Medicine and Health
RESEARCH DAY

ABSTRACT BOOK
28 April 2025

Örebro University, Faculty of Medicine and Health,
School of Health Sciences and **School of Medical Sciences**, Örebro Sweden

ÖREBRO UNIVERSITY

Preface

Dear colleagues

We are proud to present this abstract book, featuring research from the 2nd Research Day of the Faculty of Medicine and Health at Örebro University on 28 April 2025. This joint initiative by the Schools of Health Sciences and Medical Sciences highlights recent advancements across diverse research groups, reflecting strong regional, national, and international collaboration.

This collection showcases the breadth of ongoing research in medicine and health at our university. We remain committed to supporting a vibrant scientific culture, encouraging dialogue, and advancing health and medical science.

We hope you enjoy reading and feel inspired by the work presented.

Best Regards

Karin Blomberg
Dean, Faculty of Medicine and Health

Elina Mäki-Torkko
Pro-Dean, Faculty of Medicine and Health

Elisabet Welin
Head of School, School of Health Sciences

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A systems biology model of sepsis-induced immunosuppression

Niloofar Nikaein, Kaya Tuerxun, Dirk Repsilber, Gunnar Cedersund, Daniel Eklund and X-HiDE consortium

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Background/Objective: WHO has recently recognized sepsis as a world health priority which on average causes one death every 2.8 seconds, according to the global sepsis alliance foundation. Sepsis involves a hyperinflammatory phase followed by suppression of the immune system i.e., immunosuppression. Studying the dynamic behavior of immune cells and inflammatory signalling is crucial for building hypotheses about the underlying mechanisms of the condition.

Method: We have trained an ordinary differential equation (ODE)-based model of sepsis-induced immunosuppression, based on a set of time-resolved experimental data, generated by a primary human monocyte cell culture model challenged by LPS. The model is being developed building on our previous ODE models that focused on proinflammatory activation of monocytes.

Result: By developing this model, we are identifying the key components of the signaling pathways involved in sepsis-induced immunosuppression and how their interplay can explain both inflammatory phenotypes, acute inflammation as well as immunosuppression.

Conclusion: Mathematical ODE models can help us build hypotheses about the underlying mechanisms of sepsis-induced immunosuppression. In future, a validated model of inflammation in a sepsis condition could help in prognosis based on model predictions from ex vivo immune cell data, i.e. in a precision medicine setting.

An international project to enhance Parent-led pain management to Optimize neonatal Pain care: the POP Study

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Background/Objective: Hospitalized neonates are subjected to a high number of painful procedures every day. Cumulative poorly treated pain can have negative consequences on short and long-term outcomes, negative effects that are further amplified by infant-maternal separation. Research has shown that parents want to be part of their hospitalized infants pain management and that it is safe and effective. Yet, the implementation of parent-led pain management in neonatal care is sub-optimal. The overall aim of the project is to expand parent-led neonatal pain management, resulting in less infant pain and potentially better neonatal health outcomes, along with improved parent mental health and well-being.

Method: The project is carried out by an international research group with researchers and parent representatives from Canada, Finland, Italy and Sweden, and will follow the British Research Council's framework for complex interventions. It is organized into four work packages (WPs): Theory and concept (WP1), Identifying the problem (WP2), Developing an instrument and algorithm for self-audit (WP3), and Intervention and implementation (WP4). Principles for patient-public involvement will also be followed, with parent representatives involved in planning and designing the project and when applicable in data collection and publication of results.

Result: An international team consisting of clinicians, researchers and parent partners across four countries have commenced initial work from WP1: writing a position paper, performing a literature review, and conducting an analysis of the concept of parent-led pain management.

Conclusion: The POP-project builds on the contribution of parents, researchers and clinicians and has the potential to improve implementation of parent-led pain management for neonates world-wide.

Anti-Inflammatory Diet Index (AIDI) and Bladder Cancer Risk: A 22-Year Prospective Swedish Cohort Study (1998–2020)

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Background/Objective: Tobacco smoking and occupational exposure to carcinogens constitute well-established risk factors for bladder cancer (BC), while limited evidence suggest a possible effect of dietary factors and inflammation on BC risk. Dietary patterns with impact on systemic levels of inflammation have been proposed and investigated as possible determinants of cancer risk. In this cohort study, we evaluated the association between the anti-inflammatory potential of diet and the risk of BC.

Method: Using the Swedish Infrastructure for Medical Population-Based Life-Course and Environmental Research (SIMPLER), we identified a study population of N=79,292 men and women. We used a 96-item food frequency questionnaire (FFQ), completed at baseline in 1997 and repeated in 2009, to calculate the Anti-Inflammatory Diet Index (AIDI) for all participants. AIDI is a previously developed, empirically derived composite measure of dietary anti-inflammatory potential. The index comprises 16 food groups: 11 with proposed anti-inflammatory and 5 with proposed pro-inflammatory potential. We used ICD-10 code C67 to identify incident BC cases op to year 2020 in the Swedish National Cancer Register, and we used baseline study questionnaire to assess covariates, including smoking status and socioeconomic measures. We further used Cox proportional hazards regression models to estimate unadjusted and multivariable-adjusted hazard ratios (HRs) and 95% confidence intervals (95% CIs) for the association between quartiles of AIDI in the population and later BC diagnosis – overall as well as with outcome separated into non-muscle invasive (NMIBC: Ta or T1 or CIS and N0, M0) and muscle invasive (MIBC: ≤T2 or N1 or M1) BC for cases occurring after year 2004.

Result: During follow-up until 2020, 1165 BC cases occurred, of which 201 were known muscle invasive and 715 of unknown stage. Overall, we observed an inverse association between the highest quartile of AIDI (Q4 vs. Q1, representing most anti-inflammatory diet compared to most pro-inflammatory) and later BC diagnosis (multivariable-adjusted HR 0.74, 95% CI 0.61- 0.89, p-trend: 0.01). When separating outcome by stage, we observed an association for MIBC (HR 0.35, 95% CI 0.22-0.57), but not for NMIBC (HR 0.86, 95% CI 0.57-1.28).

Conclusion: We observed an inverse association between a measure of dietary anti-inflammatory potential and BC risk, particularly the risk of MIBC. Our observations support a possible implication of the inflammatory potential of diet in BC development and the more pronounced association observed for MIBC may hint at a true biological association.

Avoiding bleeding complications during surgery in patients under dual antiplatelet therapy (DAPT)

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Background/Objective: Patients experiencing a myocardial infarction or stroke reaching the emergency department are set under a regime of dual antiplatelet therapy (DAPT) as early as possible to hinder the progression of vascular occlusion. Patients surviving such an event will receive long-term if not lifelong DAPT.
While preventing ischemic recurrences, the inhibition of platelet function and aggregation by DAPT is clearly associated with an increased bleeding risk, a feared complication during surgery leading to significant morbidity and mortality.
We investigated if fucoidans, long chain sulfated polysaccharides found in various species of marine brown algae, could bypass the impeding effects of DAPT on human platelet aggregation.

Method: Aggregation of human platelets was assessed in heparinised whole blood from healthy volunteers by determining single (= non-aggregated) platelets using a hematology analyser (Swelab Alfa). Blood samples were preincubated with vehicle or DAPT (at 37°C, with stirring at 900 rpm) and then challenged with the physiological agonist collagen or with fucoidan. The data received was processed as single platelet count in resting samples (= 0% aggregation) compared to stimulated samples (wherein a count of 0 single platelets would reflect 100% aggregation).

Result: Collagen-induced platelet aggregation peaked within 2-5 min of stimulation around 80-90% and was slightly reversible; approx. 60% aggregation after 10-30 min of stimulation. Pretreatment with DAPT effectively prevented aggregation by collagen, resulting in 15-25% aggregation.
Fucoidan provoked platelet aggregation in a likewise rapid but sustained fashion; reaching approx. 75% after 2 min of stimulation, and remaining stable around 80% over up to 30 min. In the presence of DAPT, fucoidan evoked platelet aggregation within 2-5 min of stimulation up to 50-60%, which remained sustained and reached approx. 70% after 30 min.

Conclusion: Our results indicate that fucoidans might be applied to tackle bleeding and to avoid related complications during surgery in patients under DAPT.
Together with our industrial partners we are currently developing novel haemostatic patches with fucoidans as an integrated compound to be applied topically on site of a sutured but bleeding wound. In parallel we are preparing for a proof of concept study in a preclinical large animal model.

Capturing weak signals of differential regulation with help of systems biology

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Background/Objective: Strong signals of molecular dysregulation are wanted in both pre-clinical and clinical research. In the typical screening setting, signals should be strong enough to show significance in a discovery cohort to warrant further investigations and efforts for validation. However, this translates often to a search for strong signals only, also when arguing for clinical relevance or utility. We argue that, instead, more emphasis should be given to weak signals, as they might mark the actually more useful findings. Finding weak signals can be achieved when making use of available additional related information, in general. In our work we make use of public databases on molecular interactions or molecular networks. Analysis of biological networks is a field of systems biology which is advancing towards decisive importance for precision medicine.

Method: The TRRUST database contains curated information about transcription factor target gene interactions for both human and mouse. We used a published gene expression dataset on small particle stimulation of lung epithelial cells to compare a collection of network-based differential expression analysis methods, including our own proposed new algorithm. The algorithm, as published by Rush & Repsilber, is based on the widely accepted notion that regulatory changes in molecular networks are expected to affect modules in such a network, i.e. several more tightly interacting molecules, rather than single molecules without any relation to each other. We evaluate power and specificity of our proposed algorithm and a collection of similar approaches first on simulated data and finally on the example experimental dataset.

Result: Our results show that for most simulated scenarios several standard analysis methods for finding signals of differential expression in transcriptome data perform comparably, while our proposed algorithm would excel in settings with scarce data or noisy data. The evaluation based on the public experimental dataset reveals both signals of differential regulation for molecules already described in the original publication alongside with additional candidate dysregulated molecules for which the individual differential expression signal was otherwise too weak.

Conclusion: Relevant OMICs datasets for pre-clinical and clinical studies often contain either scarce or noisy datasets as variation among data from different study participants can vary considerably and large-scale molecular datasets are, still, rather expensive to collect. Algorithms to find weak signals of dysregulation in large-scale molecular datasets profit from using information on molecular network structure. Our proposed algorithm showed specific utility for otherwise difficult settings and will be used in our X-HiDE platform in collaboration with pharma industry.

Carriage of antibiotic resistant Escherichia coli in Swedish children – a nationwide study

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Background/Objective: Carriage of resistant Enterobacteriaceae is an important reservoir for antibiotic resistance determinants, and carriage is associated with an increased risk of infection and mortality. *Escherichia coli* is also the most common cause of urinary tract infection. The aim of this study was to investigate the carriage of resistant *Escherichia coli* among asymptomatic Swedish children, ≤4 years, as part of a nationwide study on dietary habits.

Method: Children in three age groups, 9, 18 months and 4 years, were invited to participate in the nationwide study ”Riksmaten young children” by the Swedish Food Agency (SFA) Uppsala, Sweden through a registry based random approach., The aim was to receive at least 300 fecal samples per age group. Fecal samples were collected by the parents and sent to SFA, where they were stored frozen. All samples were then thawed and spread on 1) Uriselect 4 chromogenic agar (Bio-Rad), 2) Uriselect 4 suplemented with vancomycin + nalidixic acid (NAL) or Trimethoprim (TMP) and 3) CHROMAgar ESBL, CHROMAgar SuperCarba (CHROMAgar) and incubated in ambient air over night. Species determination was performed using MALDI-TOF and verified *E. coli* were tested for antibiotic susceptibility using Disk Diffusion according to EUCAST.

Result: 282 (9mo), 305 (18mo) and 290 (4yrs) samples were cultured with growth of Enterobacterales in 89%, 83% and 51% of the samples respectively. The presence of *Escherichia coli* resistant were in the respective age group 13,1%, 13,0%, 12,8%, for NAL, 16,2%, 18,3%, 12,1% for TMP and 3,6%, 4,0% and 4,0% for CTX. There was no growth of carbapenem resistant Enterobacterales.

Conclusion: This is the first nationwide study investigating the carriage of resistant *E. coli* in Swedish children. The resistance rates are in line with results from previously performed smaller cohort studies in children and a nation wide study in adults indicating stable, low level, of CTX resistant *E.coli* in Swedish children. Resistance to quinolones and trimethoprim were similar in all age groups.

Correlations between Trimethylamine-N-oxide, megalin, lysine and markers of tubular damage in chronic kidney disease

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Background/Objective: Trimethylamine-N-oxide (TMAO) is a gut microbiota-derived metabolite implicated in chronic kidney disease (CKD). Megalin is a receptor expressed by renal proximal tubular cells, which is essential for albumin reabsorption. Megalin function is known to be inhibited by lysine. Both TMAO and megalin have been implicated in CKD development, but the link between them is not well studied. The aim of this study was to investigate if there are any correlations between the levels of TMAO, megalin, lysine and tubular damage in CKD.

Method: Serum samples and 24-hour urine samples from CKD stage 4–5 Swedish patients from the prospective cohort study European QUALity (EQUAL) were used in this study. Patients ≥65 years of age were included if their estimated glomerular filtration rate (eGFR) had decreased for the first time to ≤20 mL/min per 1.73 m2 during the previous 6 months (between March 2012 and February 2019). Controls ≥60 years of age were randomly selected by the Statistics Bureau of Sweden (www.scb.se). The only exclusion criteria for selecting healthy controls was a lack of willingness to participate in the study. Urinary metabolites, including TMAO, choline, L-carnitine, betaine, lysine, and creatinine, were quantified using ultra-high-pressure liquid chromatography-tandem mass spectrometry (UHPLC-MS/MS). Additionally, urinary levels of megalin, albumin, EGF, and MCP-1 were determined by enzyme-linked immunosorbent assays.

Result: Analysis revealed that choline, L-carnitine and betaine, but not TMAO, was increased in the urine of CKD patients compared to controls. Soluble megalin, albumin and lysine were also increased in the urine of CKD patients compared to controls. Markers of tubular damage such as EGF and EGF/MCP-1 were decreased, and MCP-1 was increased in CKD patients. Correlation analysis showed that both urine and serum TMAO were positively associated with soluble megalin and negatively associated with EGF/MCP-1. Soluble megalin correlated positively with lysine and albuminuria, and negatively with EGF/MCP-1. Urine choline, L-carnitine, and betaine were positively associated to soluble megalin and lysine, while choline was also associated with albuminuria.

Conclusion: In conclusion, our results shed new light on the pathophysiologic role of TMAO, megalin and lysine in CKD, which may help unravel new therapeutic targets for CKD treatment.

Development and characterization of Langat virus infectious clones as live-attenuated TBE vaccine candidates

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Background/Objective: Tick-borne encephalitis (TBE) is one of the most important tick-transmitted diseases in Europe and Asia. TBE virus (TBEV) infections lead to a diversity of outcomes ranging from mild flu-like symptoms to severe neurological disorders. There is no specific antiviral treatment available for TBE and vaccination remains the best protective measure. Repeated booster doses of commercially available inactivated TBE vaccines are required to sustain immunity. In addition, vaccine breakthroughs are reported in some patients, especially in the elderly. Live-attenuated viral vaccines are known to provide long-term, sometimes lifelong, immunity after a single dose. Langat virus (LGTV) is a naturally attenuated strain of TBEV which makes it a potential candidate for live-attenuated TBE vaccine.

Method: We used RNA- and DNA-based reverse genetic methods to produce LGTV infectious clones (ICs). Next generation sequencing (NGS) was performed to assess the genetic integrity and stability of these ICs. In addition, we performed *in vitro* and *in vivo* characterisation of one of the rescued LGTV ICs and compared it with the LGTV strain in our lab.

Result: In this study we have designed and rescued four ICs of LGTV. NGS of the rescued ICs showed that the viruses rescued by DNA-based methods were more similar to the parental LGTV sequence and they showed higher genetic stability after passaging in cell culture. The *in vitro* and *in vivo* characterisation of a DNA-launched LGTV IC exhibited growth kinetics and immune profile comparable to the LGTV strain in our lab.

Conclusion: This study provides a crucial foundation for developing a more robust live-attenuated TBE vaccine capable of providing long-lasting immunity.

Differential gene and protein expression of key regulators of the IGF, adiponectin and PPAR signalling pathways in placentas from small, appropriate and large for gestational age newborns

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Background/Objective: Foetal growth involves a complex interplay of molecular systems, including the insulin/insulin-like growth factor (IGF) system, adiponectin, and peroxisome proliferator-activated receptors (PPARs) signalling pathways. This study aimed to investigate the expression and abundance of a subset of genes and proteins associated with these pathways in placental tissue and cord blood collected from small-for-gestational-age (SGA), appropriate-for-gestational-age (AGA), and large-for-gestational-age (LGA) infants, as well as associated first-trimester maternal serum.

Method: A total of 55 LGA-, 61 SGA-, and 109 AGA-born infants were included in the study. RT-qPCR was employed to analyse placental tissue samples collected at term, focusing on differential expression of 22 key genes, including IGF1, IGF2, IGF1R, IGF2R, INSR, IGFBP1-7, PPARA, PPARB, PPARG, RXRA, RXRB, ADIPOQ, ADIPOR1, ADIPOR2, APPL1, and APPL2. A blinded assessor evaluated a subset of placental samples (n = 78) using semi-quantitative IHC analysis to validate differential gene expression at the protein level. ELISA was utilised to measure the abundance of chosen proteins (IGF1, IGF2, sIGF2R, IGFBP2, PAPP-A) in first-trimester maternal serum samples, as well as four proteins (IGF1, IGF2, sIGF2R, IGFBP2) in cord blood samples collected at term.

Result: The expression of placental genes IGF1, IGF2, IGF2R, IGFBP2, and PPARA varied among the three groups, with significant findings for IGF1, IGF2, and PPARA after multiple testing corrections. No meaningful expression of ADIPOQ was observed. With IHC analysis, strong expression of IGF1, IGF2, IGF2R was observed in the LGA group compared to the SGA and AGA groups. Strong expression of PPARA was observed in the LGA group compared to the SGA group. Weak expression of IGFBP2 was observed in both the LGA and AGA groups compared to the SGA group, with weaker expression in the LGA group compared to the AGA group. A strong positive correlation was found between cord blood IGF1 and infant birth weight ($rs = 0.73$, $p < 0.001$), and a strong negative correlation with IGFBP2 ($rs = -0.56$, $p < 0.001$). A modest positive correlation was observed for IGF2 ($rs = 0.42$, $p < 0.001$). No associations were found between maternal serum protein levels and infant phenotype.

Conclusion: This study shows for the first time in humans an association between PPARA and foetal birth weight and confirms the association between the IGF signalling pathway and birth weight.

Digital Psychological Treatment

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Objectives and key research themes:
Our vision is to **explore the full potential of digital technology in psychological treatment** by:

- Maximizing the effect of known digital treatments
- Expanding to new problem areas & new groups
- Investigating the role of therapist guidance
- Developing and testing new digital treatments
- Better predicting who will benefit

Methodologies and approaches:
Randomized Controlled Trials (RCT:s)
-Superiority
-Non-inferiority
Qualitative studies
Mixed methods
Meta-analyses

Collaborations and partnerships:
With researchers at Karolinska Institutet we are exploring digital self-care (without therapist support) for anxiety and depressive symptoms. The goal is evidence-based self-care with increased avvailability and scalability.
With researchers at Amsterdam University Medical Centers we are investigating the possibilities of digital treatment for the prevention of relapse in depression (ITFRA-collaboration).

Key achievements and future directions:
Researchers in the group has published research on Digital Psychological Treatments since 2005 with a variaty of angles, including efficacy, effectiveness, participant experiences, prediction, psychometrics, comorbidity, treatment, relapse prevention as well as the communication between therapist and patient. Digital treatment programs for depression and for individuals with autism has been developed and tested by this group.
Future research will be aimed at increased availability to evidence-based psychological treatment.

Effectiveness of a group-based time-management intervention: a randomised controlled trial

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Background/Objective: Time management skills are essential in daily life. People with ADHD, autism or mental disorders typically have time management difficulties which often causes problems in daily life. Training to use time assistive devices is the usual treatment, but the group intervention Let's Get Organized (LGO) is also promising, and needs to be evaluated. Therefore, the study aimed to evaluate the effectiveness of LGO compared to treatment as usual, to improve time management skills, parental self-efficacy and to evaluate its health economic outcome.

Method: A multi-centre, open, two-armed randomized controlled trial included 75 participants at baseline (mean age 32.3 years) of whom 28 were parents. Data were collected pre-, post- and 3 months post intervention. Instruments included e.g. Assessment of Time Management Skills, Parental Sense of Competence Scale and EQ-5D-5L. Non-parametric tests and mixed-effects models were used to analyze data.

Result: Preliminary results showed statistically significant improvement of time management skills in both groups, as well as in organisation and planning skills, emotional regulation, general self-efficacy and satisfaction with daily occupations at post-intervention. Most of the improvements were sustained after 3 months. Changes from baseline in time-management skills between LGO and TAU were not significantly different. Program completers in LGO (>=7 of 10 sessions) had better sustained time managements skills at 3 months than non-completers. Between-group comparisons of changes from baseline favoured TAU for organisation, planning and emotional regulation at post-intervention but not at 3-month follow-up.

For parents the results indicated a significant improvement in parental self-efficacy both in total score and the parenting efficacy subscale after time management interventions, but this improvement was not sustained at 3 months follow-up. There was no significant difference between groups. Parents' interest was quite high from start and remained stable at all measurement points. The two interventions were equally effective in improving QALYs, and thus a cost-minimization analysis is under way and will be reported at the research day.

Conclusion: This RCT showed that both LGO-S and individual occupational therapy are clinically useful interventions to improve time-management skills.

From the first cell division to birth - the impact of nuclear errors

Amanda Stenberg, Juliane Baumgart, Emma Adolfsson

Region Örebro County

Background/Objective: The first mitosis in embryos is , potentially causing aneuploidy and developmental arrest. Time-lapse imaging (TLI) has enabled the observation of the nuclear status at the two-cell embryo after the first mitosis. This division happens at night and therefore cannot be observed with conventional embryo culture. In our previous study, we concluded that nuclear errors (NE) could be categorised into different phenotypes, and were not only common in two-cell embryos (but also negatively correlated with the embryo's ability to form a clinically useful blastocyst. Two-cell embryos with split nucleation or different errors in each cell were the least likely to develop (whereas embryos with bi-nucleation behaved as normal embryos without NE). The aim of this study is to explore whether NE in the two-cell stage affects the pregnancy rate (PR) and live birth rate (LBR) of transferred blastocysts.

Method: In this retrospective cohort study, 2566 blastocysts transferred either fresh on day five or frozen-thawed on day 5 or 6 were assessed using TLI and grouped based on the type of NE present at the two-cell stage (44 hours post-insemination). Mononucleated and binucleated embryos were classified as normal whereas all other nuclear patterns were categorized as either multi-nucleation, micronucleation or split-nucleation. When two different NE occurred, the embryo was categorized as mixed error. All embryos were cultured in time lapse incubator (EmbryoScope, Vitrolife, Sweden) at +37°C, 6% CO2 and 5% O2 in pre-equilibrated culture media with oil overlay (Vitrolife). Outcomes in form of achieved pregnancy and live birth was obtained from laboratory records.

Result: In this cohort, the NE rate was 24.2% (622/2566), with micro-nucleation being the most common (10%), followed by multi-nucleation (8%), split-nucleation (4%), and mixed error (3%). The overall PR in the cohort was 51.8% (1330/2566), and the LBR was 36.3% (926/2552). Only split nucleation showed significantly lower PR (41.1%) (OR 0.63 (0.41-0.97), $p<.05$) and LBR (25.6%) (OR 0.59 (0.36-0.96), $p<.05$) compared to embryos without NE. All other groups showed comparable results regarding both outcomes.

Conclusion: NE in two-cell embryos affects the embryos' ability to reach the blastocyst stage; however, if the embryo did develop into a blastocyst, the PR and LBR are comparable between all NEP categories - except for split nucleation. Prolonged culture to blastocyst for all patients could therefore improve outcomes after assisted reproduction.

Health and family climate in families where a parent has deafblindness

Moa Wahlqvist, Agneta Anderzén Carlsson

Region Örebro County

Background/Objective: Research has identified that deafblindness implies challenges in daily life. Deafblindness is a combination of hearing- and vision impairment where the senses fail to compensate for each other. Consequences of deafblindness are related to taking part of information, to communicate with others and safety regarding orientation and mobility. From a system theory perspective, it is reasonable to assume that the entire family could be affected when a parent has deafblindness. However, studies focusing on parenting and family life in this context are sparse.
Hence, the objective of this project was to describe the family situation, the health and wellbeing, in family members where a parent has deafblindness.

Method: Data were collected by means of questionnaires and semi structured interviews. Family members from 16 families participated (14 parents with deafblindness, 6 partners and 18 children). Analysis of questionnaires were conducted by descriptive statistical analysis and interview data was analyzed with different qualitative methods.

Result: The parents with deafblindness described their family life and being a parent as something that gave them great joy, but the feelings were intertwined with uncertainty mainly because of lacking services and support. They wanted to take on a parental responsibility, but sometimes they felt forced to abdicate from the responsibility. An adapted environment facilitated, like support from a guide or a professional interpreter with personal knowledge of the family did. The partners experienced that the consequences of the deafblindness ruled the family. They expressed a need for rest from responsibility, and a need for support in everyday life for the couple to be able to handle their family life. The children shared experiences of a family life like their peers, doing same activities. The children also described empathy and concern for their parent with deafblindness. Negative feelings were mostly connected to lack of knowledge from others in society or from professionals. On group level, the family climate pattern was uniform; the parents with deafblindness, partners and children scored a high level of family closeness. However, health related quality of life and sense of coherence revealed a strained situation mainly on behalf of the parent with deafblindness.

Conclusion: The consequences of deafblindness affects all family memebers and the entire family. In order to maintain a healthy family life, the adults empathized a need for support to the individual family members, and for the whole family. The findings can serve as a base for family support interventions.

Healthcare visits, patterns of treatment, and related costs in children with controlled and uncontrolled atopic dermatitis in Sweden.

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Background/Objective: Pediatric atopic dermatitis (AD) is a common chronic disease. Treatment can be necessary over a period of several years. For assessing treatment outcomes, the concept of controlled and uncontrolled AD was recently introduced. The aim of the study was to estimate the healthcare resource use in terms of visits, treatments and costs in children with controlled and uncontrolled AD.

Method: The study utilised administrative data and hospital patient records. Data included children with AD treated in primary care, and specialist care at regional and university hospitals, with at least three years of follow-up. The study included 8922 children aged 0-17 years diagnosed with AD between 2015 and 2018 in three Swedish regions.

Result: About 13% of children had uncontrolled AD. In dermatology clinics, most patients with uncontrolled disease were 12-17 years-old (39%) and 17% had moderate-to-severe AD; 2% had systemic drug treatment and 7% received UVB treatment. Uncontrolled AD involved treatment changes and frequent visits in specialist care over several years compared to controlled disease.
The mean annual healthcare cost of an AD patient in the 0-17 years age group in Sweden was estimated at €4479.5. There was a statistically significant difference (around €4000) in the mean annual cost per individual between patients with uncontrolled AD and those with controlled disease.

Conclusion: AD involved high healthcare utilization, especially for children with uncontrolled disease. A high proportion of children with AD might be undertreated and risk groups, such as adolescents with uncontrolled AD, should be treated more effectively.

Identification of TRIM21 and TRIM14 as antiviral factors against Langat and Zika viruses

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Background/Objective: Flaviviruses, including mosquito- and tick-borne species, cause significant global health burdens. The ability of these viruses to evade host antiviral responses is crucial for their replication and transmission. While tripartite motif-containing (TRIM) proteins have been identified as key antiviral restriction factors, their roles in flavivirus infections remain incompletely understood. This study aims to identify TRIM proteins involved in flavivirus restriction and characterize their antiviral mechanisms.

Method: We purified the endoplasmic reticulum (ER) membrane fractions from flavivirus-infected cells and performed mass spectrometry-based proteomic analysis to identify host proteins enriched during infection. TRIM14, TRIM21, and TRIM38 were selected for further characterization based on their enrichment profiles. Functional validation of these TRIM proteins was conducted using overexpression, RNA interference, and virus replication assays, complemented by immunofluorescence microscopy to determine subcellular localization and protein interactions.

Result: Our study identified TRIM14, TRIM21, and TRIM38 as restriction factors for Zika virus (ZIKV) and Langat virus (LGTV) replication. Overexpression of TRIM14 and TRIM21 significantly reduced both ZIKV and LGTV titers, while TRIM38 specifically restricted ZIKV. TRIM14-mediated restriction of LGTV correlated with its colocalization with NS3 and NS5, whereas TRIM14 and TRIM38 colocalized with NS3 in ZIKV-infected cells. Interestingly, TRIM21 did not colocalize with viral proteins, suggesting an alternative antiviral mechanism. Additionally, TRIM14 knockdown impaired the antiviral effects of IFN-⍺, indicating its role as an interferon-stimulated gene (ISG).

Conclusion: Our findings establish TRIM14, TRIM21, and TRIM38 as key antiviral factors targeting flaviviruses. TRIM14 restricts LGTV by interacting with NS3 and NS5, while TRIM14 and TRIM38 inhibit ZIKV replication via NS3 interaction. TRIM21 acts independently of direct viral protein binding. These insights enhance our understanding of host-virus interactions and may inform future antiviral strategies against flaviviruses.

Impact of morula compaction and blastocyst morphology on clinical outcomes after assisted reproduction

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Background/Objective: IVF embryos have historically been evaluated by being removed from the incubator and quickly checked under the microscope at fixed time points and then returned to the safety of the incubator. Time lapse incubators gave the embryologists the opportunity of uninterrupted evaluation in a video format without negative consequences of exposure to suboptimal culture conditions. With time lapse (TL) all events in early embryo development can be studied, including the overlooked transition from cleavage stage embryo to blastocyst that takes place between day 3 and day 5. Morula compaction and subsequent blastocyst quality of transferred blastocysts was analyzed to understand the importance of this milestone on clinical outcomes.

Method: Retrospective study using TL images of blastocysts resulting after assisted reproduction. Oocytes were retrieved after controlled ovarian stimulation and fertilised using either conventional IVF or ICSI. All embryos were cultured in TL incubators, at +37 C, 6% CO2 and 5% O2 for up to six days. Images were obtained in several focal planes every 15 minutes.
Morulas were categorised as either **complete** (resulting from the inclusion of all daughter cells into a morula) or **partial** (exclusion of daughter cells) by studying all available images of embryo development between cleavage stage and blastocyst stage, and as either top quality blastocysts (**TQB**), good quality blastocysts (**GQB**) or low quality blastocysts (**LQB**) on day 5 or 6 of embryo development. Groups were compared for pregnancy rates and live birth rates using chi-2 test with post hoc analysis.

Result: Of the 2566 blastocysts, 1562 (64.6%) originated from complete morulas, and 854 (35.4%) from partial morulas. Complete morulas were more likely to develop to TQB compared to partial morulas, 57.8% vs 33.4%, p<.001, and less likely to develop into LQB; 5.0% vs 13.0%.
Combining morphology score (TQB, GQB, LQB) and morula compaction (complete/partial) improved differentiation in terms of pregnancy rates and live birth rates. TQB orginating from complete morulas achieved the highest pregnancy rate, 59.3%, and live birth rate, 41.8%. LQB originating from partial morulas achieved the lowest pregnancy rate, 31.7%, and live birth rate, 21.4%. Differences were statistically significant, p<.001.

Conclusion: This study adds evidence that TL captures aspects of embryo development that impacts the implantation ability of the formed blastocyst, i.e the transition phase between day 3 and day 5. Classifying each morula as complete or partial can help to identify blastocysts with the highest ability to implant and result in a live birth.

Increased proportion of circulating monocytes and neutrophils with impaired phagocytosis capacity in patients with peripheral arterial disease

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Background/Objective: Peripheral arterial disease (PAD) is a clinical manifestation of atherosclerosis, affecting arteries in the leg. Based on their symptoms and severity, PAD patients are characterized into three sub-groups: asymptomatic, intermittent claudication (IC) and critical limb ischemia (CLI). Despite its high prevalence, PAD remains under diagnosed and the role of immune cells in PAD pathophysiology remains poorly understood. In this study, we characterized the innate immune responses in PAD patients compared to healthy controls.

Method: Blood samples were collected from 30 patients with PAD (IC) and 34 healthy controls, to assess the surface and intracellular phenotype of monocytes and neutrophils by using 10-colour flow cytometry. Phagocytosis assay was performed with labelled *E.coli* bio-particles. Mann-Whitney U non-parametrical test was used for statistical comparison between PAD patients and healthy controls.

Result: A significantly higher proportion of monocytes ($p<0.05$) and neutrophils ($p<0.01$) were observed in PAD patients compared to healthy controls. Interestingly, both neutrophils and monocytes showed a significantly impaired phagocytosis capability ($p<0.001$ and $p<0.05$) and reduced expression of myeloperoxidase (MPO) ($p<0.01$). Neutrophils also had reduced levels of reactive oxygen species in PAD patients compared with healthy controls ($p<0.05$). In addition, CD14+ and CD14 +CD16+ monocytes ($p<0.01$ and $p<0.01$) also showed reduced MPO expression in PAD patients compared to healthy controls. Upon LPS stimulation, neutrophils produce increased levels of IL6 and IL8 in PAD patients compared with healthy controls ($p<0.05$).

Conclusion: Taken together, these results suggest that PAD patients have an increased proportion of monocytes and neutrophils in circulation, with impaired phagocytosis capability, but inflammatory compared to healthy controls. Currently we are assessing the intrinsic imprint of monocytes and neutrophils by evaluating global gene expression profile of sorted monocytes and neutrophils with RNA Seq. analysis.

Modelling the Gut-Brain Axis: A Novel Ex Vivo-In Vitro approach

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Background/Objective: Studying the gut-brain axis involves luminal metabolites crossing or regulating the blood-brain barrier (BBB), thereby affecting brain function and behavior. Increasing evidence highlights the role of gut microbiota-derived metabolites, such as short-chain fatty acids, in tryptophan/serotonin metabolism and regulation in gut-brain axis disorders, e.g., irritable bowel syndrome (IBS). For defining the underlying mechanisms, modelling the gut-brain axis is essential.

Method: Human dermal fibroblasts – BBB-representing cells – were cultured under physiological or oxidative stress conditions, along with serosal fluids of healthy or IBS participants, whose intestine was or wasn't exposed to 1) butyrate *in vivo* or 2) to a fiber fecal ferment *ex vivo*. After serosal fluid characterization and cell-viability/ cytotoxicity assessments, therapeutic or protective capacity was determined for 1- and 24-hour treatments. Additionally, we measured gene and protein expression of tryptophan-related membrane transporters, tryptophan uptake, and conducted metabolite profiling.

Result: Different serosal fluids were characterized by different metabolite profiles, and serosal fluid culturing did not compromise viability or had cytotoxic effects on the fibroblasts. Under non-stress, cells showed no altered expression of tryptophan membrane transporter genes, proteins or their activity. However, statistically and biologically significant changes were observed under H2O2-induced stress, especially in the preventive measure.

Conclusion: Adding serosal fluids prior to H2O2 revealed interesting patterns on gene, protein, and metabolite level, supporting a protective role. Interestingly, cells seemed fairly sensitive to treatment with fecal ferment serosal fluids. In sum, this new model allows the exploration of the direct effects of serosal contents on BBB-representing, fibroblasts across all levels and shows increased potential for expansion and personalization.

Navigating imaginary positions of masculine athlete bodies

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Background/Objective: While sport promotes enjoyment, embodied learning, and health, it also serves as a setting where people learn and navigate certain ideals and norms. Given the physical nature of sport, body norms and their impact on performance are particularly central. These body norms are intrinsically linked to gender norms. Most sports follow a binary structure, categorizing athletes as male or female, shaping expectations of how bodies should look and perform. Coaches play a key role in reinforcing these norms. For example, they have been shown to encourage weight-controlling behaviors and demand extreme weight loss, arguing that it enhances performance. Research on the athlete's body and its role in body-critical coaching practices has primarily focused on women's sports. This study aims to provide in-depth knowledge about the positioning of elite athletes as masculine-gendered beings in sports in relation to norms surrounding the masculine body.

Method: Building on the importance of the coach, 12 Swedish elite coaches from 9 different sports were interviewed about the role of body weight, shape, and size in their respective sports. Imaginary positions were used as a lens to map norms of the masculine sporting body. Exploring imaginary positions empirically involves analyzing patterns of what are known as practical ideologies—described in this case by sports coaches—and how these ideologies shape what is considered possible or impossible.

Result: Elite athletes construct themselves as masculine-gendered beings by navigating five imagined positions: the performing athlete, the fit athlete, the ironic athlete, the social athlete, and the self-regulated athlete. The greatest tension arises between the performing and fit athlete positions, as societal ideals of fitness can conflict with the demands of peak performance. However, in general, these positions largely reinforce one another. Athletes are expected to see their bodies as tools to calibrate, maintaining a detached and carefree attitude. This detachment is expressed through irony, joking about their own and others' bodies, and being social. Athletes who are introverted or sensitive about their bodies face barriers. Some exceptionally skilled athletes may bypass certain expectations, but few can resist hegemonic masculinities. Interestingly, female athletes, perceived as more sensitive, may challenge norms and influence body ideals in sport.

Conclusion: The findings present an argument for sport organizations to reconsider the traditional practice of organizing sport along gendered lines, but working with mixed-gender groups alone is insufficient. To effectively challenge gendered stereotypes, coaching practices must adopt what is termed a "gender-transformative" approach, which involves actively reshaping gender roles. While our study does not provide concrete examples of such practices, we encourage coaches and other stakeholders to critically engage with gender issues related to the masculine sporting body.

Non-Invasive Assessment of Free Steroid Hormones: Development of a High-Throughput LC-MS/MS Method for Salivary Steroid Hormone Quantification

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Background/Objective: Steroid hormone concentrations reflect diverse physiological and pathological processes and have been recognized as valuable biomarkers for disease, with growing interest in their potential for patient stratification in precision medicine. Salivary steroid concentrations should reflect the free (biologically active) steroids in circulation, as steroids in the bloodstream passively diffuse to saliva. This allows for the direct measurement of free steroids without transporter protein-bound hormones (inactive form). However, implementation of salivary steroid quantification in larger studies remains limited by challenges associated with sample preparation.

Method: We evaluated the performance of three 96-well solid phase extraction (SPE) methods and compared electrospray (ESI) versus UniSpray ionization (USI) liquid chromatography-tandem mass spectrometry (LC-MS/MS). We demonstrate a sensitive and rapid high-throughput method with SPE of 200 µL saliva in 96-well-format and USI-LC-MS/MS for major steroids (testosterone, androstenedione, cortisone, cortisol and progesterone) in saliva.

Result: The method detection limits (MDL) range 1.1-3.0 pg/mL and linearity is $r2$ = 0.99. Intra-plate and inter-plate coefficient of variation (CV) was below 7% and 22% using USI. The method was then applied to 97 authentic saliva samples (41 male and 56 female). Median concentrations for males and females were 93 pg/mL and 8.5 pg/mL for testosterone, 159 pg/mL and 113 pg/mL for androstenedione, 16041 pg/mL and 13482 pg/mL for cortisone and 3496 pg/mL and 3152 pg/mL for cortisol. Among male participants, significant intercorrelations between salivary steroids were observed. Moreover, significant correlations between age, BMI and androgen levels were observed in both sexes.

Conclusion: The proposed 96-well SPE USI-LC-MS/MS method is well-suited for determining steroid hormones in saliva with potential usefulness in large-scale studies and clinical settings.

Nutritional neuroimaging – the exemplary case of probiotics for gut-brain axis research

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Background/Objective: Modulating the gut-brain axis via probiotic supplementation has emerged as a strategy to promote mental well-being across the entire lifespan.

Method: We have conducted a randomised, double-blinded, placebo-controlled crossover study assessing four-weeks probiotic intake in 22 healthy young to middle-aged adults; and a randomised, double-blinded, placebo-controlled parallel study comparing six-weeks probiotic intake in two different formulations in 90 healthy, community-dwelling elderly. One third of the latter study population was followed up four to six weeks after they stopped the intake of the probiotic supplementation.
In all studies, participants (female to male ratio circa 2:1) were intensively examined at baseline, rated their mental health including perceived stress, anxiety and depression symptoms, sleep quality – using validated psychological rating scales, and underwent structural and functional magnetic resonance imaging (fMRI), the latter for assessment of resting state functional connectivity. In some of the studies, participants underwent cognitive testing with or without task-related fMRI, as well as donated blood, faecal and/or saliva samples for assessment of biomarkers related to various gut-brain signalling routes and of importance for cognitive functioning and mental well-being.

Result: The results across our studies show distinct effects of probiotics on brain morphometry and functional connectivity during rest as well as while subjected to cognitively demanding negative emotional or stress stimuli. Generally, there were only few indications of probiotic effects on psychological symptom scores and cognitive performance, which often derived from longitudinal changes within groups. Analyses of various blood markers are indicative of a possible involvement of circulating serotonin or brain-derived neurotrophic factor in signal transduction, and alterations in the immunological gut-brain communication pathway.

Conclusion: fMRI is a sensitive method to detect subtle effects of mild and short-term nutritional interventions to a greater extent than alternative and classical assessments, especially in a healthy population, and possibly before effects may be noticed subjectively. Analyses of relevant blood markers and immune cell populations can give insights into potential gut-brain signalling routes, hence modes-of-action. So far, the various outcomes of each of those studies have been analysed individually. Future in-depth analyses focusing on the correlation of various outcomes could inform about predictive factors leading towards a positive and long-term probiotic effect on brain health to a priori identify so-called responders and non-responders to interventions.

Parents' experience of their own, other peoples', and their shared knowledge of congenital limb reduction differences

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Background/Objective: Congenital limb reduction difference is a rare diagnosis and knowledge about its consequences and treatment options is expected to be gained by health care providers. However, according to previous research, this has not been implemented. Therefore, the aim of this study was to describe parent's experiences of the knowledge they have acquired and managed concerning their child with limb difference.

Method: We used a descriptive design with a qualitative approach. Purposive sampling was used to identify parents from a variety of geographical settings, representing different experiences of treatments and encounters with health care providers. A study specific interview guide was developed. Upon ethics approval and informed consent online video telephony (*n*=14) or face-to-face (n=3) semi-structured interviews were conducted with 17 parents (12 mothers) of children with upper and/or lower limb difference (age 2-12 [md 5] years). The interview data were analysed using qualitative content analysis with an inductive approach.

Result: The overall theme describe *A need to know but also to understand*, and the four underlying categories are:

- *Request knowledge to trust (facts)* - Describes parents' demand for trustworthy information to rely on for reaching an understanding of why their child has a limb difference and for knowledge about appropriate interventions.
- *Reaching own knowledge and understanding* - Different ways of how to reach knowledge and understanding of what the limb difference will mean for the child.
- *Differences in knowledge – between levels of care and one's own knowledge* – Describes experiences of knowledge received from different health care providers, in relation to their own knowledge.
- *Shared perspective and understanding – more than facts* - Opportunities for the parents to exchange experiences, information, knowledge are sometimes of greater value than facts.

Conclusion: The parents' experiences show positive and challenging aspects regarding the knowledge of their child's condition and treatment interventions. Based on information and knowledge received from different sources, the parents develop their own understanding on which to base their parenting and decisions. The findings in this study support the need for specialized units with multidisciplinary competences, based on expected knowledge about potential causes for the condition and evidence-based treatments for the children.

Pre-Clinical Development of a Novel Tick-Borne Encephalitis Vaccine for Mucosal Immunization

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Background/Objective: Tick-borne encephalitis (TBE) is a significant disease in Europe and Asia, with a rising incidence due to the spread of the TBE virus (TBEV) and its vectors. Current TBE vaccines provide good protection, but they have a complex immunization schedule and lower efficacy in the elderly, leading to occasional vaccine failures. The aim of the current study is to develop a novel TBE vaccine to provide better protection with fewer doses through mucosal immunization.

Method: This work covers a pilot study that evaluates live-attenuated TBE vaccine using the Langat virus (LGTV) as a platform. Therefore, we developed and rescued an LGTV infectious clone (LGTV IC) and assessed its safety and efficacy in a murine model. Using intranasal and intramuscular administration at low and high doses, we evaluated viremia, viral presence in cerebrospinal fluid, general health outcomes, and immunogenicity.

Result: Mucosal immunization with LGTV IC demonstrated strong immunogenicity while maintaining a favorable safety profile in a dose-dependent manner. Low-dose intranasal administration was well tolerated, with no clinical signs, no weight loss, and no detectable virus in the central nervous system. It also elicited robust humoral responses, with anti-TBEV IgG detected across all groups, and induced strong cellular immunity, characterized by TBEV NS3-specific IFNg and IL-2 secretion. Notably, low-dose mucosal immunization outperformed both high-dose intranasal and intramuscular administration in generating a balanced immune response. In contrast, high-dose intranasal immunization, while inducing the highest IgG levels, resulted in significant weight loss and minimal virus presence in cerebrospinal fluid, suggesting potential adverse effects.

Conclusion: Our findings highlight the potential of mucosal immunization as an effective and well-tolerated strategy for inducing protective immunity. Ongoing work include further attenuation of LGTV IC which is necessary to improve safety for future use.

Screening Performance of Biomarkers for Intracranial Injury Within Six Hours of Injury and Beyond

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Background/Objective: The Scandinavian NeuroTrauma Committee (SNC) guidelines recommend S100 calcium-binding protein B (S100B) as a screening tool for early detection of Traumatic brain injury (TBI) in patients presenting with an initial Glasgow Coma Scale (GCS) of 14-15. The objective of the current study was to compare S100B's diagnostic performance within the recommended 6-h window after injury, compared with glial fibrillary acidic protein (GFAP) and UCH-L1. The secondary outcome of interest was the ability of these biomarkers in detecting traumatic intracranial pathology beyond the 6-h mark.

Method: The Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI) core database (2014-2017) was queried for data pertaining to all TBI patients with an initial GCS of 14-15 who had a blood sample taken within 6 h of injury in which the levels of S100B, GFAP, and UCH-L1 were measured. As a subgroup analysis, data involving patients with blood samples taken within 6-9 h and 9-12 h were analyzed separately for diagnostic ability. The diagnostic ability of these biomarkers for detecting any intracranial injury was evaluated based on the area under the receiver operating characteristic curve (AUC). Each biomarker's sensitivity, specificity, and accuracy were also reported at the cutoff that maximized Youden's index.

Result: A total of 531 TBI patients were included, of whom 24.9% (n = 132) had radiologically confirmed intracranial injury. The AUCs of GFAP (0.86, 95% confidence interval [CI]: 0.82-0.90) and UCH-L1 (0.81, 95% CI: 0.76-0.85) were statistically significantly higher than that of S100B (0.74, 95% CI: 0.69-0.79) during this time. There was no statistically significant difference in the predictive ability of S100B when sampled within 6 h, 6-9 h, and 9-12 h of injury. Overlapping AUC 95% CI suggests no benefit of a combined GFAP and UCH-L1 screening tool over GFAP during the time periods studied.

Conclusion: Targeted analysis of the CENTER-TBI core database, with focus on the patient category for which biomarker testing is recommended by the SNC guidelines, revealed that GFAP and UCH-L1 perform superior to S100B in predicting CT-positive intracranial lesions within 6 h of injury. GFAP continued to exhibit superior predictive ability to S100B during the time periods studied. S100B displayed relatively unaltered screening performance beyond the diagnostic timeline provided by SNC guidelines.

Soluble immune inhibitory checkpoint proteins: potential liquid biopsy biomarkers for penile cancer

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Background/Objective: Immune checkpoint proteins are recognized as critical regulators of the immune system and play an important role in the defence against cancer. However, cancer cells evade the immune destruction by overexpressing inhibitory checkpoint proteins, hence creating a favourable tumour microenvironment. Recently, it has been proposed that immune checkpoint proteins can be detected in soluble form in body fluids. This is important since a blood sample is less invasive than a tissue sample and hypothetically has the potential to be more representative. The aim of this study was to evaluate the concentrations of soluble immune inhibitory checkpoint proteins (sICs) in men with and without penile cancer.

Method: The circulating levels of ten soluble immune inhibitory checkpoint proteins (TIM-3, CD152, HVEM, IDO, LAG-3, BTLA, CD80, PD-1, PD-L1 and PD-L2) were assessed in plasma of 206 men with penile cancer (cases) and 46 men free from penile cancer (controls) using a multiplex Luminex assay. Mean concentrations of sICs were calculated and bootstrap resampling together with Welch's t-tests were used to assess differential expression and distribution of sICs between cases and controls.

Result: HVEM was detectable in 87% of the samples. PD-L1 was only detectable in 43.3% and therefore excluded from further analyses. The remaining markers were detectable in all samples. When comparing the mean concentrations of soluble immune inhibitory checkpoint proteins, nine sICs were found in higher concentrations in cases compared to controls, out of which seven (HVEM, TIM-3, CD80, PD-1, IDO, CD152, and LAG-3) reached statistical significance.

Conclusion: Our study indicates that men with penile cancer have higher concentrations of soluble immune inhibitory checkpoint proteins in plasma compared to penile cancer-free men. Further studies are needed to evaluate their prognostic value.

The ongoing effects of trauma experienced in women's artistic gymnastics

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Background/Objective: Women's artistic gymnastics (WAG) has since the "2016 USA Gymnastics Sex Abuse Scandal" and the 2020 Netflix documentary "Athlete A" gained mainstream and worldwide attention for being abusive. A large body of research confirms that gymnasts globally experience all forms of physical, psychological and sexual abuse, and physical, psychological, and educational neglect. Researchers are now also beginning to recognise that abuse and neglect suffered in sport can traumatise athletes and have ongoing trauma effects. The aim of this presentation is to map the ongoing trauma effects women's gymnasts experience.

Method: Data was generated through the project "#gymnastalliance: An international study on women's artistic gymnasts speaking out about abuse". The study was conducted using a trauma-informed qualitative research methodology that entailed a purposeful sampling strategy and individual semi-structured online interviews. 19 women from 12 countries (three continents; 5 languages), aged 20-50 years, consented to participate in the study. All had trained at the elite-level of gymnastics. The interviews covered six themes: Entrance into and career in WAG; life after retirement; realisation that experiences were abusive; decision to speak out; meanings made from speaking out; and demands for change and hopes for the future, and were between 90-180 minutes long. Data analysis followed a deductive thematic analysis protocol.

Result: The 19 former gymnasts experienced all forms of abuse and neglect. Both male and female coaches were identified as the abusers. Three of the former gymnasts recounted sexual abuse by male coaches, two of which were convicted and sentenced to imprisonment. The ongoing trauma effects were (1) direct causes of abuse/neglect, such as hyperextended knees, slipped vertebra bones, reconstructive surgeries, eating disorders, depression, and no positive gymnastics memories; (2) re-traumatisation later in life, such as not being listened to or believed when reporting abuse; and (3) re-victimisation, such as through a violent partner or being publicly discredited when reporting abuse to gymnastics organisations. All 19 former gymnasts reported ongoing medical, psychological, and psychiatric treatment since leaving WAG.

Conclusion: The abuse and neglect gymnasts experience is pervasive and has extensive ongoing physical, cognitive, emotional, mental health, behavioural, relational, educational, professional, and economic trauma effects. What is further concerning is that the recognition and treatment of trauma effects is delayed, for some by decades, and are suffered in privacy, and without financial or other support from sporting organisations.

The role of the gut in Parkinson's disease pathophysiology

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Background/Objective: Gastrointestinal symptoms in patients with Parkinson's disease (PD) are very similar to symptoms of irritable bowel syndrome (IBS), with constipation being virtually universal in PD. Such manifestations can appear years before the characteristic motor symptoms associated with PD, caused by protein aggregates of alpha-synuclein that degenerate dopaminergic neurons in the brain. Emerging research show that PD might start in the gut. The microbe *Akkermansia muciniphilia* has shown to strengthen the gut barrier but has an uncertain contradicting role in PD. A disrupted gut barrier as in IBS may contribute to PD pathophysiology. In line with this, IBS patients show 17-40% risk of developing PD over time but no study has yet shown any pathophysiological overlap that could explain this. The objectives of this project are to 1) study the effect *Akkermansia muciniphila* cells and its membrane protein (AMP) on colonic permeability 2) identify groups at risk of developing PD by studying shared colonic presence of alpha-synuclein in IBS and PD.

Method: We recruited early-stage PD patients (n=16) from the neurology department at Örebro University Hospital. All participants filled out questionnaires regarding their gastrointestinal health (Gastrointestinal Symptoms Rating Scale). Biopsies from the sigmoid colon were mounted in the Ussing chambers for studies of permeability. The biopsies were stimulated with *Akkermansia muciniphilia* (10^8 cells), AMP (7.5 ug), both with and without the addition of the barrier-disruptor Compound (C) 48/80 (10 ng/ml). Additional biopsies from PD patients, as well previously collected biopsies from IBS patients (n=15) and healthy controls (n=7), were used for immunohistochemical semi-quantification of several forms of alpha-synuclein.

Result: The Gastrointestinal Symptoms Rating Scale showed that PD patients experience bowel issues, dominated by constipation. The Ussing chamber experiments showed that C48/80 increased both para-and transcellular permeability but co-stimulation with AMP significantly attenuated this effect. Stimulation with *Akkermansia muciniphilia* cells increased paracellular permeability both with and without C48/80 but had no effect on transcellular permeability. Immunohistochemical analysis revealed widespread distribution of aggregated alpha-synuclein throughout the colonic mucosa in PD (n=9/9), but no positive stains in healthy controls. Among the IBS samples, 5 out 15 showed positive stains for aggregated alpha-synuclein.

Conclusion: We are the first to show that *Akkermansia muciniphilia* cells might disrupt the gut barrier function in PD patients. However, the membrane protein might instead show protective effects and could have therapeutic potential. The presence of aggregated alpha-synuclein in IBS colon warrants further studies to evaluate its PD predictive value.

TLR4 signalling and bacterial expulsion in urinary tract infection

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Background/Objective: The toll-like receptor (TLR)4 is a key part of the innate immune system. It is a pattern recognition receptor able to recognise LPS, a surface component of gram-negative bacteria such as *E. coli*. Uropathogenic *E. coli* (UPEC) are frequently involved in urinary tract infections, which in turn is one of the most common infections worldwide. The objective of this project is to map out the interaction between different variants of E. coli, that express different virulence factors, and the umbrella cells lining the inside of the urinary bladder.

Method: The system biology study combines literature knowledge on TLR4 signalling and *E. coli* interaction with host cells into a mechanistic knowledge model that can be used to both visualise and reason about the encoded knowledge. Formal knowledge representation enables the use of propositional logic and automated reasoning to formally test the hypothesis that any knowledge model constitutes.

Result: We present a detailed mechanistic knowledge model of TLR4 signalling and of how UPEC interacts with and invades umbrella cells. The knowledge based is visualised in a network representation and different scenarios can be tested by simulation.

Conclusion: Formalisation and compilation of knowledge into mechanistic knowledge models are critical to build and analyse the complex hypotheses necessitated by the ever-increasing scope and detail of data. This, in turn, is essential for the transformation of data/knowledge into actionable understanding.

Translational Bioinformatics for Gamma Delta T Cell-Based Immunotherapy

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Background/Objective: Recent advancements in cancer immunotherapy, including immune checkpoint inhibitors and CAR-T cell therapy, have transformed cancer treatment. Among emerging strategies, using Gamma Delta T cells stand out due to their unique properties, such as non-alloreactivity, potent tumor cell lysis, and broad antigen recognition. To explore their therapeutic potential, computational tools are essential for reconstructing Gamma Delta T-cell receptor (TCR) repertoires from high-throughput sequencing data, providing insights into their diversity, antigen specificity, and functional dynamics in both tumor and non-tumor environments.

Method: Computational approaches have been instrumental in characterizing tumor-immune interactions, predicting patient-specific responses, and optimizing the application of Gamma Delta T-cell therapies in cancers such as neuroblastoma and medulloblastoma. To enhance the accuracy and reproducibility of Gamma Delta TCR predictions, we present a computational strategy designed to systematically comparing different prediction models for Gamma Delta T-cell repertoires.

Result: By benchmarking various methods, this approach facilitates the evaluation of sequencing-based reconstructions, aiding in the standardization and refinement of computational strategies in Gamma Delta T cell research

Conclusion: By integrating predictive modeling, immune profiling, and comparative analysis tools, computational methods are driving forward the development of Gamma Delta T-cell-based immunotherapies. These advancements not only refine our understanding of tumor-immune dynamics but also contribute to the broader goal of improving precision immunotherapy strategies.

Treatment patterns, healthcare utilization, and related costs for prurigo nodularis in Sweden

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Background/Objective: Prurigo nodularis (PN) is a chronic, inflammatory skin condition that negatively affects quality of life. In Sweden, PN affects a significant portion of the population, mostly the elderly and patients with coexisting atopic dermatitis (AD). Recalcitrant PN often requires the use of several treatments and forces patients to seek health care repeatedly.
This study aimed to investigate the healthcare utilization, including treatment patterns and direct costs for specialist care for PN in Sweden

Method: Linkage cohorts were created from large-scale linked data from national Swedish patient and prescription registers and the cost-per-patient database of PN adults in specialist care in Sweden from 2015 to 2020.

Result: About 875 patients were registered annually with a specialist diagnosis of PN in Sweden, and there were 3,548 specialist visits per year on average. 33% of patients were in specialist care for more than one year. In patients with severe PN with AD, topical treatment with corticosteroids was often (32.6%) followed by systemic prednisolone and methotrexate. 31.7% of patients in outpatient care received phototherapy and 7.3% lubrication treatment. In outpatient care, the cost per type of contact was higher for team visits (€555.8) followed by single visits (€249.5) and telephone contact (€216.3). Considering in- and outpatient care together, the mean cost per visit was €458.6 and per patient per year around €1,859.3. The total annual cost of PN patients is estimated to be around 1.6 million euros.

Conclusion: A high proportion of patients affected by PN seek care for several years, receiving diverse, often systemic, treatment combinations for at least one year before attaining disease control or remission. Targeted treatments for PN might improve patients' quality of life and reduce the high related costs for the healthcare system.