIEF LC-MS/MS) and targeted antibody-based proteomics (Olink Explore). Several thousand proteins quantified by either platform were analyzed using machine learning to identify proteins contributing to accurate classification of NSCLC and control samples. The analysis revealed multiple multivariate protein signatures capable of effectively discriminating between cases and controls. These findings demonstrate the potential of plasma proteomics to aid in the early detection of NSCLC and warrant further validation in additional cohorts.

POSTER PRESENTATIONS

Ig Germline Prerequisites Shape Individual Influenza A Hemagglutinin-Specific Antibody Responses

Name: Alexandra Fischer

Poster Number: 1

Abstract:

Background: Human immunoglobulin (Ig) heavy, kappa and lambda genes exhibit extensive allelic and copy number variation forming the genetic basis of individual adaptive immune control of infections. Current knowledge is limited regarding the impact of polymorphisms in B cell receptor (BCR) variable (V), diversity (D), and junctional (J) genes on antigen-specific responses and as a consequence, clinical disease severity and prognostic outcomes. Methods: Biotinylated H1N1pdm2009-like influenza monomeric head, trimeric stem domain and full trimer hemagglutinin (HA) probes were used to isolate HA-specific memory B cells by index sorting. Single-cell cDNA libraries, multiplex nested PCR and well-barcoding enabled high-throughput full-length paired heavy and light chain V(D)J identification. Retailed PCR-products were directly (ligation-free) cloned into human IgG1, IgK1 or IgL2 expression vectors for monoclonal antibody (mAb) expression and functional/biophysical characterization. Results: A total of 761 paired HC and LC V(D)J transcripts were obtained from three donors and assigned to the donor-specific Ig genotypes using the software IgDiscover. Clonally related sequences were grouped based on allele usage and CDR3 similarity. The HA-specific antibody gene usage was highly donor-specific and a diverse range of V allele pairings, such as IGHV3-9*01/IGKV1-33*01 or IGHV2-70*01/IGLV3-9*01. A panel of mAbs (n=37) targeting the head or stem domain of HA were expressed, of which 26 demonstrated neutralizing activity, including four that cross-neutralized Influenza A group 1 subvariants including H5. The use of cryo-EM of HA-Fab complexes revealed both known and novel binding modes. Conclusions: We developed a technique that couples rapid and high-throughput antigen-specific BCR sequencing with donor-specific Ig germline genotyping. This highly versatile tool can be applied across diverse antigens, disease contexts and study designs, providing biologically and clinically relevant insights into BCR response dynamics.

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

Name: Ana Varas Sánchez

Poster Number: 2

Abstract:

Protein translation unfolds in three sequential 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 because of gene code degeneration, complex tRNA secondary structure and their extensive post-transcriptional modifications. 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. We termed that score, theoretical translation efficiency (tTE). 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 based on their research needs. 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.

Engineering CD38 in NK Cells for Combination Therapy of Anti-CD38 Antibodies to Treat Multiple Myeloma

Name: Anna Pumpe

Poster Number: 3

Abstract:

Adoptive transfer of natural killer (NK) cells and administration of daratumumab as treatment for patients with multiple myeloma (MM) have independently been shown to be benefical. However, daratumumab induces fratricide of NK cells which express CD38 themselves, thereby decreasing their number and limiting their anti-tumour activity. Therefore, preventing NK cell fratricide by genetically engineering CD38 in NK cells to avoid daratumumab recognition is explored to increase treatment efficiency. The novelty of the approach investigated here is based on retaining endogenous functions of the multifunctional CD38 receptor. Currently, generation of CD38 engineered NK cells will be achieved by knockout (KO) of CD38 using CRISPR/Cas9 via electroporation with subsequent lentiviral transduction of engineered CD38 constructs. Optimisation of this process into a one-step procedure using base editing or homology-directed repair will be investigated. Engineered NK cells will be assessed in terms of daratumumab evasion and resistance to fratricide as well as their functionality against target cells including cytotoxic capacity and cytokine secretion. Additionally, functions of engineered CD38 as an adhesion receptor and enzyme will be evaluated. Two single amino acid mutations have been found to evade recognition by daratumumab. Using electroporation of CRISPR/Cas9 components for KO of CD38 in primary NK cells is feasible and an efficient crRNA has been identified resulting in 80 % downregulation. Preliminary data indicate that CD38 engineered NK cells have similar levels of CD107a expression in reponse to K562 target cells. Genetically engineering CD38 on NK cells that are targeted by the therapeutic antibody daratumumab as well harbours the potential to address clinical issues in the treatment of MM. The evasion procedure investigated here can potentially be applied in therapies targeting other tumour antigens also expressed on effector cells and in therapies using not only antibodies but other targeting agents such as CAR engineered cells.

Multi-dimensional analysis of MASLD signatures: discovering novel targets and biomarkers

Name: Carlos Gallardo Dodd

Poster Number: 4

Abstract:

Metabolic dysfunction-associated steatotic liver disease (MASLD) is a growing global health concern affecting one in three adults worldwide. It occurs when excessive fat accumulates in the liver, often due to poor diet and lifestyle factors, increasing the risk of inflammation, fibrosis, and even liver cancer. Despite the growing repertoire of available diagnostic tools, there is a need for simple non-invasive tests that can accurately identify patients with MASLD, especially at the early stages of the disease. Moreover, while some drugs against obesity-driven MASLD have started to emerge, effective and long-lasting solutions are still lacking. To address this, we have conducted an in-depth characterization of gene expression changes throughout MASLD progression by combining data from both preclinical models and patients. We systematically evaluate the effect of hormone and small molecule inhibitor treatments, uncovering a novel mechanism by which lipid accumulation is regulated in liver cells. Furthermore, we establish a computational framework empowering large-scale integration of high-throughput sequencing data from over 1,000 patients with MASLD. We investigate gene biosignatures and alternative splicing events at various MASLD stages and assess their potential as biomarkers. Collectively, our findings reveal novel candidates for non-invasive MASLD diagnosis and pharmacological intervention.

Sleep timing, sleep duration and serum metabolites in healthy adults

Name: Charlotte Sørensen

Poster Number: 5

Abstract:

Study objectives: Short and long sleep duration as well as poor sleep quality have been linked to higher prevalence of metabolic disorders. However, it is still unclear how diverse sleep variables relate to different metabolic pathways. This study examines how different features of sleep health relate to serum metabolites. Methods: The study used data from 197 healthy individuals aged 20-79 (Females n=103) from the IronAge study performed at Karolinska Institutet in Sweden. Sleep variables were assessed with the Karolinska Sleep Questionnaire, where the following variables were computed: sleep duration, sleep debt, midpoint, social jetlag (i.e., the discrepancy between midpoint on free and workdays), napping frequency and sleep quality. Morning fasting blood samples were collected and 1H NMR spectroscopy was utilized for metabolomic analysis. The metabolites were categorized according to their major metabolic pathways: amino acid, lipid, carbohydrate, energy and gut microbiota. Linear regressions were performed to examine the relationship between each sleep variable and metabolite. Results: Sleep duration, midpoint of sleep on free days, social jetlag and chronotype associated with eight metabolites at a significance level of $p<0.01$. Notably, midpoint associated with most metabolites spanning multiple pathways. A later midpoint was associated with higher levels of metabolites in the lipid pathway, and lower levels in the amino acid and energy pathway. Conclusion: These observations indicate that sleep timing features, midpoint and social jetlag, have a stronger relationship with morning metabolism than other sleep health dimensions. Following replication in larger samples, these complex relationships may hold potential for health promotion.

Antiviral nucleotide analogues trap chemoresistance factor SAMHD1 in an inactive tetrameric state

Name: Christopher Dirks

Poster Number: 6

Abstract:

Objectives: SAMHD1 is a deoxynucleoside triphosphohydrolase (dNTPase) that regulates cellular dNTP levels and has recently been implicated as a resistance factor to nucleoside analogue antimetabolite chemotherapy. This makes SAMHD1 an attractive target for inhibitor development, but no cell-active compounds have been reported so far. In this project we therefore aim to improve our understanding of SAMHD1 biology, especially of its allosteric activation, oligomerisation and catalytic mechanisms. We aim to diversify the modes of inhibition towards SAMHD1 and provide a starting point to rationally develop allosterically targeting molecules. Methods: We use mainly biochemical and biophysical methods to study modulators of SAMHD1 activity. This includes enzyme activity assays (high-throughput biochemical endpoint assay & continuous NMR-based kinetic assay), a competitive binding assay to study allosteric site affinity and chemical crosslinking to study SAMHD1 oligomerisation. Results: Antiviral guanine nucleotide analogues Acyclovir- and Ganciclovir-triphosphate can mimic the endogenous allosteric activator GTP, inducing the formation of enzymatically competent homotetramers. However, depending on the analogue activator and dNTP substrate identity, the resulting catalytic activity can be drastically reduced. We also observe dNTPase activity with mixtures of endogenous and non-natural allosteric site 1 activators, suggesting the formation of mixed occupancy homotetramers. Conclusions: By studying the modulation of SAMHD1 dNTPase activity via nucleotide analogues we identify new avenues of inhibiting this challenging target by trapping it in a stable, inactive tetramer. In addition, we present a novel mode of SAMHD1 allosteric activation through a combination of endogenous activators and nucleotide analogues. We thereby improve our understanding of the allosteric activation process and of SAMHD1’s dNTPase activity in the context of its oligomerisation.

Can cardiac magnetic resonance imaging safely defer invasive coronary angiography in patients with suspected non-ST-elevation myocardial infarctions?

Name: Daniel Andersson

Poster Number: 7

Abstract:

Introduction Patients with suspected NSTEMI constitute a majority of patients evaluated for suspected MI. Early cardiac magnetic resonance (CMR) has the potential to reclassify diagnoses and influence management in over half of suspected NSTEMI cases. We aimed to evaluate if an early CMR examination can be used to defer patients with suspected NSTEMI from invasive coronary angiography (ICA) and improve diagnosis. Methods Patients with suspected NSTEMI referred for an ICA were prospectively enrolled. Of 36 patients, 4 patients could not undergo CMR. CMR was done using a 1.5T Siemens Sola and included cine imaging, T1- and T2 mapping, and LGE. CMR images from 32 patients were interpreted by 2 independent blinded observers and cases of discrepancies adjudicated in consensus with 3 readers. Subsequent clinical management including revascularization decision-making was performed without knowledge of the CMR results. Results Of 22 patients that underwent revascularization, 10 patients had CMR evidence of acute ischemic injury, 2 patients had myocarditis, 2 had chronic MI and 8 had normal CMR. Two patients had ICA complications; 1 stroke and 1 peri-procedural MI. Patients with CMR findings of an acute event (11 with acute myocardial infarction, 5 with acute non-ischemic findings) had significantly higher mean Troponin-T than patients with no acute findings on CMR (400 ± 605 vs. 74 ± 137 ng/L, $p < 0.001$*). There was no CMR evidence of acute myocardial infarction in patients with TnT levels < 140 ng/L. CMR identified an acute event in all but two patients with TnT > 140 ng/L, and in none with TnT < 50 ng/L. Conclusions There is a discrepancy between revascularization based on ICA findings and CMR evidence of acute ischemic injury in patients with suspected NSTEMI. In patients with TnT > 140 ng/L, CMR could potentially have deferred an urgent ICA in the 35% of patients who had non-ischemic findings. *TnI = 42ng/L for 1 patient

Translation termination in mammalian mitochondria

Name: Daria Kovalchuk

Poster Number: 8

Abstract:

Mitochondrial translation relies on specialized mitoribosomes and dedicated release factors (RFs) to ensure accurate synthesis and proper termination of 13 proteins involved in oxidative phosphorylation (OXPHOS). While sharing features with both prokaryotic and eukaryotic systems, mitochondrial translation is uniquely adapted to accommodate deviations from the standard genetic code, including the use of non-canonical stop codons AGA and AGG. In human mitochondria, the RF mtRF1a is known to recognize canonical stop codons (UAA/UAG), whereas mtRF1 has recently been elucidated to decode non-canonical stop codons AGA and AGG present in the open-reading frames (ORFs) of COX1 and ND6, respectively. However, the presence of mtRF1 in mammalian species lacking AGA/AGG stop codons like in mouse or rat raises questions regarding its conserved function. Herein, we performed comparative analyses of human and murine mitochondrial translation by combining biochemical assays, mitoribosome profiling, and siRNA screening. Our results reveal species-specific adaptations: in murine mitochondria, mtRF1 mediates an alternative mechanism for COX1 termination, whereas in human mitochondria, the absence of mtRF1 leads to COX1 degradation via the mitochondrial degradosome, while ND6 translation is rescued by mtRF1a through a stalling-induced read-through that leads mitoribosomes to encounter a downstream canonical stop codon. Furthermore, our deep mitoribosome profiling analysis of RF-deficient models reveals widespread mitoribosome stalling on unprocessed mt-transcripts. Together, our findings uncover evolutionarily tailored release mechanisms in mammalian mitochondria that ensure the fidelity of OXPHOS protein synthesis and maintain mitochondrial function.

Spatial Transcriptomic Profiling of Mediobasal Hypothalamus in Murine Model of Anorexia Nervosa

Name: Emmy Erskine

Poster Number: 9

Abstract:

Anorexia Nervosa (AN) is a psychiatric disorder characterized by restriction of food intake and weight loss. Individuals can maintain a negative energy balance despite presence of evolutionary mechanisms that should support energy homeostasis and prevent self-starvation. AN affects 4% of females and 0.3% of males with high chronicity and mortality rates alongside co-morbidities with other major psychiatric disorders. Currently there are no pharmacologically available treatments for AN. Genome wide association studies have identified differential gene expression associated with metabolic and anthropometric traits indicating a possible dysregulation of metabolic signalling required for regulation of energy balance. Such genetic studies have also highlighted hypothalamic involvement and genes associated with microglia in AN. Two neuronal populations in the arcuate hypothalamus (ARC) expressing agouti related peptide hormone (AgRP) and pro-opiomelanocortin (POMC) regulate energy through communication with peripheral hormones including insulin, ghrelin and leptin which typically initiate or inhibit feeding behaviours. An anorectic murine model demonstrates microglial activation in the ARC and several other hypothalamic regions including the paraventricular hypothalamus (PVH), dorsal medial hypothalamus (DMH) and lateral hypothalamus (LHA).

We propose that there is a genetic hypothalamic dysregulation regulated by microglia underpinning the negative energy balance in AN. To investigate the molecular footprint of starvation in AN we performed spatial transcriptomic profiling of microglia, AgRP neurons and POMC neurons in several hypothalamic regions in the anx/anx mice compared to wild-type mice. The whole transcriptomic profiling was performed in the GeoMX platform for omics and analysis was performed using Nanostring DSP software.

We identified several differentially expressed genes (DEGs) in the microglia surrounding degenerating neurons in the anx/anx mice, several of which relate to complement proteins such as C4b and C1q(a-c) which are known to be implicated in synapse engulfment. Moreover, DEGs in AgRP and POMC expressing neurons indicate altered gene expression in these neuronal populations which are essential for maintenance of energy balance. This suggests a potential divergent role for microglial mediated synaptic pruning of ARC neurons in AN and taken together with other genetic studies indicates a potential metabo-psychiatric basis of AN.

Estrogen receptor mediated neuroprotection in models of Alzheimers disease

Name: Heba Ali

Poster Number 10

Abstract:

Objectives Middle-aged women are 2-3 times more likely than men to develop Alzheimer’s disease (AD) later in life. While women tend to live longer, factors like sex hormones, genetics, and environment heighten their AD risk. Understanding sex differences in AD has been complex. This project aims to uncover the molecular underpinnings of the female sex hormone estrogen in AD models and relate these findings to human disease. Methods We are using APPNLGF mice, which exhibit clear AD pathology by 6 months of age, to study the effects of biological sex and sex hormones on memory and AD pathology at 6 and 12 months. Surgical menopause is induced in young adult female mice and castration in male mice. Preliminary data indicate neuroprotective effects of estrogen receptor beta (ERβ) in APPNLGF mice. Consequently, we crossed ERβ-/- mice with APP-KI mice to study the effects of ERβ loss on AD pathology, utilizing single-cell RNA sequencing of hippocampal brain cell populations. Results Our ongoing analysis provides insights into ERβs role in brain cell functions and identifies sex-dependent alterations in gene activity. Preliminary data show that ERβ has neuroprotective effects in APPNLGF mice. We will anchor our findings to human disease by studying gene and pathway regulations in human AD brains and analyzing GWAS data from women with or without AD diagnosis and with or without different menopausal hormonal treatments. Conclusions Collectively, these findings offer insights into mechanisms underlying sex-specific susceptibility to AD and identify regulatory proteins for potential treatments targeting sex-dependent AD pathology. Understanding the role of estrogen and ERβ in AD could lead to targeted therapies addressing the heightened risk in women. Keywords: Estrogen; Estrogen receptor beta; Alzheimer’s disease; APP-KI Mice.

Discovery of diagnostic biomarkers for early detection of Non Small Cell Lung Cancer (NSCLC

Name: Irene Villanueva Sanz

Poster Number:11

Abstract:

We propose that there is a genetic hypothalamic dysregulation regulated by microglia underpinning the negative energy balance in AN. To investigate the molecular footprint of starvation in AN we performed spatial transcriptomic profiling of microglia, AgRP neurons and POMC neurons in several hypothalamic regions in the anx/anx mice compared to wild-type mice. The whole transcriptomic profiling was performed in the GeoMX platform for omics and analysis was performed using Nanostring DSP software.

Investigation of the Anti-Inflammatory Effects of Aucklandia lappa Extract for the Treatment of Rheumatoid Arthritis

Name: Janika Welzel

Poster Number:12

Abstract:

Purpose: Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by joint inflammation and progressive tissue damage. Modern treatments have greatly improved the management of the disease, but many patients still do not achieve treatment outcomes, highlighting the need for alternative therapeutics. This study investigates the potential of traditional Chinese herbal medicine, specifically Aucklandia lappa, in mitigating RA-related inflammation. Methods: Using a combination of in vitro bioassays and the KRN T cell transfer model of arthritis in vivo, we explored the anti-inflammatory properties of the aqueous extract from A. lappa. The aqueous extract was obtained by extraction in organic solvent followed by an extraction in water/acetonitrile. A. lappa is part of a Chinese herbal formulation that is used in the clinics in China for the treatment of RA and consists of eight more plants that are prepared as a hot water decoction. Results: Our findings demonstrate that the extract exerts inhibitory effects on several key inflammatory signaling pathways, including NF-κB, NFAT, STAT3, and STAT5, across diverse immune cell types. Additionally, the extract significantly suppressed prostaglandin production in synovial fibroblasts and cytokine secretion in primary B cells. In vivo, treatment with the extract resulted in reduced joint swelling and decreased autoantibody levels in arthritic mice. Using different analytical methods, we could identify two structurally very similar major compounds of this extract that were active in the cellular assays, offering insights into the molecular basis of its effects. Conclusions: Our findings demonstrate some anti-inflammatory and anti-arthritic effects of this plant and point towards a predominant functional role in the formulation. Further studies are warranted to validate these results and elucidate the underlying mechanisms.

Comparative studies of microglia-like cells from patients with anorexia nervosa vs healthy controls

Name: Jingjing Xu

Poster Number: 13

Abstract:

The psychiatric disorder anorexia nervosa (AN) affects around 4% of females and 0.3% of males, and both mortality and relapse rates are high. A puzzling part of the disorder is the paradoxical response to negative energy balance, leading to continued loss and maintenance of low body weight. Intricate neuronal circuits originating in the hypothalamus are fundamental in regulating energy balance, metabolism, and food intake. Signals from long-term energy stores and short-term meal-related signals instruct the hypothalamus about the energy status, thereby altering the neuronal activity to synchronize appetite with energy needs. In addition, interactions between hypothalamic neurons and microglia are central to this regulation referred to as energy homeostasis. Furthermore, genetic enrichment studies support microglial involvement in AN. Based on the above findings, we hypothesize that a primary genetic vulnerability in AN resides with a dysfunction of hypothalamic microglia. In this study, we collected blood samples and skin biopsies from AN patients and non-psychiatric controls and induced them into microglia-like cells (iMG), hypothalamic neurons, and cortical neurons. Synaptosomes were extracted from the neurons and fed to iMG to assess their phagocytic capacity. We found that iMG derived from AN patients have a lower phagocytic capacity of hypothalamic synaptosomes compared to healthy controls, indicating the possibility of aberrant synaptic pruning of the hypothalamic circuits regulating food intake. Interestingly, no such difference was seen when feeding the same iMG cortical synaptosomes. In addition, the phagocytic capacity of hypothalamic synaptosomes by patient-derived iMG was impaired upon treatment with meal-related signals, indicating potential dysfunction of AN microglia in response to such signals. Taken together our data suggest a deviant microglia-driven synaptic pruning of hypothalamic neurons in AN that we speculate to be involved in the puzzling maintained negative energy balance of the disorder.

External validation of a machine learning based classification algorithm for ambulatory heart rhythm diagnostics using smartphone- hotoplethysmography: the SMARTBEATS-ALGO study

Name: Jonatan Fernstad

Poster Number: 14

Abstract:

Aims: Smartphone-photoplethysmography (PPG) can be used for heart rhythm diagnostics. According to current guidelines, ECG verification is required for a new diagnosis of atrial fibrillation (AF). The aim of this study was to perform an external validation of an automatic machine learning algorithm for heart rhythm diagnostics using smartphone-PPG recorded by patients with AF and atrial flutter (AFL) pericardioversion in an unsupervised ambulatory setting. Methods: Ph.D. candidate Jonatan Fernstad has created a smartphone application that patients can use with their own smartphone at home to receive a diagnosis of their heart rhythm. Patients undergoing cardioversion performed 1-min heart rhythm recordings pericardioversion at least twice daily for 4–6 weeks, using an iPhone 7 smartphone running a PPG application (CORAI Heart Monitor) simultaneously with a single-lead ECG recording (KardiaMobile). The algorithm uses support vector machines (SVM) to classify heart rhythm from smartphone-PPG. The algorithm was trained on PPG recordings made by patients in a separate cardioversion cohort. PPG recordings in the external validation cohort were analysed by the algorithm. Diagnostic performance was calculated by comparing the heart rhythm classification output to the diagnosis from the simultaneous ECG recordings (gold standard). Results: In total, 460 patients performed 34 097 simultaneous PPG and ECG recordings, divided into 180 patients with 16 092 recordings in the training cohort and 280 patients with 18 005 recordings in the external validation cohort. Algorithmic classification of the PPG recordings in the external validation cohort diagnosed AF with sensitivity, specificity and accuracy of 99.7%, 99.7%, and 99.7%, respectively, and diagnosed AF/AFL with sensitivity, specificity and accuracy of 99.3%, 99.1%, and 99.2%, respectively. Conclusion: A machine learning-based algorithm demonstrated excellent performance in diagnosing atrial fibrillation and atrial flutter from smartphone-PPG recordings in an unsupervised ambulatory setting, minimizing the need for manual review and ECG verification, in elderly cardioversion populations.

Genetic diversity of Plasmodium falciparum vaccine candidate merozoite surface protein 2 across sub-Saharan Africa

Name: Julia Zerebinski

Poster Number: 15

Abstract:

Genetic diversity in the malaria parasite Plasmodium falciparum is a significant hurdle to the development of efficacious vaccines. We investigated the genetic diversity of the highly polymorphic blood stage antigen MSP2 in 2761 P. falciparum isolates from across sub-Saharan Africa where malaria is endemic. Using PCR-based genotyping and high-fidelity long-read sequencing, we found that some msp2 variants were more prevalent than others even across geographical, transmission intensity, and temporal groups. We determined that msp2 variants were made up of multiple sequence variants, although dominant sequences were usually detected. Our findings suggest the true diversity of msp2 is much more extensive than shown with previous genotyping tools. Our findings also indicate some biological advantage of size variants, and of specific sequence variants, to the parasite.

Improving the efficiency of CAR-T cell therapies in solid tumors using synthetic co-stimulatory receptors

Name: Julian Fischbach

Poster Number: 16

Abstract:

CAR-T cell therapies have so far shown limited efficiency in treating solid tumors, which is mainly attributed to the immunosuppressive tumor microenvironment (TME) inducing CAR-T cell dysfunction and exhaustion. Synthetic co-stimulatory receptors (SRs) consisting of an extracellular inhibitory domain linked to an intracellular co-stimulatory domain can convert immunosuppressive signals in the TME into activation signals and have therefore emerged as a promising strategy to overcome immunosuppression. However, there is an extensive pool of potential candidates for SRs making individual testing in vivo unfeasible. In this project, we are therefore performing a pooled knock-in screening approach using a big library of SRs to identify those synthetic receptors that enhance CAR-T cell function and activation. By performing amplicon-seq as well as single-cell-RNA-seq, we are investigating the effect of each SR on the CAR-T cell proliferation and phenotype in the tumor in vivo. Since solid tumors are very diverse with distinct TMEs, we are using multiple in vivo mouse models replicating different types of solid tumors. This comprehensive approach enables us to broadly screen for SRs improving CAR-T cell functionality across diverse solid tumors. Our findings may significantly contribute to the development of the next generation of CAR-T cells that might eventually be translated into improved therapies for solid tumors in the clinics.

Network-based Analysis of Acute Myeloid Leukemia: Integrating Large Language Models for Enhanced Module Annotation

Name: Justin Seby

Poster Number: 17

Abstract:

Acute Myeloid Leukemia (AML) presents significant heterogeneity, challenging conventional methods for interpreting genetic alterations. The gap between genetic data and actionable insights is a barrier to precision medicine, as traditional approaches struggle to capture the interplay between mutations and biological networks. Here, we present an integrative framework combining machine learning, network biology, and large language models (LLMs) to enhance the interpretation of genetic alterations. We developed a protein-protein interaction (PPI) classification model using proteomics data from 118 AML patients, demonstrating increased accuracy with GenePT embeddings. Using this model, we constructed a high-confidence PPI network under FDR control (0.01) exhibiting a scale-free topology consistent with biological networks. Louvain clustering identified 222 distinct modules, systematically annotated using a hybrid system that fuses traditional enrichment methods with LLMs (GPT and DeepSeek). Semantic similarity using Sentence-BERT revealed a strong correlation between LLM confidence and alignment with known annotations. High-confidence but moderately similar annotations pointed to biologically plausible yet underexplored pathways. The analysis revealed that SRSF2 mutations lead to decreased expression of INTS3, a known effect; however, we observed similar patterns in other members of the integrator complex, suggesting INTS3 may play a more central role in maintaining the integrity of the complex than previously recognized. We developed a chatbot interface with an explainable AI component, making the framework accessible. In summary, our work demonstrates how integrating AI with biological networks can transform omics data into interpretable insights, advancing precision medicine by closing the gap between data generation and meaningful discovery.

Illuminating the Hidden Structure of the Mitotic Chromosome

Name: Kaja Harton

Poster Number: 18

Abstract:

Mitotic chromosomes represent the most condensed state of DNA during the cell cycle. Despite decades of research, the mechanisms underlying their iconic X-shape remain poorly understood. In this study, we investigate whether DNA arrangement within mitotic chromosomes is random or influenced by sequence-derived properties. By integrating cell biology and sequencing approaches, we demonstrate that the periphery of prometaphase chromosomes exhibits a reproducible arrangement. The outermost fragments are consistently AT-rich and enriched in polyA mononucleotide tracks. These findings suggest that DNA folding in mitotic chromosomes may not be entirely random, offering new insights into their structural organization.

Repurposing Antidiabetics for Parkinson's Disease – A genetically informed study

Name: Katalin Vincze

Poster Number: 19

Abstract:

Introduction: Type 2 diabetes and Parkinson's disease (PD) have common pathophysiological processes. Considering this link, it is critical to investigate whether repurposing currently licensed anti-diabetic drugs could aid the primary prevention of PD. Materials and Methods: We conducted a two-sample Mendelian randomization (MR) study using GWAS summary statistics from COURAGE-PD and IPDGC. The drug targets we investigated correspond to antidiabetic drugs. Instrumental variables were selected as the genetic variants coding for the drug target proteins. We proxied antidiabetic drug use with genetically predicted low levels of glycemic traits. We used three different MR models to assess the causal effect between genetically predicted effects of antidiabetic drugs and PD risk, as well as age at onset – with separate analyses. Results: TBD

Scattering and absorption free confocal imaging of 3D samples

Name: Louise Gsell

Poster Number: 20

Abstract:

3D samples, such as organoids and spheroids, have emerged as essential tools in biology, designed to replicate organ and tissue physiology while enabling rapid, reproducible experiments. The transition from traditional 2D cell cultures and animal models to these advanced 3D systems is accelerating in biomedical research. However, a major challenge remains in imaging these cultures due to their size, opacity, and structural complexity, limiting standard microscopy techniques effectiveness. Confocal microscopy, the current gold standard for imaging 3D cell cultures, often faces issues with light attenuation caused by absorption and scattering, making it difficult to obtain accurate, quantitative data across the entire sample. To address this, we have developed a novel approach to quantify light attenuation by leveraging the properties of fluorescent molecules. Our method integrates an imaging protocol with post-processing adjustments to correct for light attenuation, allowing for precise, quantitative analysis using conventional confocal microscopes. With this method, we aim to achieve robust quantitative imaging in 3D cell cultures, paving the way for more accurate experimental comparisons in biomedical research.

HIF Regulatory Pathways Control CD8+ T Cell Fate and Differentiation During Acute Viral Infection

Name: Madara Brice

Poster Number: 21

Abstract:

CD8+ T cells play a critical role in adaptive immunity and must rapidly adapt their metabolism in response to changing microenvironments, including oxygen and nutrient availability. This metabolic plasticity is regulated in part by HIF transcription factors, which are themselves modulated by the oxygen-dependent inhibitors FIH and VHL. In this study, we extended our investigation of HIF regulation in CD8+ T cells using an LCMV Armstrong infection model. We adoptively transferred a 1:1 mixture of WT (Cre-) and T cell-specific FIH, VHL, or double FIH/VHL knockout OT-I cells into WT hosts, followed by infection with LCMV-OVA the following day. We analyzed OT-I T cell responses in blood (days 5 and 7) and spleen (day 7). We observed that FIH deficiency mildly promoted effector differentiation, with minimal impact on expansion or survival. In contrast, VHL-deficient CD8+ T cells failed to proliferate efficiently and exhibited reduced expression of proliferation marker Ki67. Interestingly, these cells resisted terminal differentiation, as shown by lower levels of KLRG1, CX3CR1, and PD1, while maintaining elevated expression of cytotoxic markers such as Granzyme B and Perforin. Strikingly, cells lacking both FIH and VHL displayed signs of severe dysregulation, potentially due to unrestrained HIF activity. These double knockout cells showed severely impaired expansion, suggesting that excessive HIF signalling may drive metabolic stress and cell death. These findings provide further mechanistic insight into how individual and combined HIF regulatory pathways shape CD8+ T cell differentiation, function, and survival during acute viral infection.

Subcutaneous Allergen-Specific Immunotherapy for Allergic Rhinitis: Divergent IgA Responses in Nasal Mucosa and Blood with Validation of B Cell Class-switching in Lymph Nodes and Blood

Name: Maryam Jafari

Poster Number: 22

Abstract:

Background: Subcutaneous immunotherapy (SCIT) has been a cornerstone treatment for allergic rhinitis (AR) for over 50 years, consistently demonstrating symptom reduction and modulation of immune responses. Despite this, the underlying mechanisms responsible for the efficacy of SCIT remain incompletely understood, especially with regard to local immune responses in lymph nodes and nasal mucosa. Aim: To determine the impact of SCIT treatment on immunoglobulin production in blood and nasal mucosa, as well as B cell class-switching in blood and lymph nodes. Methodology: Blood, nasal lavage (NAL), and fine-needle aspirates (FNA) of inguinal lymph nodes were collected from 23 patients with birch and/or timothy pollen-induced AR before and after SCIT updosing. General response to SCIT was evaluated via symptom and medication scores, as well as allergen-mediated activation of basophils. Allergen-specific IgE, IgA, IgG, and IgG4 were measured in blood and NAL visa ELISA. B-cell class-switching was assessed in blood and FNAs by flow cytometry. Results: AR symptoms, medication use, and basophil sensitivity to allergens was reduced after SCIT updosing. Interestingly, the plasma levels of allergen-specific IgA, IgG, and IgG4 increased after SCIT updosing, while the levels of allergen-specific IgE and IgA decreased in NAL at this timepoint. Moreover, these results were accompanied by an increase in class-switched conventional (IgD-CD27+) and unconventional (IgD-CD27-) memory B cells in blood and lymph nodes, respectively. Conclusion: This study highlights the differential impact of SCIT on local and systemic immunity and forwards the systemic increase in allergen-specific IgG4 and IgA as a key determinant of SCIT efficacy. Moreover, the rise in class-switched memory B cells reported in this study suggests a progression towards sustained tolerance. Finally, this study underscores the importance of assessing mucosal immune responses in SCIT evaluations, as evidenced by the local decrease in allergen-specific IgA in NAL.

5-HT1B receptors mediate dopaminergic inhibition of GABA release from striatonigral synapses

Name: Maya Molinari

Poster Number: 23

Abstract:

Besides releasing dopamine (DA) in the striatum—the input structure of the basal ganglia—DAergic neurons of the Substantia Nigra compacta (SNc) also release DA from dendrites in the Substantia Nigra pars reticulata (SNr), a basal ganglia output nucleus. While striatal DA release modulates the activity of medium spiny projection neurons (MSN) to regulate behavior, the behavioral impact of dendritic DA release in the SNr remains unknown. One potential role of DA in the SNr is to modulate GABA release from the axons of D1 receptor-expressing MSNs. However, whether DA directly influences GABA release from D1-MSN synapses in the SNr is unclear. We tested the effect of DA on GABA release in the SNr by performing optical recordings of vesicular fusion and presynaptic calcium influx at D1-MSN synapses, as well as postsynaptic patch-clamp recordings of optogenetically-induced GABA currents in SNr neurons in brain slices. We found that DA exposure inhibited D1-MSN GABA release; however, this effect was independent of D1R activation. Previous studies have suggested that DA releases 5-HT, which inhibits GABA release via 5-HT1B receptors. Notably, we found that DA did not inhibit GABA release in the presence of NAS181, a 5-HT1B receptor antagonist, nor in slices obtained from mice treated with reserpine, which depletes monoamines from the brain. Using a serotonin-sensitive fluorescent biosensor, g5HT3.0, we found that DA increases extracellular 5-HT levels in the SNr, either by interfering with reuptake or by triggering non-exocytic release through the serotonin reuptake transporter (SERT). Treatment with citalopram and GBR12909, which blocks 5-HT and dopamine reuptake, respectively, increased SNr 5HT levels in vivo, as measured by fiber photometry. We show that DA and 5-HT cooperatively fine-tune basal ganglia output activity, which may play a role in the effects of psychostimulant medications and the symptoms of movement disorders such as Parkinson’s disease.

Spatial mapping of DNA synthesis reveals dynamics and geometry of human replication nanostructures

Name: Michael Hawgood

Poster Number: 24

Abstract:

DNA replication is essential to life and ensures the accurate transmission of genetic information, which is significantly disturbed during cancer development and chemotherapy. While DNA replication is tightly controlled in time and space, methods to visualise and quantify replication dynamics within 3D human cells are lacking. Here, we introduce 3D-Spatial Assay for Replication Kinetics (3D-SPARK), an approach enabling nanoscale analysis of DNA synthesis dynamics in situ. 3D-SPARK integrates optimised nucleotide analogue pulse labelling with super-resolution microscopy to detect, classify, and quantify replication nanostructures in single cells. By combining immunofluorescence techniques with click chemistry-based nascent DNA labelling and transfection of fluorescent nucleotide derivatives, we map multi-colour DNA synthesis events in relation to established replication proteins, local RNA-protein condensates or large subnuclear domains. We demonstrate quantitative changes in size, relative abundance and spatial arrangement of nanoscale DNA synthesis events upon chemotherapeutic treatment, CDC6 oncogene expression and loss of chromatin organiser RIF1. The flexibility, precision and modular design of 3D-SPARK helps bridging the gap between spatial cell biology, genomics, and 2D fibre-based replication studies in health and disease.

Impact of Non-Verbal Reasoning and Baseline Individual Differences in Cognitive Training to Enhance Mathematical Abilities

Name: Nieves Ruiz Ibáñez

Poster Number: 25

Abstract:

Enhancing spatial abilities has been suggested as a promising approach to improving mathematical skills. We hypothesized that training with non-verbal reasoning (NVR) tasks would positively influence mathematical learning and that the benefits of training would vary depending on individual differences. We included 1,028 children, aged 5–9 years, who used an adaptive mathematical and cognitive training program for 4 weeks. Participants were randomly assigned to training plans that varied in the proportions of NVR and visuospatial working memory (VSWM) tasks, with equal amounts of mathematical training. Data from the first week of training — including measures of reaction times, accuracy, and trial counts of all tasks — were input into a gradient boosting regressor that predicts the final performance on a number line task. This model was trained on an independent dataset of 33,000 children. Predicted performance (level) was included as a covariate for analyzing the new data. The amount of time spent on NVR tasks was generally associated with greater improvements in math performance. However, there was a negative interaction between the amount of NVR training and baseline performance, such that children with greater mathematical difficulties at baseline, as defined by the prediction algorithm, benefited more from NVR training, while children with higher performance at baseline showed greater improvements training on VSWM tasks instead of NVR. These findings highlight the importance of individualizing cognitive training. They also emphasize the potential of machine learning tools to optimize education, offering personalized strategies to meet each child’s unique needs.

Can γδ CAR T Cells Withstand the Immune Suppressive Milieu of Ovarian Cancer?

Name: Paula Hahn

Poster Number: 26

Abstract:

Ovarian cancer is the leading cause of gynecological cancer-related death. About half of treated patients experience relapse after conventional treatments, so alternative and more efficient therapies are urgently needed. Chimeric antigen receptor (CAR) T cells prove high efficacy in certain hematological malignancies, but have not yet shown sufficient success in solid tumors. Mesothelin has been proposed as a target antigen for ovarian cancer due to its overexpression in ovarian cancer cells. One hurdle to their application in solid tumors is the lack of access, fitness and survival of the T cells in an immune suppressive environment, in particular in autologous settings. Allogeneic options using αβ T cells pose the risk of graft-versus-host-disease (GvHD). γδ T cells however, may be more suitable in this setting due to their non-MHC dependence and their inherent anti-tumor properties. Most previous studies have focused on Vδ2 CAR T cells, but since Vδ1 T cells have stronger tissue-homing and potent anti-tumor functions, we suggest the use of a mixed population. Therefore, we aim to assess the usability and fitness of allogeneic γδ CAR T cells, by exposing them to a tumor microenvironment (TME)-like milieu. Female T cells are transduced with mesothelin-directed CAR T cells, and αβ T cells and γδ T are sorted, separately expanded, and cultured in a hypoxic, patient-derived ascites suspension. Phenotype, gene expression, metabolism, and functionality will be assessed by various methods. Preliminary results showed that γδ T cells can efficiently be transduced with CARs and expanded, retaining both Vδ1 and Vδ2 fractions. Furthermore, cytokine profiles of patient ascites could be associated with survival. A change in gene expression patterns can be observed upon TME-like culture in all cell populations. Planned experiments will show which of both T cell types will better survive and overcome patient-derived immunosuppressive ascites environment, to kill their targets.

Unveiling the Link Between Respiration and Pupil Dynamics: Insights from Machine Learning and Statistical Modeling

Name: Reza Ebrahimian Baboukani

Poster Number: 27

Abstract:

Deciphering the impact of RNA binding proteins on post-transcriptional regulation in disease and evolution

Name: Riccardo Mosca

Poster Number: 28

Abstract:

RNA functionality is a key determinant of cell identity, with its levels tightly regulated to support homeostatic processes such as self-renewal, proliferation, and differentiation. RNA regulation occurs at both transcriptional and post-transcriptional levels, with RNA binding proteins (RBPs) playing a central role in post-transcriptional regulation by interacting with regulatory RNA molecules to modulate cellular processes1. To investigate the functions of RBP, it is crucial to identify their interactome. At this purpose we developed a novel, in vitro, RBP-centric technology that discovers and quantifies RBP binding sites in any given transcriptome/species of interest. RAPseq is an in vitro binding assay between a recombinant purified RBP and native total chemically fragmented RNA. The bound RNA molecules are recovered and sequenced on an NGS platform. Our custom NGS data processing pipelines then deconvolute the RBP binding sites. RAPseq enables cross-species comparisons of RBP binding. Using this method, we analyzed HUR, a divergent ELAV family member, across six vertebrates, showing that binding strength is influenced by amino acid changes without affecting uracil triplet recognition. As a second application, we performed a comprehensive analysis of publicly available data to identify fetal-specific RBPs that are re-activated in liver cancer and performed RAPseq with the selected candidates. Gene ontology and pathway analysis of the RBP CAPRIN1 revealed enrichment in proliferation and cell cycle-related terms. In cellulo knockdown of CAPRIN1 impaired cancer cell proliferation suggesting a tumorigenic role to be further investigated through comprehensive RNAseq and flow cytometry-based cell cycle analyses. 1- Gebauer F et al. Nature Reviews Genetics 22.3 (2021): 185-198. 2- Good, Peter J. "A conserved family of elav-like genes in vertebrates." Proceedings of the National Academy of Sciences 92.10 (1995): 4557-4561. 3- M. Cardoso-Moreira et al., “Gene expression across mammalian organ development,” Nature, vol. 571, no. 7766, pp. 505–509, Jul. 2019.

Apolipoprotein B100 associated antibodies in atherosclerotic plaques contribute to plaque vulnerability through engaging Fc-gamma receptor and transporter

Name: Shiying Lin

Poster Number: 29

Abstract:

Atherosclerosis is chronic inflammation in vascular wall in which multi-factorial immune responses are involved. Low-density lipoprotein (LDL) as one of the main atherogenesis factors constructs atherosclerotic plaques under vessel endothelial dysfunction. Over time, advanced plaque develops more complicated characteristics and tends to rupture, causing acute cardiovascular symptoms. LDL is actively involved in adaptive immunity due to its apolipoprotein (apo) B100 molecule that harbors many immune epitopes. Antibodies with varying LDL reactivity deposit into plaque and form apoB-immune complexes, which subsequentially engage with intraplaque immune cells and profoundly influence atherosclerosis, from lesion characteristics to clinical manifestations. Our study observed that intraplaque antibodies are associated with different plaque morphologies, on which our hypothesis is based that antibodies and their apoB-immune complexes contribute to plaque vulnerability. Antibodies from morphologically defined human atherosclerotic plaques (n=30) from carotid endarterectomy were quantified using immunohistochemistry (IHC). The reactivity towards apoB and immune complex formation was evaluated using immunoassays in both plaques and plasma in a separate cohort of carotid stenosis patients (n=70). Our IHC results show that antibodies in plaques are associated with plaque vulnerability characteristics, including collagen levels, fibrous caps, and smooth muscle cells. Consistently, apoB-specific antibodies are more commonly found in plaques with more complex pathogenic characteristics from symptomatic patients. On the other hand, these symptomatic plaques simultaneously display lower levels of apoB-immune complexes. This purported immune complex consumption is likely mediated through the Fc-gamma receptor and transporter, which process immune complex through endocytosis and release antibodies via exocytosis. We present a conceptual framework of how apoB-immune complex and plaque macrophages engage through Fc-gamma receptor and transporter, through which proinflammatory cytokines (e.g. MCP1, TNF-α) are invoked. The effectiveness of Fc-gamma receptor and transporter in interacting with apoB-immune complexes is correlated with the abundance of matrix metalloproteinase 9 (MMP9), which is particularly related to plaque rupture.

Aging compromises microglia plasticity and increases monocyte-derived macrophage infiltration in the CNS

Name: Stefan Bencina

Poster Number: 30

Abstract:

The central nervous system (CNS) homeostasis is principally maintained by brain-resident macrophages that are divided into parenchymal microglia and non-parenchymal border-associated macrophages (BAMs). During inflammation or injury, local tissue debris or pro-inflammatory mediators can attract monocyte-derived macrophages (MDMs) to migrate into the tissue. During aging, there is an increase in the proportion of MDMs in the CNS, and accumulating evidence supports their pathogenic role in neurodegenerative disease. However, the precise role of MDMs, whether they are protective or detrimental is context dependent, but remains elusive in aging. To investigate the role of MDMs infiltration in the CNS and discern age-related changes, we used the CX3CR1cre-Rosa26DTA mouse model to induce a tamoxifen dependent microglia depletion in young (2 months) and old mice (24 months) mice. The mice received 3 doses of intraperitoneal tamoxifen injection to deplete microglia. To maximize the infiltration of MDMs in the brain, the mice received two rounds of additional tamoxifen-induced depletion within the time window of 3 weeks. Seven days post last tamoxifen injection, mice were sacrificed and myeloid and lymphoid cells isolated from brains were analyzed with flow cytometry. In young mice microglial repopulation was observed after tamoxifen-induced microglial ablation. However, the capacity of microglia to repopulate in old mice was abolished. Infiltration of MDMs occurred in the brains of young and old mice, with further enrichment in aged mice. Concomitantly, increased inflammatory T-cells infiltration was observed in the brains in aging in the absence of microglia repopulation. Our findings suggest that MDMs infiltration into the CNS may cause a detrimental effect, triggering a pro-inflammatory response, especially in aging.

“The health worker tells you about the pills but she doesn’t take them”: Young women’s experiences of peer support for oral PrEP use, Kampala, Uganda

Name: Yunia Mayanja

Poster Number: 31

Abstract:

Background Peer-led HIV prevention interventions among adolescent girls and young women (AGYW) have previously involved brief interactions through peer-delivered test kits and oral pre-exposure prophylaxis (PrEP). Peer support through education offers a more sustained, learning-based approach. This study explored how a peer education intervention influenced PrEP use among AGYW vulnerable to HIV in Kampala, Uganda. Methods Between January 2023 and February 2024, we audio-recorded qualitative in-depth interviews with consenting 14-24-year-old AGYW purposively sampled from those assigned to peer support for oral PrEP use in a randomized controlled trial. Eighteen baseline interviews explored prior experiences with peer support for oral PrEP. Using an explanatory sequential model, 17 follow up interviews were conducted post intervention to explore how it influenced PrEP use. Data were analyzed thematically and follow up interviews interpreted using the situated information, motivation behavioral skills (sIMB) model. Results Before the study, participants had limited PrEP knowledge and no peer support experience. Negative community perceptions were a barrier. Those uninterested in PrEP at baseline did not initiate use. Peer education enhanced knowledge, motivation, and behavioral skills, improving PrEP uptake and adherence. AGYW received accurate information about PrEP. Personal motivation was through HIV risk awareness and positive attitudes while social motivation came from observing peers and receiving psychosocial support. Behavioral skills included self-efficacy, incorporation of PrEP use in daily routines, discreet use, and accessing PrEP while mobile. Non-disclosure helped avoid stigma and accidental sex work disclosure. However, contextual factors like mobility, partner disapproval and ill health limited adherence use. AGYW preferred private, accessible PrEP services with strong health education. Conclusion Peer education positively influenced PrEP use among AGYW. Programs should incorporate peer education and address contextual barriers. Community education, long-acting PrEP and adequate counselling when PrEP is prescribed concurrently with other oral drugs may further support adherence.