Charles University

Translational Research: Innovation Born of Need

22ND INTERNATIONAL MEDICAL DOCTORAL CONFERENCE 2025

Abstract Book

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About IMDC

Since 2005 the Faculty of Medicine in Hradec Králove has been annually organizing an international conference of PhD students from medical faculties – the International Medical Doctoral Conference in Hradec Králové.

The number of European participants is increasing every year (students as well as evaluators). The level of individual conference papers and the prestige of the conference are constantly rising.

Organizing Committee

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Support

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Under the Auspices of

Her Magnificence, Rector of the Charles University Milena Králíčková

and Spectabilis, dean of Medical Faculty in Hradec Králové Jiří Manďák.

Programme

The programme is subject to change.

Wednesday November 19, 2025

Lecture Hall, Educational Center FM

9:00 **Opening ceremony**

Lectures

Session 1

Chairs: **Hana Langrová, Romana Koberová Ivančaková**

9:15 **Qasem Marwan M Kh (1st Faculty of Medicine, Charles University, Czech Republic):** Detection of steatotic liver disease in type 2 diabetes mellitus via utilising retinopathy screening pathways

9:30 **Benada Matyas (Faculty of Medicine in Hradec Králové, Charles University, Czech Republic):** Retrospective Analysis of Pharmacokinetically Guided Busulfan Dosing in Two Different Dosing Regimens in Patients Undergoing Conditioning for Allogeneic Stem Cell Transplantation

9:45 **Afshari Moeina (Faculty of Medicine in Hradec Králové, Charles University, Czech Republic):** CD200 and CD200R1 as part of the regulatory mechanisms in atopic dermatitis

10:00 **Polojintef-Corbu Roxana (Medical University of Vienna, Austria):** Preoperative pregabalin reduces the Cp50 for skin incision during target-controlled propofol infusion: A randomized, placebo-controlled, double-blind clinical trial

10:30 **Coffee break**

Session 2

Chairs: **Milan Kaška, Pavel Žák**

10:45 **Bedoshvili Ana (Faculty of Medicine, David Tvildiani Medical University, Georgia):** Impact of cerebral visual impairment on neurodevelopmental outcome in children at high risk of cerebral palsy

11:00 **Habeš Dominik (Faculty of Medicine in Hradec Králové, Charles University, Czech Republic):** Does mesh surgery alter oxidative stress levels in patients with pelvic organ prolapse?

11:15 **Luyten Julien Antonio (Faculty of Health, Medicine & Life Sciences, Maastricht University, Netherland):** Safe surgery for perihilar cholangiocarcinoma without preoperative biliary drainage: A retrospective multicentre analysis of data from 2067 patients.

11:30 **Blichová Tímea (Jessenius Faculty of Medicine in Martin, Comenius University in Bratislava, Slovakia):** Association of HLA Alleles with IgA Nephropathy and Its Recurrence After Kidney Transplantation

11:45 **Short break**

Session 3

Chairs: **Ilja Tachecí, Vladimír Koblížek**

11:50 **Hildebrand Nicole (Faculty of Health, Medicine, and Life Sciences, Maastricht University, Netherland):** Prognostic host phenotypes based on body composition and systemic inflammation predict survival in patients with periampullary cancer: results of a nationwide cohort study

12:05 **Emam Mohamed (Semmelweis University, Budapest, Hungary):** The Effect of Cervicogenic Headache on the Myoelectrical Activities of Suboccipital Muscles, Range of Motion and Functional Activities of the Neck at Different Ages

12:20 **Al Akkad Marwan (Faculty of Medicine and Dentistry, Palacký University Olomouc, Czech Republic):** Mind the Gap: Can 3D Printing Provide a Translational Solution to the Inherent Marginal Discrepancy of Computer-Aided Design / Computer-Aided Manufacturing CAD/CAM in Fixed Prosthodontics?

12:35 **Lunch**

13:30 **MSc. Samira Eissazadeh, Ph.D.: Evaluation of the Anti-Endoglin Monoclonal Antibody on Endoglin Expression and Signaling During Liver Sinusoidal Endothelial Dysfunction**
Invited speaker (Terasom Ltd. / Faculty of Pharmacy, Charles University, Czech Republic)

Dr. **Samira Eissazadeh** is a Pharmacologist with a strong background in Cellular and Molecular Biology. During her PhD at the Faculty of Pharmacy in Hradec Králové, Charles University, she investigated the role of Endoglin (ENG), a TGF-β co-receptor involved in angiogenesis, in liver sinusoidal endothelial dysfunction. Her research focused on ENG-related signaling in hepatic impairment and on the therapeutic potential of the anti-ENG monoclonal antibody Carotuximab (TRC105) in experimental models of cholestasis and metabolic dysfunction–associated steatohepatitis (MASH). Her findings highlighted ENG as a promising target for reducing liver inflammation and fibrosis, opening new avenues for translational research and leading to publications in top-tier, peer-reviewed journals. Dr. Eissazadeh received the prestigious Minister of Education, Youth and Sports Award of the Czech Republic (2025) in the doctoral category, recognizing exceptional accomplishments in research, experimental development, and innovation. She currently works as a Scientist at Terasom Ltd. in Prague, contributing to exosome-based diagnostics and cancer immunotherapies.

14:30 **Short break**

Session 4

Chairs: **Martina Řezáčová, Emil Rudolf**

14:35 **Chrzan Natalia (Medical University of Lodz, Poland):** Metabolic phenotype determines melanoma cell sensitivity to copper – delivering agents

14:50 **Kalkušová Kateřina (2nd Faculty of Medicine, Charles University, Czech Republic):** Chronic inflammasome activation in cancer: promoting tumor progression and immune escape

15:05 **Miškufová Viktória (Faculty of Medicine, Pavol Jozef Šafárik University in Košice, Slovakia):** Unraveling the antiproliferative mechanisms of indole phytoalexin 1-methoxyisobrassinin in cervical cancer cells

15:20 **Vladyka Ondřej (2nd Faculty of Medicine, Charles University, Czech Republic):** Genotype Phenotype Evaluation of Statistical Association using PhenoPackets: Advancing the Automated Analysis of Monogenic Disease Phenotypes

15:35 **Coffee break**

Posters

16:00 – 17:40 **Poster presentation 1 - 10**
Chairs: **Milan Kaška, Romana Koberová Ivančaková**

18:00 **Dinner, Social evening**

Thursday November 20, 2025

Lecture Hall, Educational Center FM

Lectures

Session 5

Chairs: **Aleš Ryška, Jan Kremláček**

8:30 **Ptáčková Hana (1st Faculty of Medicine, Charles University, Czech Republic):** New phenotype in SARS2 deficiency

8:45 **Morávek Alexander (Faculty of Medicine in Hradec Králové, Charles University, Czech Republic):** Assessing directional asymmetry in mandibular bone mineral radiodensity: Insights from voxel-based morphometry

9:00 **Chebernina Inna (Medicine, State Establishment "Lugansk State Medical University", Ukraine):** Investigation of Microglial Activation in the Hippocampus of Rats with Experimentally Induced Colorectal Carcinogenesis

9:15 **Al-Redouan Azzat (2nd Faculty of Medicine, Charles University, Czech Republic):** Basal Ganglia Are Compromised by Status Epilepticus in Immature Animal Experimental Model of Mesial Temporal Lobe Epilepsy: Translational Research into Neuroimaging Diagnostics and Potential Neuromodulator Therapeutics in Epileptic Pediatric Patients

9:30 **Merkl Tomáš (Military Faculty of Medicine, Hradec Králové, University of Defence, Czech Republic):** Effect of exogenous surfactant on contused lung - experimental animal study

9:45 **Coffee break**

Session 6

Chairs: **Otto Kučera, Aleš Ryška**

10:05 **Ferčáková Annamária (Faculty of Medicine, Pavol Jozef Šafárik University in Košice, Slovakia):** From Tumor to Culture Dish: A Journey of Cancer-Associated Fibroblasts from PDAC

10:20 **Veselá Šárka (1st Faculty of Medicine, Charles University, Czech Republic):** A Novel Cellular Model for Investigating Experimental Therapy in Alpha-1-antitrypsin Deficiency

10:35 **Vakhnovska Khrystyna (Medicine, State Establishment "Lugansk State Medical University", Ukraine):** Ultrastructural Changes in the Bloodstream and Anatomical Structures of the Kidney of White Laboratory Rats during Severe Dehydration and Rehydration

10:50 **Leonard Sophie Victoria Louise (Hull York Medical School, University of Hull, United Kingdom):** Oxygen Concentration Plays a Fundamental Role in the Regulation of Platelet Activity

11:05 **Short break**

Session 7

Chairs: **Jan Kremláček, Martina Řezáčová**

11:10 **Wawrzyniak Piotr (Medical University of Lodz, Poland):** IFN-γ drives phenotypic changes in melanoma cells and potentiates cell sensitivity to GLUT1 inhibition

11:25 **Harazimová Adéla (Faculty of Medicine, University of Ostrava, Czech Republic):** Gene expression of methylation and demethylation enzymes in HPV-negative OSCC

11:40 **Colborn Lauren Brooke (Hull York Medical School, University of Hull, United Kingdom):** Spatial Transcriptomic Profiling Reveals IL1β^{+} Macrophages as Major Drivers of Senescence in Chronic Wounds

11:55 **Muhammad Hashim (Medical University of Vienna, Austria):** YB-1 regulates PD-L1 and PD-L2 expression in Pleural Mesothelioma

12:10 **Speakers award: The best lecture (start of voting)**

12:15 **Lunch**

Posters

13:15– 14:50 **Poster presentation 11 - 20**
Chairs: **Martina Řezáčová, Emil Rudolf**

14:50 **Coffee break**

15:00 **Meeting of the organizing committee / Free time**

18:00 **Evaluation of the best presentations, music performance "Young accordions and strings"**

19:30 **Raut, social evening**

Friday November 21, 2025

Lecture Hall, Educational Center FM

Invited speakers:

09:00 **Prof. Markus Hecht, MD: Immune-modulation by local radiotherapy**
Invited speaker (Saarland University/Saarland University Hospital, Homburg, Germany)

Since 2022, Prof. **Markus Hecht** has been Director of the Clinic for Radiation Therapy and Radio-Oncology at Saarland University Hospital and W3 Professor of Radiation Oncology at Saarland University. He specializes in head-and-neck cancer and radio-immunotherapy, studying how local irradiation reshapes tumor immunity and influences responses to checkpoint inhibitors. His group's recent **IMPORTANCE / KEYNOTE-717** work suggests that irradiating one metastatic site can boost the overall effectiveness of **pembrolizumab** in metastatic head-and-neck cancer without adding major toxicity. His lecture will also cover findings from long-term collaborations with Rainer Fietkau and Udo S. Gaipl (FAU Erlangen–Nürnberg/University Hospital in Erlangen).

10:00 **doc. Mgr. Jan Křivánek, Ph.D.: Ever-Growing Teeth: Infinite Source of Stem Cells**
Invited speaker (Faculty of Medicine, Masaryk University, Czech Republic)

Assoc. Prof. Jan Křivánek leads the Dental Development and Regeneration Research Group at the Department of Histology and Embryology at the Faculty of Medicine, Masaryk University in Brno. His lab investigates several fundamental research topics, including the stem-cell dynamics and plasticity, regeneration and healing of teeth and bones, tissue micropatterning and others. Recently, his team developed the BEE-ST method, enabling the quantification of hard-tissue development, growth and remodelling (published in Science Advances), for which he received the MUNI Scientist Award 2023. The most recent work (Lavicky et al., JDR, 2025) shows that activating a defined set of transcription factors can program stem cells toward the odontoblast lineage, outlining new translational avenues for dentin regeneration. He integrates developmental biology with regenerative dentistry and leads nationally funded projects on mechanosensing, stem-cell niche adaptation and dental healing with clear clinical relevance.

11:00 **Coffee, sandwiches and cakes, Farewell**

Posters

1) **Artimovič Peter (Faculty of Medicine, Pavol Jozef Šafárik University in Košice, Slovakia):** Cross-tissue Transcriptomics Identifies Immune Crosstalk Connecting Psoriasis and Recurrent Implantation Failure
2) **Doležal Ondřej Jan (Military Faculty of Medicine, University of Defence, Czech Republic):** Radioprotective Potential of Modified Nanoparticles
3) **Dubaj Maciej (Doctoral School, Discipline: Medical Sciences, Medical University of Lublin, Poland):** In the Shadow of Cancer: Searching for Predictors of Malnutrition in Patients with Multiple Myeloma – A Systematic Review
4) **Gulová Slavomíra (Faculty of Medicine, Pavol Jozef Šafárik University in Košice, Slovakia):** Extracellular Vesicles from Hoffa's Fat Pad-Derived Mesenchymal Stem Cells in Osteoarthritis Therapy
5) **Havlínová Barbora (Faculty of Medicine in Hradec Králové, Charles University, Czech Republic):** Anti-Müllerian Hormone as a Marker of Ovarian Reserve in Safety of Radioiodine Treatment for Premenopausal Women with Thyroid Carcinoma
6) **Háziková Viktória (Faculty of Medicine, Pavol Jozef Šafárik University in Košice, Slovakia):** Molecular and Functional Analysis of ABC Transporter Modulation
7) **Holmannova Drahomira (Faculty of Medicine in Hradec Králové, Charles University, Czech Republic):** Vitamin D Supplementation in the Czech Republic: Socioeconomic Determinants and Public Awareness Gaps
8) **Cherednychenko Daria (Medicine, Lugansk State Medical University, Ukraine):** Optimization of Diagnosis and Treatment of Skin Lesions Associated with Lyme Borreliosis in Military Personnel
9) **Kováčová Gabriela (Faculty of Medicine, Pavol Jozef Šafárik University in Košice, Slovakia):** Differential Expression of Angiogenesis-Related Genes in Female Reproductive System Pathologies
10) **Kriváková Eva (Faculty of Medicine, Pavol Jozef Šafárik University in Košice, Slovakia):** Role of Hyaluronic Acid Metabolism in Endometrial Receptivity: Insights from RNA-seq and Cellular Models

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11) **Kuchyňka Jiří (Faculty of Medicine in Hradec Králové, Charles University, Czech Republic):** Automated Sleep Staging Using Sequential XGBoost and Multi-Scale Temporal Fusion
12) **Lamačová Lucie Josefa (Third Faculty of Medicine, Charles University, Czech Republic):** Effects of a Highly Hydrophilic Mitochondria-Targeted Iron Chelator
13) **Lonek Jan (2nd Faculty of Medicine, Charles University, Czech Republic):** Methodological Aspects of Nociceptive Flexion Reflex Assessment. A Pilot Normative Study
14) **Matouskova Laura (2nd Faculty of Medicine, Charles University, Czech Republic):** Liquid Biopsy, Solid Findings: New Insights into Pathogenesis and Cisplatin Resistance in TGCTs
15) **Matraszek Veronika Viktoria (3rd Faculty of Medicine, Charles University, Czech Republic):** Screening for Anticardiolipin Antibodies in Early Pregnancy: Findings and Implications
16) **Matyskova Kubisova Michaela (Faculty of Medicine in Hradec Kralove, Charles University, Czech Republic):** Management of Kidney Transplant Outpatients With COVID-19: A Single Center Experience
17) **Mečiaková Martina (Jessenius Faculty of Medicine in Martin, Comenius University Bratislava, Slovakia):** Genetic Variants of G Protein-Coupled Estrogen Receptor (GPER) and Their Association with Prostate Cancer Susceptibility in Slovak Population
18) **Pásler Adam (Military Faculty of Medicine, University of Defence, Czech Republic):** The Effect of Hyperbaric Environment on the Physiological Functions of Military Divers in the Czech Armed Forces
19) **Sabová Jana (Faculty of Medicine, Pavol Jozef Šafárik University in Košice, Slovakia):** Tissue Repair Potential of Agrimonia eupatoria L. Extract in Advanced 3D Skin Models
20) **Sukharieva Liliia (Kharkiv National Medical University, Ukraine):** Morphological Features of the Lungs of Offspring that Developed In Utero Under Maternal Genitourinary System Chronic Inflammatory Process Conditions

Abstracts

Abstracts are listed alphabetically by presenting author.

Title	**CD200 and CD200R1 as part of the regulatory mechanisms in atopic dermatitis**
Author	**Moeina Afshari**
Affiliation(s)	Department of Clinical Immunology and Allergy, Faculty of Medicine, Charles University

Introduction: Atopic dermatitis (AD) is a condition that affects a significant number of people worldwide, causing varying degrees of symptoms in their daily lives. The underlying mechanisms and participating molecules, which could also serve as biomarkers, are only partially understood.

Methods: In our study, we followed the serum levels of sCD23, sCD200, sCD200R, and IL-24 in 103 patients with atopic dermatitis and 39 healthy individuals. Patients received the treatment either with conventional or biological therapy (Dupilumab). Patients were also stratified according to the seasonal collection of samples. Serum markers were measured by ELISA and correlated with the clinical scores, which reflected the patients' condition.

Results: While IL-24 and sCD23 did not respond to the treatment, significant differences were observed between groups when comparing sCD200 and sCD200R1. Interestingly, these parameters were significantly increased in patients treated with dupilumab ($p < 0.05$). The seasonal effect was not definitive: sCD200 levels were only increased in summer samples from patients receiving Dupilumab, reaching a significantly higher level than in patients receiving conventional treatment ($p = 0.006$). Both clinical scores were much lower in patients with dupilumab treatment ($p < 0.00001$).

Discussion: Using Dupilumab, as well as other means of stimulating the CD200-CD200R1 axis in AD patients, may bring clinical benefits.

Conclusion: Our results suggest that CD200 and CD200R are likely involved in regulating inflammation in patients with AD.

Title	**Mind the Gap: Can 3D Printing Provide a Translational Solution to the Inherent Marginal Discrepancy of Computer-Aided Design / Computer-Aided Manufacturing CAD/CAM in Fixed Prosthodontics?**
Author	**Marwan Al Akkad [1,2]**
Co-Authors	**I. Voborná [1], T. Taylor [3], O. Hamadah [4], B. Savas Yigit [1], V. Prokupek [5], M. Matoušek [6], J. Sorensen [7], O. Fasanya [8], R. Mounajjed [1,2]**
Affiliation(s)	1) Institute of Dentistry and Oral Sciences, Faculty of Medicine and Dentistry, Palacký University Olomouc, Olomouc, Czech Republic. 2) Clinic, Hradec Kralove, Czech Republic. 3) Department of Reconstructive Sciences, UConn School of Dental Medicine, Farmington, Connecticut, USA. 4) Department of Oral Medicine, Faculty of Dental Medicine, Damascus University, Damascus, Syria. 5) Department of Experimental Physics, Faculty of Science, Palacky University Olomouc, Olomouc, Czech Republic. 6) Stomatologické centrum U svaté Anny, Vimperk, Czech Republic. 7) Department of Restorative Dentistry, School of Dentistry, University of Washington, Seattle, Washington, USA. 8) Department of Biostatistics and Data Science, School of Public Health, Louisiana State University Health Sciences Center, New Orleans, USA

Introduction

Milling machines struggle to reproduce thin margins, particularly in zirconia. This presentation delves into three studies, highlighting the importance of polishing and finishing CAD/CAM copings and exploring 3D-printed resin models as a potential translational tool to optimize marginal fit.

Methods

Palacky University supported part of this work with the grant IGA_LF_2024_009.

The first study included 18 metal copings, which underwent finishing and polishing F&P.

The second study included 20 zirconia copings. 10 of them were produced by a full digital workflow, and the other 10 by a hybrid workflow. Copings from both workflows were measured before and after F&P.

The third study included 30 zirconia copings. 15 of them underwent F&P with a 3D printed model. Whereas the other 15 underwent F&P without a model.

The marginal fit of all the copings from the three studies was measured systematically under a digital optical microscope.

Results

Copings had a mean of 62 ± 60, 24.90 ± 23.88, 30.62 ± 32.63, 21.03 ± 16.65, 18.93 ± 18.27, 15.17 ±14.48, and 12.45 ± 14.09 for the first study samples, full digital without F&P, full digital with F&P, hybrid without F&P, hybrid with F&P, F&P with 3D model, and F&P without 3D model, respectively.

Discussion

Mean value represents precision, while standard deviation represents trueness. The workflow, the presence of F&P, and the way of F&P impact the marginal fit.

Conclusions

F&P might improve marginal fit. Resin 3D models lack sufficient dimensional stability and offer no benefit for F&P.

Title	**Basal Ganglia Are Compromised by Status Epilepticus in Immature Animal Experimental Model of Mesial Temporal Lobe Epilepsy: Translational Research into Neuroimaging Diagnostics and Potential Neuromodulator Therapeutics in Epileptic Pediatric Patients**
Author	**Azzat Al-Redouan**
Co-Authors	Hana Kubova, Rastislav Druga
Affiliation(s)	Department of Anatomy, Second Faculty of Medicine, Charles University.

Introduction

The basal ganglia (BG) are not primary trigger for seizures but play role in controlling cortical seizure activity. This study provides new insight about the sensitivity and vulnerability of individual BG nuclei in epilepsy during postnatal development.

Methods

Status epilepticus (SE) induced morphological neurodegeneration in BG was investigated in lithium−pilocarpine Wistar albino rats model of mesial temporal lobe epilepsy (MTLE). Age was set at 12-25 days old pups (corresponds to 1-3 years old toddlers). SE was induced in 120 animals at post-SE intervals of 4 hours to 1 week (correspond to 5 days-8 months in humans). FJB-positive neurons were profiled: 1) Stereotaxic map distribution pattern. 2) Quantification and measurement of perikarya long-axis.

Results

Neuronal damage in the dorsal striatum was persistence, started at age 18 days pups (corresponds to ~1 year and 7 months old human) and peaked 12hr post SE (corresponds to ~2.5 weeks in human), distributed in its periphery-extending-medially. The ventral striatum was compromised with less severity. It developed at age of 25 days pups (corresponds to ~2.5 years old human) and peaked at 24hr post SE, then declined.

Discussion

SE neuronal damage in the striatum was age dependent with specific distribution. The BG system of hyperactivity of afferent systems coupled with inhibitory neurons may be the underlying cause of the confined neuronal damage.

Conclusions

The BG post-SE damaged neuronal distribution can correspond to epileptic pediatric patients MRI. The GABAergic confined inhibitory neurons can be considered for electrical stimulation and pharmacological neuromodulatoion in MTLE.

Title	**Cross-tissue Transcriptomics Identifies Immune Crosstalk Connecting Psoriasis and Recurrent Implantation Failure**
Author	**Peter Artimovič [1]**
Co-Authors	Monika Švecová [1], Vladimíra Nagyová [2], Nicole Fabianová [1], Janette Baloghová [2], Mária Mareková [1], Miroslava Rabajdová [1]
Affiliation(s)	[1] Department of Medical and Clinical Biochemistry, Faculty of Medicine, Pavol Jozef Šafárik University in Košice, Slovakia [2] Department of Dermatovenerology, Faculty of Medicine, Pavol Jozef Šafárik University in Košice, Slovakia

Introduction

Immune dysregulation is increasingly recognized as a driver of infertility, especially in conditions such as recurrent implantation failure (RIF). Psoriasis, a chronic inflammatory disease mediated by IL-23/IL-17 and TNF-α signaling, has been epidemiologically associated with reduced fertility and adverse pregnancy outcomes in women of reproductive age. However, the molecular basis of this link remains poorly defined.

Methods

Cross-tissue transcriptomic analysis was performed using RNA-seq datasets from mid-secretory endometrium (GSE106602) and psoriatic skin (GSE121212). Shared differentially expressed genes were integrated into protein–protein interaction networks. The top 29-gene immunoregulatory module was evaluated by enrichment analysis, transcriptional regulation, correlation with immune cell deconvolution, and classification models (Random Forest, SVM, Logistic Regression).

Results

Module consisted of cytokines, chemokines, and immune checkpoints. It was upregulated in psoriatic lesions but suppressed in RIF endometrium, reflecting divergent regulation of a conserved immune program. Immune deconvolution revealed opposite shifts in $CD4^+$ effector/memory T cells, $CD8^+$ naïve T cells, and neutrophils across the two tissues. Classification ensemble models trained on this module achieved robust performance (AUC > 0.95) in both datasets.

Discussion

These findings reveal a shared transcriptomic signature reflecting the Th17/IL-17–neutrophil axis, pathologically activated in psoriasis but attenuated in RIF. This contrast provides molecular context for epidemiological links between systemic inflammation and reproductive failure.

Conclusions

This study identifies a conserved immune module that bridges chronic inflammation and implantation failure. The signature may serve as a biomarker of immune-mediated infertility and highlights IL-17 and immune checkpoint pathways as potential therapeutic targets in personalized reproductive medicine.

Title	**Impact of cerebral visual impairment on neurodevelopmental outcome in children at high risk of cerebral palsy**
Author	**Ana Bedoshvili [1,2]**
Co-Authors	Nini Valishvili [2], Nino Chankseliani [2], Tinatin Giuashvili [1] , Sofia Tatishvili1[1,2] , Nana Tatishvili [1],Roslyn N Boyd[3], Andrea Guzzetta[4]
Affiliation(s)	1.David Tvildiani Medical university 2. Iv. Bokeria Neurodevelopment Centre 3. The University of Queensland 4. University of Pisa

Introduction

Cerebral palsy (CP) is the most common childhood-onset neurodevelopment disorder affecting movement and posture, which is accompanied by cerebral visual impairment (CVI) in 1 in 10 children with CP.

Aims

The study, conducted as part of the international VISIBLE study and supported by Shota Rustaveli national Science Foundation of Georgia. The aim of this study is to identify early markers of CVI in infants from Birth till 12 months of age (corrected age), who are at high risk of CP. Study examines relationship between General Movements and CVI assessment scores, and impact of early diagnosis and intervention for CVI on neurodevelopment outcome.

Method

Prospective cohort study including 120 high-risk newborns, commencing in the Neonatal Intensive Care Unit. Inclusion criteria are: Prematurity (born <32 weeks gestation), stroke, Neonatal Encephalopathy. They will be assessed with following stages: baseline - corrected age up to 12 months, and final - corrected age 12-24 months, with following tools - general movements (MOS-R) and CVI assessment tools (Ricci vision assessment scale and Pisa Infant battery for vision scale), Gross and fine motor function – (HINE, BSID-III, PDMS-2) and parent questionnaires.

Results/Conclusion

Research commenced on June 24, 2024, and has successfully enrolled 73 infants at high risk of CP. 14 newborns have progressed to enrolment in the VISIBLE RCT to receive intervention for CVI. Continued monitoring and analysis of our participants will provide valuable insights into early development of infants with CVI and effective intervention strategies, contributing to better long-term outcomes for children at risk for CP.

Title	**Retrospective Analysis of Pharmacokinetically Guided Busulfan Dosing in Two Different Dosing Regimens in Patients Undergoing Conditioning for Allogeneic Stem Cell Transplantation**
Author	**Matyas Benada**
Co-Authors	Zavrelova A., Radocha J., Libra A., Visek B. , Lanska M. , Mertova J. , Zibridova K. , Zak P. , Malakova J. , Rozsivalova P ., Sima M
Affiliation(s)	Charles University, Faculty of Medicine in Hradec Králové

Introduction

Busulfan is an essential component of conditioning regimens before allogeneic stem cell transplantation, particularly in acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS). We performed a retrospective analysis to compare pharmacokinetics, especially the area under the curve (AUC), clinical outcomes, and two different dosing regimens.

Methods

We analyzed 90 adult patients with AML or AML-type MDS who received busulfan (12.8 mg/kg i.v.) plus fludarabine prior to transplantation. Most also underwent in vivo T-cell depletion. Busulfan was given once daily in 47 patients and in four divided doses every 6 hours in 43 patients. Plasma concentrations were monitored, and pharmacokinetic parameters calculated using the NLME method.

Results

AUC values were comparable between regimens, owing to dose adjustments targeting 5500–6000 µmol·min/day. The best predictor of pharmacokinetics was dosing based on ideal body weight (IBW) with a 40% correction, superior to the commonly used 25%. No significant differences were found in overall survival, relapse-free survival, or relapse incidence. At 2 years, overall survival was 73% vs. 71%, relapse-free survival 59% vs. 58%, and relapse incidence 30% vs. 38% for the four-times-daily and once-daily schedules, respectively.

Discussion

These findings indicate that once-daily busulfan dosing achieves comparable pharmacokinetics and clinical outcomes to the conventional regimen. Importantly, the once-daily schedule provides practical advantages by reducing nursing workload, simplifying drug monitoring, and optimizing patient care. Our results are consistent with previously reported data supporting the feasibility of once-daily administration. The main limitation of this study is its retrospective design and relatively small cohort, which may limit generalizability. Prospective randomized studies are warranted to confirm these results and further refine dosing strategies, particularly with respect to IBW-based corrections.

Conclusions

Once-daily busulfan dosing is pharmacokinetically and clinically equivalent to the standard regimen while offering operational advantages. It represents an effective and practical alternative for conditioning prior to allogeneic transplantation.

Title	**Association of HLA Alleles with IgA Nephropathy and Its Recurrence After Kidney Transplantation**
Author	**Tímea Blichová**
Co-Authors	**Graňák K[12], Vnučák M[12], Kleinová P[12], Kollár A[12], Čereš A[3], Dedinská I[12]**
Affiliation(s)	[1]Transplant-Nephrology Department, University Hospital Martin, Martin, Slovakia [2]Department of Internal Medicine I, Jessenius Faculty of Medicine, Comenius University, Martin, Slovakia [3]Department of Clinical Immunology and Medical Genetics, University Hospital Martin and Jessenius Faculty of Medicine, Comenius University, Martin, Slovakia

Introduction

The recurrence of IgA nephropathy (IgAN) after kidney transplantation (KT) varies between 9% and 51%. We aimed to identify risk and protective HLA alleles for the development of IgAN and its recurrence after KT.

Methods

This retrospective single-center analysis included all patients after KT who underwent HLA typing prior to being listed on the waiting list for KT. Comparisons were performed with a cohort of 10,000 healthy donors from the Eurotransplant registry.

Results

A total of 470 patients were included. Biopsy-proven IgAN was found in 7.2% (n=48), of whom 77% were male. The DRB1*11 allele was present in 47,9% and was *identified as a significant risk factor for IgAN (OR 2.09, P=0.0048). The DRB*1*03 allele was detected in 4,17%, and we identified it as potentially protective (OR 0.2, P=0,5472). Recurrence of IgAN was detected in 20,8%, all male, with a mean time to confirmation of 56.1 months. The DRB1*11 risk allele was present in 77.8% of patients with confirmed recurrence but was not an independent risk factor (HR 2.3967; P=0.3956). Recurrence significantly correlated with development of donor-specific antibodies (DSA) after KT (r=0.3980, P=0.0218).

Discussion

The DRB1*11 allele was a risk factor for IgAN in native kidneys but was not confirmed as an independent risk factor for recurrence. The DRB1*03 allele was more common in healthy controls, suggesting a protective effect. Recurrence was usually confirmed by indication biopsy, with management focused on supportive care.

Conclusions

IgAN recurred in 20.8% of KT patients, with 77.8% carrying DRB1*11 allele which we also identified as a risk allele for the development of IgAN in native kidneys. De novo DSA after KT was correlated with IgAN recurrence.

Title	**Spatial Transcriptomic Profiling Reveals IL1β⁺ Macrophages as Major Drivers of Senescence in Chronic Wounds**
Author	**Lauren B. Colborn**
Co-Authors	Laden Fenercioglu[1], Leah Cooksey[1], Nina Rocha[2], Alexander Johns[2], Matthew J Hardman[1,2] and Holly N. Wilkinson[1,2]
Affiliation(s)	[1]Centre for Biomedicine, Hull York Medical School, University of Hull, UK, [2]Skin Research Centre, Hull York Medical School

Introduction:

Chronic non-healing wounds affect over 40 million individuals worldwide, yet effective therapies remain lacking due to limited understanding of the cellular mechanisms underlying impaired healing. We previously demonstrated that cellular senescence is a driver of poor healing in mice. In the present study, we thus characterised the cellular and molecular drivers of senescence in human chronic wounds to identify therapeutic targets.

Methods:

Spatial transcriptomics (Xenium, 10X Genomics) and protein multiplex imaging (MACSima, Miltenyi Biotec) was conducted on human chronic wound tissue. Complimentary *in vivo* studies were carried out in diabetic mice, with wound healing outcomes and immune cell senescence assessed via histology and flow cytometry.

Results:

We generated the first single-cell spatial atlas of human chronic wounds. Transcriptomic analysis identified highly senescent myeloid and fibroblast clusters driving the senescent niche and revealed significant upregulation of IL1β and CXCL5 in high-senescent wounds. IL1β and CXCL5 showed strong co-localisation within a specific myeloid cluster, and CellChat analysis confirmed strong predicted ligand-receptor interactions between this myeloid cluster and keratinocyte populations. Functional *in vivo* experiments corroborated our findings, where blockade of IL1β in diabetic mice reduced immune cell senescence and significantly improved wound repair.

Discussion:

Our data validate senescence as a hallmark of chronic wound dysfunction, where immunosenescence drives sustained inflammation and impaired healing. IL1β-driven immune-epithelial crosstalk emerged as a key mechanism in this process, identifying IL1β as a promising therapeutic target.

Conclusions:

These findings provide a foundation for precision therapies aimed at targeting senescence to improve wound healing outcomes in patients.

Title	**Radioprotective Potential of Modified Nanoparticles**
Author	Dolezal O. J.
Co-Authors	Carrillo A., Sinkorova Z., Cizkova J.
Affiliation(s)	Department of Radiobiology, Military Faculty of Medicine, University of Defence, Hradec Králové, Czech Republic

Introduction

Ionizing radiation causes severe damage to biological systems. Radioprotective agents act by limiting oxidative stress and DNA damage, thereby enhancing post-exposure recovery. Nanoparticles, particularly those based on biocompatible polymers, have shown potential to improve the delivery and efficacy of such protective compounds. The aim of the study was to evaluate the radioprotective potential of hyaluronic acid nanoparticles (HANPs), amifostine-modified HANPs, WR-1065 (amifostine), vitamin C, and their combination in an *in vitro* model.

Methods

Human T and B lymphocyte cell lines (Jurkat and Ramos) were seeded in 96-well plates (5,000 cells/well) and pretreated with HANPs, amifostine (WR-1065), or vitamin C prior to ^{60}Co gamma irradiation at doses of 4 and 15 Gy. Cell viability was assessed after 24 h using the MTS assay, and cell cycle alterations were analyzed using the BD Cycletest™ Plus DNA kit.

Results

HANPs alone exhibited a mild radioprotective effect, which was further enhanced when combined with other mentioned compounds. The most effective concentrations (HANPs, 0.35 mg/mL; vitamin C, 3 µM; amifostine, 0.5 µM) also reduced the proportion of cells in the G2/M phase, suggesting a decrease in radiation-induced cell arrest.

Discussion

The data indicate that HANPs can reduce radiation-induced cytotoxicity and potentially modulate DNA damage response pathways. Their natural biocompatibility and stability make them promising candidates for developing advanced radioprotective formulations.

Conclusions

Hyaluronic acid nanoparticles demonstrated measurable radioprotective potential *in vitro*. Their combination with established agents such as amifostine and vitamin C warrants further investigation in *in vivo* models.

Title	**In the shadow of cancer: searching for predictors of malnutrition in patients with multiple myeloma – a systematic review**
Author	**Maciej Dubaj (1)**
Co-Authors	Karol Bigosiński (1), Aneta Szudy-Szczyrek (2), Teresa Małecka-Massalska (3), Iwona Homa-Mlak (3)
Affiliation(s)	(1) Doctoral School, Medical University of Lublin, Poland (2) Department of Hematooncology and Bone Marrow Transplantation, Medical University of Lublin, Poland (3) Deparment of Human Physiology, Medical University, Lublin, Poland

Introduction

Multiple myeloma (MM) is the second most common hematological cancer, accounting for up to 2% of all oncological diseases. Although it is an incurable disease, recent years have seen significant improvements in MM treatment methods, contributing to an increase in patient survival to up to 10 years. One of the factors limiting the effectiveness of therapy and prognosis is malnutrition. The aim of this study was to present predictors of malnutrition in MM.

Methods

A systematic review was conducted in the PubMed, Scopus, Embase, and Google Scholar databases of publications from 2015 to 2025. Five publications from this period describing predictors of malnutrition in multiple myeloma were found.

Results

Malnutrition occurs in 12.5-71% of MM patients. Predictors of this condition with proven effectiveness include: levels of C-reactive protein (CRP) >54 mg/L (OR=5.94) and interleukin (IL) 1β >6.7 pg/mL (AUC=0.788), as well as rs1143634 polymorphism in the *IL1B* gene (AUC=0.72). The combination of CRP and IL-1β levels was the most effective (AUC=0.956). In addition, Growth Differentiation Factor 15 (GDF-15) and soluble transferrin receptor (sTfR) levels correlated negatively with albumin levels (r=-0.51, r=-0.26, respectively), which is an indicator of nutritional status in patients with MM. A similar relationship was observed in the case of reduced miR-192-5p expression.

Discussion

One of the main pathomechanical pathways of malnutrition in MM is inflammation. Its main indicator is CRP, and IL-1β is one of proinflammatory cytokines.

Conclusions

Effective predictors of malnutrition in MM include: CRP >54 mg/L and IL-1β >6.7 pg/mL levels.

Title	**The Effect of Cervicogenic Headache on the Myoelectrical Activities of Suboccipital Muscles, Range of Motion and Functional Activities of the Neck at Different Ages**
Author	**MOHAMED A. EMAM**
Co-Authors	**FATMA S. AMIN*, DOAA I. AMIN*, and RADWA AZMY****.
Affiliation(s)	PhD student at János Szentágothai Neurosciences Division, Semmelweis University, 1085 Budapest, Hungary The Departments of Basic Sciences, Faculty of Physical Therapy* and Neurology, Faculty of Medicine**, Cairo University

Introduction

Cervicogenic Headache (CGH) represents a major health problem, aggravating Quality of Life (QOL) and work productivity. The Suboccipital Muscles (SOM) have been identified as playing a role in cervical pain, and are therefore a target for rehabilitation.

Methods

Thirty patients with CGH and thirty normal subjects of both genders participated in this study, their ages ranged from 18-55 years old. They were randomly assigned into 2 experimental groups: Group A (18- 35 years)-group B (36-55 years) & 2 control groups: Group C (18-35 years)-group D (36-55 years). Myoelectrical activities was measured by Natus nicolet vikingquest to analyze the motor unit potentials by quantitative measures & neck range of motion was measured by Cervical Range of Motion (CROM) device and functional activities of the neck was measured by Neck Disability Index (NDI).

Results

There was non significance increase in myoelectrical activities of the suboccipital muscles in cervicogenic patients than normal subjects with (p-value=0.147). And there was statistical significant decrease in all ROM values and functional activities in cervicogenic patients than normal subjects in cervicogenic patients than normal subjects with (p-value <0.05).

Discussion

The study found increased myoelectrical activity in suboccipital muscles among cervicogenic headache (CGH) patients, though not statistically significant. Cervical ROM was significantly reduced in CGH subjects indicating functional impairment. Quality of life was also notably lower in CGH groups, highlighting the condition's impact on daily activities and well-being.

Conclusions

This study provides sound evidence for SOM alterations in in myoelectrical activities in patients with CGH.

Title	**From Tumor to Culture Dish: A Journey of Cancer-Associated Fibroblasts from PDAC**
Author	**Annamária Ferčáková[1]**
Co-Authors	Jana Sabová[1], Lenka Varinská[1], Lukáš Urban[1,2], Matúš Čoma[1,2] and Peter Gál[1,2]
Affiliation	[1] Department of Pharmacology, Faculty of Medicine, Pavol Jozef Šafárik University in Košice, 040 11 Košice, Slovak Republic [2] Department of Biomedical Research, East-Slovak Institute of Cardiovascular Diseases Inc, Ondavská, 040 11 Košice, Slovak Republic

Introduction

Cancer-associated fibroblasts (CAFs) drive tumor progression and therapy resistance in Pancreatic Ductal Adenocarcinoma (PDAC). Reliable CAF isolation from patient tissue is essential for functional and molecular studies. This study aimed to establish a protocol for CAF isolation from surgical PDAC samples.

Method

Fresh tumor specimens were obtained from the First Department of Surgery, L. Pasteur University Hospital and P. J. Šafárik University in Košice. Specimens were transported in DMEM/F-12 medium supplemented with a fivefold higher-than-standard concentration of penicillin, streptomycin, amphotericin B, and gentamicin. Adipose and necrotic tissue were removed, samples were minced and directly plated or enzymatically digested with trypsin. Tissue fragments were plated in six-well dishes and cultured in DMEM/F-12 with fetal bovine serum. Antibiotics in the culture medium were gradually tapered from threefold the standard concentration to standard levels during the first week. Fibroblast growth was monitored microscopically. Cells were harvested, expanded, and validated by immunofluorescence (IF) and Western blot (WB).

Results

Seventeen of 42 PDAC specimens yielded viable CAF cultures. Enzymatic digestion showed higher success (90%) than mechanical mincing (73.3%). Fibroblast-like cells appeared within 4-14 days, displaying spindle-shaped morphology and typical proliferation. Expression of vimentin, α-SMA, fibronectin and PDGFR-β was confirmed by IF and/or WB. Stepwise antibiotic reduction prevented contamination.

Discussion

This protocol consistently generated fibroblast cultures. Enzymatic digestion proved superior to mechanical mincing, and gradual antibiotic reduction preserved culture stability.

Conclusions

We present a reliable protocol for CAF isolation from PDAC tissue, providing a platform for downstream analyses and adaptable to other tumor types.

Title	**Extracellular vesicles from Hoffa´s fat pad - derived mesenchymal stem cells in osteoarthritis therapy**
Author	**[1]Slavomíra Gulová**
Co-Authors	[2]Alexander Otahal, [2]Karina Kramer, [2]Markus Rothammer, [3,4]Zsombor Lacza, [1]Denisa Harvanová, [2,5]Stefan Nehrer & [2]Andrea De Luna
Affiliation(s)	1 Associated Tissue Bank, Faculty of Medicine, P.J. Safarik University and L. Pasteur University Hospital in Kosice, Kosice, Slovakia 2 Center for Regenerative Medicine, Department for Health Sciences, Medicine and Research, University for Continuing Education Krems, Krems, Austria 3 Department of Sport Physiology, University of Physical Education, Budapest, Hungary 4 Inst. Clinical Experimental Research, Semmelweis University, Budapest, Hungary 5 Department of Orthopaedics and Traumatology, Universitätsklinikum Krems, Krems, Austria

Introduction

Osteoarthritis is a common degenerative joint disease in adults, with treatment being mostly symptomatic, while disease progression often leads to total joint replacement in the end stage. This study evaluates the potential of mesenchymal stem cells (MSCs)-derived extracellular vesicles (EVs) as a regenerative and anti-inflammatory therapy for osteoarthritis.

Methods

Hoffa's fat pad-derived MSCs (HFP-MSCs) were expanded on microcarriers in vertical-wheel bioreactors. After reaching plateau, MSCs were primed with fetal calf serum, platelet-rich plasma (PRP), or hyperacute serum. EVs were isolated from conditioned media by ultrafiltration and characterized by cryo-electron microscopy, nanoparticle tracking analysis, and Western blot. CFSE-labeled EV uptake by chondrocytes and synovial fibroblasts was assessed using confocal microscopy. To mimic the osteoarthritis environment, chondrocytes and synovial fibroblasts were co-cultured with M1 macrophages. Gene expression was analyzed by RT-qPCR and cytokine release by ELISA.

Results

HFP-MSC-EVs suppressed the expression of inflammatory genes (CCL5, COX2) in synovial fibroblasts and catabolic enzymes (MMP3, MMP13) in chondrocytes. In co-cultures, HFP-MSC-EVs enhanced the expression and release of the anti-inflammatory cytokine IL-10 by M1 macrophages.

Discussion

The effect of HFP-MSC-EVs may be donor age-dependent, indicated by elevated type II collagen expression in chondrocytes in response to EVs from a young compared to an old donor. There is evidence of superior effects of PRP-primed HFP-MSC-EVs over the other priming conditions. To support the hypothesis, repeated studies with multiple donors are required.

Conclusions

HFP-MSC-EVs have potential as a cell-free therapy for osteoarthritis, with anti-inflammatory and anti-catabolic properties with reduced safety concerns compared to cell-based approaches.

Title	**Does mesh surgery alter oxidative stress levels in patients with pelvic organ prolapse?**
Author	**Dominik Habeš**
Co-Authors	Martin Štěpán, Ondřej Dvořák, Iva Sedláková, Jiří Špaček
Affiliation(s)	Department of Obstetrics and Gynecology, Charles University, Faculty of Medicine in Hradec Králové

Introduction

Oxidative stress (OS) reflects an imbalance between oxidants and antioxidants, leading to the generation of reactive species that damage cellular molecules and impair function. Their by-products also participate in signaling; for example, increased advanced glycation end products (AGEs) stimulate matrix metalloproteinase expression, resulting in collagen degradation. In pelvic organ prolapse (POP), weakening of supportive and suspensory structures leads to organ descent with major impact on quality of life. While OS has been shown to be elevated in POP tissues, it remains unclear whether corrective suspensory surgery can reduce OS levels. This study assessed whether surgical correction of POP decreases markers of OS in vaginal fluid.

Methods

Seventy-two women with ≥ stage II POP, treated at PGK FNHK between February 2021 and June 2023, were enrolled. Exclusion criteria included active inflammation, malignancy, autoimmune disease, prior suspensory surgery, and recent sexual activity. Each participant underwent standardized urogynecological assessment, POP-Q, and 3D ultrasound before and one year after surgery (sacrocolpopexy, n=38; pectopexy, n=34). Vaginal fluid was sampled at both time points, and concentrations of 8-hydroxy-2'-deoxyguanosine (8-OHdG) and AGEs were quantified using ELISA.

Results

Mean age was 61 years, mean BMI 26.6. Ba point improved from +2.5 to –2.1 at one year. Mean 8-OHdG levels decreased (3.075 → 2.577 pg/ml) but did not reach statistical significance (Wilcoxon W=904, p=0.070; CLES=0.593). AGE levels showed minimal change (2.311 → 2.124 μg/ml; W=1160, p=0.939).

Discussion

Although 8-OHdG levels trended downward, neither marker demonstrated significant reduction postoperatively. AGE appeared insensitive in vaginal fluid.

Conclusions

Suspensory surgery for POP did not normalize OS marker levels, suggesting that its clinical benefit derives mainly from mechanical correction rather than biochemical modification of oxidative stress.

Title	**Gene expression of methylation and demethylation enzymes in HPV-negative OSCC**
Author	**Mgr. Adéla Harazimová**
Co-Authors	Ing. Kateřina Smešný Trtková, Ph.D.
Affiliation(s)	University of Ostrava, Faculty of Medicine, Ostrava

Introduction

Oral squamous cell carcinoma (OSCC) represents most head and neck squamous cell carcinomas (HNSCC) and is often diagnosed at advanced stages with poor prognosis. Rising incidence in younger patients without typical risk factors is alarming and highlights the need for new biomarkers. Epigenetic mechanisms may offer insights, regarding perineural invasion (PNI) and human papillomavirus (HPV) status.

Methods

Tumour samples from 17 HPV negative OSCC patients following resection therapy at University Hospital Ostrava divided into PNI-positive and PNI-negative groups were used for RNA isolation. Gene expression levels of DNA methyltransferases and TET enzymes were analysed using quantitative reverse transcription real-time PCR (RT-qPCR). Data analysis was performed using Microsoft Excel software.

Results

ΔCt value of DNMT1 gene expression was increased compared to DNMT3A and DNMT3B. Normalized values of DNMT1 in PNI-positive group were increased compared to PNI-negative group, and on the contrary, DNMT3A and DNMT3B normalized values were increased in PNI-negative group. Both groups of analysed patients showed increased ΔCt expression value of TET3 compared to TET1 and TET2 as well. Further, PNI-negative group showed increased normalized values of TET1 and TET3.

Discussion

Distinct methylation patterns indicate different methylation and demethylation process in HPV-negative OSCC patient and may differ in their impact on pathogenesis compared to HPV-positive OSCCs patients.

Conclusions

Given the complexity of epigenetic changes in HPV-driven cancers, further research with a larger number of patients is needed to explore the potential of molecular and therapeutical targeting of DNA methylation pathways in both HPV-negative and HPV-positive OSCCs.

Title	**Anti-Müllerian Hormone as a Marker of Ovarian Reserve in Safety of Radioiodine Treatment for Premenopausal Women with Thyroid Carcinoma**
Author	**Barbora Havlínová**
Co-Authors	Ilona Součková, Jiří Doležal
Affiliation(s)	Charles University, Faculty of Medicine in Hradec Králové

Abstract text

Introduction

Aims of the project are to determine ovarian reserve assessed by anti-Müllerian hormone (AMH), to determine the absorbed dose of ^{131}I in the ovary of women undergoing radioiodine treatment based on the magnitude of ^{131}I activity administered, to evaluate the relationship between absorbed dose of ^{131}I and change in AMH level.

Methods

Within a period of three years, 74 serum samples were drawn from women with thyroid carcinoma and 4 serum samples from healthy premenopausal women. AMH levels were compared before and after therapy in regular intervals 4–6 months, a total of 5 times, using the ELISA method.

Results

We found a significant effect on reducing AMH levels and thus ovarian reserve after ^{131}I (median 3.56 versus median 1.25, $p < 0.0001$). There was a strong correlation with age ($r = -0.616$ and $- 0.752$, respectively) – AMH decreases with increasing age. The relationship between changes in AMH and menstrual cycle disturbance has not been demonstrated.

Discussion

Differentiated thyroid carcinoma is the most common endocrinological malignancy with women being more frequently affected. There are discussions about adverse effects of ^{131}I on ovarian function and female fertility. AMH is regarded as the best endocrine marker for evaluating the physiological loss of oocytes in healthy women with regard to age.

Conclusions

The question of possible long-term side effects of radioiodine remains open and therefore the need to inform patients. Consequently, predicting the end of ovarian function by assessing a simple serum biomarker could help to select an appropriate treatment strategy for young women planning pregnancy.

Title	**Molecular and Functional Analysis of ABC Transporter Modulation**
Author	**Viktória Háziková[1]**
Co-Authors	Ondrej Franko[1], Martina Čižmáriková[1], Martin Kello[1], Radka Michalková[1], Sergio M. Marques[2,3], David Bednář[2,3], Viera Habalová[4], Mária Vilková[5], Atila D. Homolya[6]
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Introduction

Efflux mediated by ATP-Binding Cassette (ABC) transporters plays a key role in multidrug resistance (MDR), and numerous compounds are assessed for their potential to influence transporter expression or function. We explored various approaches for evaluating transporter expression, activity, and compound interaction, focusing on their suitability for studying ABC transporters.

Methods

qRT-PCR and Western blotting were used to evaluate the gene and protein expression of ABCB1, ABCC1, and ABCG2, and to examine the effects of the tested compound (1C) on these transporters in COLO 320 colon carcinoma cells. Transporter activity was evaluated using Efflux-ID Green assay, while the interaction of compound 1C with ABCB1 was analysed through rhodamine-123 accumulation, ATPase activity assay, and molecular docking.

Results and Discussion

All tested transporters were expressed in cancer cells, but gene expression did not consistently correlate with protein levels or function. ABCC1 protein was reduced after compound treatment despite stable mRNA levels. ABCG2 showed strong protein expression without corresponding activity (MDR activity factor below 25). Antibody performance varied, with Abcam antibodies proving more sensitivity than CST antibodies. Rhodamine-123 and ATPase assay results aligned with molecular docking predictions.

Conclusions

Our results demonstrate that evaluating ABC transporters and their modulation requires an integrated set of complementary methods.

Title	**Prognostic host phenotypes based on body composition and systemic inflammation predict survival in patients with periampullary cancer: results of a nationwide cohort study**
Author	**Nicole D. Hildebrand, MD** [a,b];
Co-Authors	David P.J. van Dijk, MD, PhD [a,b,c] ; Jisce R. Puik, MD [d, e, f]; Anne Claire Henry, MD, PhD [g]; Paul Andel, MD [g, h]; Esther N. Dekker, MD [i]; Nynke Michiels, MD [j] ; Lloyd Brandts, MSc, PhD [k]; Ralph Brecheisen, MSc, PhD [b]; Leonard Wee, MSc, PhD [l,m] ; Sebastiaan Festen, MD, PhD [n]; Koop Bosscha, MD, PhD [o]; Jennifer M. J. Schreinemakers, MD, PhD [p] ; Fennie Wit, MD [q]; Marion B. van der Kolk, MD, PhD [r]; J. Sven D. Mieog, MD, PhD [j]; Mike S.L. Liem, MD, PhD [s]; Vincent B. Nieuwenhuijs, MD, PhD [t]; Ignace H. J. T. de Hingh, MD, PhD [u, v]; Judith de Vos-Geelen, MD, PhD [w]; Jens T. Siveke, MD, PhD [x,y], Joost M. Klaase, MD, PhD [z]; Vincent E. de Meijer, MD, MSc, PhD [z]; Robbert de Haas, MD, PhD [aa]; Bas Groot Koerkamp, MD, PhD [i]; Babs M. Zonderhuis, MD, PhD [d, f]; Geert Kazemier, MD, PhD [d, f]; Marc G. Besselink, MD, MSc, PhD [f, bb]; I Quintus Molenaar, MD, PhD [g, h]; Lois A. Daamen, MD, PhD [g]; Marcel den Dulk, MD, PhD [a,b]; Sander S.M. Rensen, MSc, PhD [b]; Hjalmar C. van Santvoort, MD, PhD [g, h]; Steven W.M. Olde Damink, MD, MSc, PhD [a,b,x, cc] for the Dutch Pancreatic Cancer Group (DPCG)
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Introduction: The prognosis of periampullary cancer remains poor. Current predictive models for survival often disregard the tumour-host interaction. This study aims to define host phenotypes based on systemic inflammation and body composition to predict overall survival in patients undergoing resection for periampullary cancer.

Methods: A post-hoc analysis of the nationwide PORSCH-trial including patients with periampullary cancer was performed. The primary outcome was overall survival. A multivariable-adjusted Cox-proportional hazard analysis was performed. Body composition analysis was performed using preoperative abdominal computed tomography scans using automatic segmentation (MosaMatic™). Host phenotypes, ranging from low, intermediate, to high risk, were identified by stratifying sarcopenia, myosteatosis, and systemic inflammation.

Results: 923 patients were included. Systemic inflammation, sarcopenia, and myosteatosis were associated with survival in univariate analysis. The high-risk host phenotype was based on the combination of sarcopenia, myosteatosis, and systemic inflammation. In multivariable analysis, host phenotypes were associated with overall survival (hazard ratio [HR] 1.27 [95%CI 1.06-1.51] and HR 1.57 [95%CI 1.25-1.98] for intermediate and high risk, respectively) independent of histopathological diagnosis. Median overall survival was significantly different (low: 35 months [95%CI 28-41], intermediate: 25 months [95%CI 21-28], high risk: 18 months [95%CI: 13-24], $p<0.0001$).

Discussion: The presented findings are in line with previous evidence, where each individual adverse host factor negatively impacts prognosis. Combining them into distinct host phenotypes improved the prognostic assessment of the host.

Conclusions: Host phenotypes based on systemic inflammation, sarcopenia, and myosteatosis predict overall survival of patients with periampullary cancer independent of histopathological diagnosis, underscoring the importance of tumour-host interaction.

Title	**Vitamin D Supplementation in the Czech Republic: Socioeconomic Determinants and Public Awareness Gaps**
Author	**Drahomíra Holmannová**
Co-Authors	Jan Hodac, Lenka Borska, Eva Cermakova, Lenka Hodacova
Affiliation(s)	Charles University, Faculty of Medicine in Hradec Králové

Introduction

Vitamin D deficiency is a worldwide health concern linked to bone, immune, cardiovascular, and cognitive health problems. In the Czech Republic, the prevalence of deficiency is high, yet little is known about supplementation practices and public and public awareness of its effects on human health.

Methods

In 2023 a cross-sectional survey was conducted on a representative sample of 1,812 people aged 15+ across the Czech Republic. Data were collected via standardized face-to-face interviews. Supplementation patterns and knowledge of vitamin D functions were assessed. Statistical analysis included chi-square tests and logistic regression.

Results

Only 13.5% of participants reported regular year-round vitamin D supplementation, while 51.5% never supplemented. Women (OR = 2.47), older adults 65+ (OR = 2.49), those with higher education (OR = 2.18), married (OR = 1.97) and widowed (OR = 2.68) individuals, and mental workers (OR = 2.20) had significantly higher odds of supplement use. Higher income was also positively associated. Knowledge of vitamin D was mostly limited to bone (65.6%) and immune health (67.5%), while awareness of cardiovascular, neurological, and metabolic benefits was low, and misconceptions persisted.

Discussion

Our findings confirm that supplementation in the Czech Republic remains low and is strongly influenced by socioeconomic factors. Knowledge gaps suggest that public awareness is focused narrowly on bone and immunity, neglecting other health aspects.

Conclusions

Targeted prevention strategies and educational campaigns are needed, particularly for men, younger individuals, and those with lower education. Equally important is education of healthcare professionals to provide consistent evidence-based recommendations.

Title	**Investigation of Microglial Activation in the Hippocampus of Rats with Experimentally Induced Colorectal Carcinogenesis**
Author	**Inna Chebernina**
Co-Authors	—
Affiliation(s)	Horbachevsky Ternopil National Medical University of the Ministry of Health of Ukraine, Ternopil, Ukraine State Establishment "Lugansk state medical university", Rivne, Ukraine

Introduction

Peripheral tumors, including intestinal ones, can activate microglia in the brain, particularly in the hippocampus.

Methods

The experiment was carried out on 48 white rats (190±20 g) injected with dimethylhydrazine (7.2 mg/kg). Hippocampal samples were stained with Iba-1 antibodies and analyzed using a PreciPoint M8 Digital Scanning Microscope and ImageJ software. Data were processed in Microsoft Excel and STATISTICA 12.0**.**

Results

In controls, the density of Iba-1-positive microglial cells in the dentate gyrus was 100.45 ± 10.3 cells/mm². After 1 month of dimethylhydrazine (DMH) exposure, the number rose 1.2-fold (120.3 ± 12.9). At 2 months, it increased 1.34-fold (134.1 ± 9.1), at 3 months 1.64-fold (164.9 ± 15.3). The maximum density was reached at 4 months, doubling control values (200.6 ± 19.9; $p<0.001$). Decline followed: month 5 – 143.7 ± 13.1, month 6 – 110.6 ± 8.9. Morphometric analysis revealed significant soma enlargement ($p<0.05$), peaking at month 6 with a 3.19-fold increase.

Discussion

Microglia showed activation-related changes: hypertrophied somata, shortened processes, and reduced branching. The peak at 4 months reflected acute neuroinflammation, while later decline suggested glial exhaustion or transition to chronic inflammation.

Conclusions

DMH-induced carcinogenesis provokes dynamic microglial activation, with maximal response at month 4 and remodeling persisting through month 6.

Title	**Optimization of Diagnosis and Treatment of Skin Lesions Associated with Lyme Borreliosis in Military Personnel**
Author	**Daria Cherednychenko**
Co-Authors	—
Affiliation(s)	State Establishment “Lugansk state medical university”, Rivne, Ukraine

Introduction

The symptoms of Lyme borreliosis (LB) in military personnel are often masked as fatigue, flu-like conditions, joint injuries, stress disorders, or allergic reactions, which complicates timely diagnosis. Delayed diagnosis in military personnel reduces the effectiveness of standard treatment regimens, leading to chronic and atypical forms of Lyme borreliosis.

Methods

We examined 42 military personnel patients with suspected co-infection of LB. Diagnostic methods included clinical examination, serological testing (ELISA, IFA), and PCR. Treatment outcomes were compared between two groups: one received standard antibiotic therapy, while the other was treated with a combined regimen of antibiotics, recombinant interferon alpha-2b, and physiotherapy.

Results

Standard therapy showed 25% lower efficacy in Lyme borreliosis, with prolonged clinical symptoms (erythema migrans, arthralgia, neurological signs, asthenia), persistently elevated inflammatory markers (CRP, ESR, IL-6, TNF-α), and less pronounced reduction of IgM/IgG antibody titers to Borrelia burgdorferi (ELISA, Western blot).

Discussion

The inferior response to standard therapy in Lyme borreliosis highlights the need for combined treatment approaches that address both infection and immune dysregulation.

Conclusions

Incorporating immunotropic agents into standard regimens may enhance clinical recovery and reduce the persistence of inflammatory manifestations in military personnel with Lyme borreliosis.

Title	**Metabolic phenotype determines melanoma cell sensitivity to copper – delivering agents**
Author	**Natalia Chrzan**
Co-Authors	Justyna Suwara, Małgorzata Sztiller-Sikorska, Piotr Wawrzyniak, Malgorzata Czyz, Mariusz L. Hartman
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Introduction

About 50% of melanomas harbor *BRAF* mutations leading to the overactivation of the MAPK pathway, which promotes cell survival and proliferation. $BRAF^{V600}$ and MEK1/2 inhibitors improve patient prognosis, but long-term treatment often leads to the acquisition of resistance. Therefore, adjuvant therapies that sensitize drug-resistant cells to cell death induction are needed. In this respect, increasing intracellular copper levels might offer a potential therapeutic approach for melanoma patients, including those with acquired resistance to molecularly targeted drugs.

Methods

We used drug-naïve $BRAF^{V600E}$ melanoma cell lines derived from different surgical specimens. Drug-resistant cell lines were obtained by continuous exposure to increasing concentrations of the combination of $BRAF^{V600}$ and MEK1/2 inhibitors. To mimic the melanoma microenvironment more accurately, cells were cultured under reduced (6%) oxygen concentration. Sensitivity of melanoma cells to copper-delivering agents (copper ionophores) was assessed by flow cytometry, qRT-PCR, and assays aimed at determining the metabolic phenotype.

Results

Drug-resistant cells were more sensitive to copper ionophore-induced cell death than parental drug-naïve cells. Both drug-resistant and drug-naïve melanoma cells exhibited lower sensitivity to copper ionophores in 6% O_2 than in 21% O_2, which was accompanied by increased glucose uptake and lower mitochondrial dependence.

Discussion

Copper ionophore-induced cell death has been already suggested to rely on the metabolic state of cancer cells. Notably, targeted drug-resistant melanoma cells exhibit intensified oxidative phosphorylation compared to drug-naïve cells.

Conclusions

Our findings suggest an association between the mode of ATP production in melanoma cells and their susceptibility to copper ionophore-induced cell death.

Title	**Chronic inflammasome activation in cancer: promoting tumor progression and immune escape**
Author	**Kateřina Kalkušová**
Co-Authors	Dmitry Stakheev, Pavla Táborská, Jiřina Bartůňková, Isabelle Cremer, Daniel Smrž
Affiliation(s)	Department of Immunology, Second Faculty of Medicine, Charles University and Motol University Hospital

Introduction

The NLRP3 inflammasome plays a dual role in cancer, promoting anti-tumor immunity acutely but supporting tumor progression chronically. However, its precise function, particularly within the immune tumor microenvironment (TME), remains unclear.

Methods

In this *in vitro* study, we investigated NLRP3 function in prostate cancer (PCa) and non-small cell lung cancer (NSCLC) using cancer cell lines and patient-derived immune cells. We employed the selective NLRP3 inhibitor MCC950 and small interfering RNA (siRNA) to modulate inflammasome activity. Functional assays assessed cancer cell proliferation, epithelial-mesenchymal transition (EMT), immune checkpoint expression, cytokine secretion, and lymphocyte cytotoxicity. RNA sequencing was performed to identify broader NLRP3-regulated pathways in NSCLC.

Results

In PCa, MCC950 treatment enhanced long-term cytotoxicity of lymphocytes, improving their control of cancer cell growth. Notably, the response to MCC950 positively correlated with patients' clinical stage. NLRP3 inhibition also directly suppressed cancer cell proliferation, downregulated PD-L1 and EMT-associated molecules, and decreased secretion of tumor-promoting cytokines IL-8 and TGF-β. Similarly, RNA sequencing in NSCLC revealed NLRP3 involvement in EMT, proliferation, DNA repair, and immune escape pathways.

Discussion

Our exploratory study highlights the role of the NLRP3 inflammasome two distinct cancer diagnoses, PCa and NSCLC. We showed its contribution in shaping the immune TME and supporting the cancer progression. Although limited to *in vitro* models, our data propose NLRP3 inflammasome inhibition as a promising potential therapeutical strategy, particularly in combinational therapy.

Conclusions

Altogether, we described the role of NLRP3 inflammasome in PCa and NSCLC, demonstrating its involvement in tumor progression and immune escape, and suggesting NLRP3 as a potential therapeutic target.

Title	**Differential Expression of Angiogenesis-Related Genes in Female Reproductive System Pathologies**
Author	**Kováčová Gabriela**
Co-Authors	Tóthová Ivana, Švecová Monika, Artimovič Peter, Rabajdová Miroslava
Affiliation(s)	Pavol Jozef Šafárik University in Košice, Faculty of Medicine, Department of Medical and Clinical Biochemistry

Introduction

Angiogenesis is a crucial biological process involved in endometrium tissue regeneration after menstrual phase as well as the progression of pathological conditions of the female reproductive system (FRS). Dysregulation of angiogenic factors contributes to disorders such as endometriosis, endometrioid ovarian adenocarcinoma, and endometrial carcinoma. This pilot study aimed to analyze the expression of selected angiogenic genes in various FRS cell lines, representing both physiological and pathological states.

Methods

Cell lines of endometriotic and ovarian/endometrial origin (12Z, A2780, RL-95-2, SK-UT-1) and a control cell line (HME1) were cultured. Total RNA was isolated and reverse transcribed into cDNA. Quantitative Real-Time PCR was performed to evaluate VEGF-A, TGF-β1, ANG1, ANG2, and HIF-1α expression. Data were normalized to β-actin and analyzed with respect to angiogenic balance, hypoxia, and invasive potential.

Results

The study revealed marked heterogenity among angiogenic profiles. Endometriotic 12Z cells demonstrated the highest invasiveness, with elevated VEGF-A/TGF-β1 ratios and upregulation of ANG2/ANG1 and HIF-1α. A2780 cells showed low VEGF-A/TGF-β1 ratios but high TGF-β1 expression. RL-95-2 and SK-UT-1 lines displayed increased ANG2/ANG1 expression, whereas HME1 cells maintained baseline angiogenic gene expression.

Discussion

The findings highlight significant variability in angiogenic signaling pathways across distinct pathological FRS cell types. Hypoxia-inducible factor HIF-1α emerged as a key regulator, supporting the role of hypoxia-driven angiogenesis as central molecular mechanism in FRS pathologies.

Conclusions

The identification of dominant angiogenic profiles provides insight into the pathophysiological mechanisms of FRS disorders and may contribute to the development of personalized diagnostic and therapeutic strategies targeting angiogenesis.

Title	**Role of Hyaluronic Acid Metabolism in Endometrial Receptivity: Insights from RNAseq and Cellular Models**
Author	**Eva Kriváková**[1]
Co-Authors	Fabianová N.[1], Marčišin T.[4], Raptová P.[3], Kubala L. [2,3,4], Rabajdová M. [1]
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Despite long-term research, the percentage of successfully implanted embryos during in vitro fertilization (IVF) process stays low (ca. 30%) creating a significant number of patients with so called non-receptive endometrium pathological condition. The extracellular matrix (ECM) of the endometrium, the initial interface between the embryo and the endometrial lining, may play a crucial role in embryo implantation. This matrix contains various adhesive molecules that facilitate temporary adhesion, allowing subsequent biological processes to support implantation. Hyaluronic acid (HA), a key ECM component, has been identified as critical in this interaction.

This study investigates the role of HA metabolism in endometrial receptivity by analyzing bulk and single-cells RNA sequencing (RNAseq) datasets from the GEO database. We compared datasets from GEO database of endometrial samples from healthy women with successful pregnancies to those with repeated IVF failures. Furthermore, we utilized functional receptivity assay to test changes in receptivity of endometrial epithelial cell line Ishikawa to choriocarcinoma cell line Jar, which is used as trophoblast surrogate in this *in vitro* model. We modulate receptivity of Ishikawa cells using cytokines and hormones as the main regulators of receptivity *in vivo*. Changes in HA metabolism and receptivity markers were further studied on both gene and protein level using methods such as RT-PCR and immunocytochemistry.

Our reanalysis of GEO datasets from bulk RNAseq revealed significant downregulation of HA metabolism in the latter group. Differences in HA metabolism in the two studied groups were confirmed also in epithelial cells in GEO datasets from single-cell RNAseq. The results from *in vitro* experiments showed alterations in HA-related gene expression and protein levels, consistent with the differential HA gene expression observed in human endometrial samples. These findings suggest that impaired HA metabolism may contribute to the non-receptive state of the endometrium, providing a potential target for enhancing implantation success in assisted reproduction techniques (ART).

Conclusion: Altered HA metabolism may play a significant role in endometrial receptivity, highlighting its potential as a therapeutic target to improve ART outcomes.

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Title	**Automated Sleep Staging Using Sequential XGBoost and Multi-Scale Temporal Fusion**
Author	**Jiří Kuchyňka**
Co-Authors	Oldřich Vyšata
Affiliation(s)	Charles University, Faculty of Medicine in Hradec Králové

Introduction

Manual sleep stage classification is time-consuming, requiring 1-2 hours per recording. Automated solutions often struggle with complex patterns. This study develops a practical method combining multi-scale temporal fusion with sequential XGBoost processing to improve accuracy while maintaining computational efficiency for clinical use.

Methods

We analyzed polysomnographic data at multiple time scales (30, 15, and 5 seconds) using XGBoost algorithm. Sequential processing incorporated temporal context from previous epochs. The method was validated on 224 clinical recordings and the Sleep-EDF expanded database. Performance was evaluated using accuracy, Cohen's kappa, and F1-scores.

Results

The approach achieved 81.5% accuracy (κ=0.742) on clinical data and 91.5% (κ=0.826) on Sleep-EDF data. Sequential processing enhanced N1 stage detection with F1-score improvements of 27-61% across datasets. Training required approximately 12 minutes on standard hardware for 170 recordings.

Discussion

Multi-scale analysis captured both brief sleep events and longer transitions, addressing limitations of single-window methods. Sequential processing proved valuable for transitional stages where temporal context is crucial. Computational efficiency enables laboratories to develop customized models for their specific scoring patterns and populations.

Conclusions

Combining multi-scale fusion with sequential XGBoost provides effective automated sleep staging with competitive accuracy and computational efficiency accessible to clinical settings. Further research should validate performance across diverse populations and recording environments.

Title	**Effects of a Highly Hydrophilic Mitochondria-Targeted Iron Chelator**
Author	**Lucie Josefa Lamačová[1]**
Co-Authors	Jan Lj. Miljković[2], Michael P. Murphy[2], Jan Trnka[1]
Affiliation(s)	[1] Department of Biochemistry, Cell and Molecular Biology, Third Faculty of Medicine, Charles University, Prague, Czechia [2] MRC Mitochondrial Biology Unit, University of Cambridge, Cambridge, UK

Introduction

Mitochondrial iron is a potential cancer therapy target due to its crucial role in energy generation for high-demand cancer cells. The widely used mitochondria-targeting triphenylphosphonium (TPP^+) moiety ensures mitochondrial membrane potential ($\Delta\Psi_m$)-dependent accumulation of compounds into mitochondria. However, lipophilic TPP^+-based compounds can inhibit the electron transport chain (ETC). Therefore, we designed a hydrophilic derivative of the iron chelator deferiprone (MitoDFP) to selectively deplete mitochondrial iron while minimising the inhibitory effects of TPP^+ moiety.

Methods

We measured uptake into rat heart mitochondria (RHM) using RP-HPLC. We confirmed the iron-complexing ability using calcein and UV spectrophotometry. Cellular respiration was measured using a Seahorse XF Pro Analyzer. We analysed changes in protein levels using SDS-PAGE. We measured TMRM accumulation by flow cytometry to investigate mitochondrial membrane potential.

Results

MitoDFP accumulates in RHM in a membrane potential-dependent manner. The iron-complexing ability of deferiprone is not impaired upon derivatization with TPP^+ moiety. Incubation of PANC-1 cells with MitoDFP depletes cellular iron, as evidenced by increase in transferrin receptor 1 and decrease in cytosolic ferritin protein levels, while also reducing maximal respiration. We did not observe the same decrease in respiration in cells treated with control TPP^+-compound incapable of binding iron.

Discussion

MitoDFP affects cellular iron metabolism in a manner similar to untargeted deferiprone. However, its effect on mitochondrial respiration is greater, possibly due to mitochondrial iron depletion and dysfunction of the iron-containing complexes of the ETC.

Conclusions

New mitochondria-targeted deferiprone derivative accumulates in mitochondria and influences both energetic and iron metabolism in PANC-1 cells.

Title	**Oxygen Concentration Plays a Fundamental Role in the Regulation of Platelet Activity**
Author	**Sophie Leonard**
Co-Authors	Dr Zoe Booth, Dr Giordano Pula, Dr Simon Calaminus
Affiliation(s)	Centre for Biomedicine, Hull York Medical School, Hull, United Kingdom.

Introduction:

Oxygen (O_2) is a key determinant for cellular function. In the cardiovascular system the arteries and veins have markedly different O_2 environments (12% and 5% respectively), in disease states such as COPD this can fall further to hypoxic levels (1%). Low O_2 environments are prothrombotic, therefore we investigated the role of O_2 in platelet regulation, specifically investigating how the two key inhibitory signalling pathways prostacyclin (PGI_2) and nitric oxide (NO), were affected.

Methods:

Whole blood samples were incubated at either 1%, 5%, 12% or 21% O_2 and treated with PGI_2 or NO mimetic (8-pCPT-cGMP) before completion of thrombus formation assays, granule secretion and integrin $\alpha_{IIb}\beta_3$ activation via FACs analysis and signalling analysis via western blotting.

Results:

PGI_2 signalling is lost as O_2 concentration decreases, PGI_2 failed to mediate inhibition of platelet function at 1% and 5% O_2. In contrast, NO maintained its inhibitory effect even under hypoxic conditions. Interestingly, the PGI_2 receptor (IP) surface expression was unchanged, and the cAMP signalling pathway was able to work with other agonists (Iloprost and PGE_2). Therfore, we propose that PGI_2 breakdown is enhanced at 1% and 5% O_2, preventing it inhibiting platelets.

Conclusions:

The ability of O_2 concentrations to alter PGI_2 illustrates the requirement for two signalling pathways to inhibit platelet function, PGI_2 for arteries, NO for veins. This has implications for diseases such as diabetes where endothelial dysfunction reduces NO production allowing platelets to be more active and pose an elevated risk of driving pathological thrombus formation.

Title	**Methodological Aspects of Nociceptive Flexion Reflex Assessment** **A Pilot Normative Study**
Author	Jan Lonek
Co-Authors	Jiří Kozák, Rudolf Černý
Affiliation(s)	Second Faculty of Medicine, Charles University and Motol University Hospital

Abstract text

Introduction

The nociceptive flexion reflex (NFR) is an objective physiological marker associated with pain, reflecting spinal nociceptive activity. It is widely used for evaluating central sensitization, a key mechanism in neuropathic pain. Because NFR thresholds are influenced by technical and physiological factors, normative data are essential for accurate interpretation. The aim of this study was to establish normative threshold values in healthy volunteers and to identify influencing factors.

Methods

Forty-three healthy volunteers (21 women, 22 men; mean age 37.9 years) were examined. The NFR was elicited by electrical stimulation of the sole of the foot and recorded from the tibialis anterior muscle. For each subject, stimulation intensity (mA), subjective pain (NRS), electrical noise (μV), and skin impedance (kΩ) were measured. Statistical analyses included correlation testing between NFR threshold and influencing factors (JASP 0.18.3)

Results

The mean NFR threshold was 9.75 mA (SD 4.8). Average subjective pain during testing was 3.1/10 on the NRS scale. A moderate positive correlation was found between NFR threshold and subjective pain intensity ($r = 0.61$). Skin impedance demonstrated a strong negative correlation with NFR threshold ($r = –0.8$). Age, gender, and electrical noise showed no significant effect.

Discussion

The results demonstrate that NFR threshold values in this cohort are consistent with international standards. Skin impedance was identified as the most critical factor, highlighting the importance of monitoring and standardizing electrode–skin conditions. This may improve the reliability of NFR testing and support its wider use in both clinical practice and pain research.

Conclusions

Skin impedance is a significant determinant and must be controlled for reliable application of the NFR in both clinical and research settings.

Title	**Safe surgery for perihilar cholangiocarcinoma without preoperative biliary drainage: A retrospective multicentre analysis of data from 2067 patients.**
Author	Julien A. Luyten 1,2
Co-Authors	Julien A. Luyten 1,2 Pim B. Olthof (MD, PhD)4,5,6, Sander M.J. van Kuijk (PhD)7, Silvio Nadalin (MD, PhD)8, Hauke Lang (MD, PhD)9, Ruslan Alikhanov (MD, PhD)10, Joris I. Erdmann (MD, PhD)11, Johann Pratschke (MD, PhD)12, Shishir K. Maithel (MD, PhD)13, Roberto Troisi (MD, PhD)14, Andreas A. Schnitzbauer (MD, PhD)15, Ernesto Sparrelid (MD, PhD)16, Peter Lodge (MD, PhD)17, Massimo Malagò (MD, PhD)18, Ulf P. Neumann (MD, PhD)3, Erik Schadde (MD, PhD)19, Hassan Z. Malik (MD, PhD)20, Keith J. Roberts (MD, PhD)21, Baki Topal (MD, PhD)22, Frederik J.H. Hoogwater (MD, PhD)23, Jeroen Hagendoorn (MD, PhD)24, Andrea Ruzzenente (MD, PhD)25, Concepcion Gomez (MD, PhD)26, William R. Jarnagin (MD, PhD)27, Matteo Cescon (MD, PhD)28, Luca Aldrighetti (MD, PhD)29, Bas Groot Koerkamp (MD, PhD)5, Maxime J.L. Dewulf (MD, PhD)1#, Steven W.M. Olde Damink (MD, PhD)1,2,3#, on behalf of the Perihilar Cholangiocarcinoma Collaboration Group
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Introduction: There is no consensus on the use of preoperative biliary drainage (BD) for resectable perihilar cholangiocarcinoma (pCCA). This retrospective cohort study aims to explore the association of BD with postoperative mortality and morbidity.

Methods: In this retrospective observational cohort study, resected patients with histologically confirmed pCCA from the pCCA Collaboration Group database across 27 Western hepato-biliary centres (2000–2022) were included. To correct for baseline differences between drained and undrained patients, propensity score weighting (PSW) was applied. Outcomes were compared using propensity score-weighted regression (PSWR) and multivariable analysis.

Results: Overall, 2067 patients were included, of whom 350 (16.93%) did not undergo BD. Before PSW, undrained patients had fewer Bismuth III-IV cases (78.9% vs. 84.3%, $p<0.001$), lower median bilirubin levels (12.0μmol/L vs. 85.5μmol/L, $p<0.001$), and underwent more left hepatectomies (42.9% vs. 26.4%, $p<0.001$). After PSWR, the drained group had a higher likelihood of 90-day mortality (OR: 1.46, 95%CI: 0.92–2.34, $p=0.11$), though not significant. However, drained patients were more likely to experience major postoperative complications (OR: 1.43, 95%CI:1.04-1.95, $p=0.027$) and post-hepatectomy liver failure (PHLF) (OR: 2.12, 95%CI:1.25-3.58, $p=0.005$). After multivariable analysis, only PHLF remained significant (OR: 1.90, 95%CI:1.09-3.31, $p=0.024$).

Discussion: In this retrospective PSW analysis, preoperative BD was associated with a higher incidence of PHLF in resectable pCCA. There was also a trend toward higher 90-day mortality in drained patients, though not statistically significant.

Conclusions: These findings suggest that a subgroup of pCCA patients can be safely operated without BD. The indication of preoperative BD should be carefully considered on a case-by-case basis.

Title	**Liquid biopsy, solid findings: new insights into pathogenesis and cisplatin resistance in TGCTs**
Author	**Laura Matouskova [1,2]**
Co-Authors	Violeta Bakardjieva-Mihaylova[1], Martina Zwyrtkova[1], Kristyna Soffrova[1], Lucie Winkowska[1], Jan Stuchly[1], Karolina Skvarova Kramarzova[1], Ludmila Boublikova[1,2]
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Introduction

Testicular germ cell tumors (TGCTs) are the most common solid tumors in young adult men. Although highly curable due to their exceptional sensitivity to cisplatin (cDDP), a subset of patients develops cDDP resistance, leading to disease progression and death. The mechanisms underlying cDDP resistance and TGCT pathogenesis remain unclear.

Methods

We performed whole-exome sequencing using Illumina platform on a unique cohort of 30 refractory patients, analyzing 130 samples comprising primary tumors, metastases, cell-free DNA (cfDNA) collected over the disease course, and germline DNA as a control.

Results

Somatic variants with allele frequencies ≥ 5% detected in at least two patients were further examined for their relevance in TGCTs. We identified variants in genes linked to carcinogenesis and/or testis development (*TPTE2, RBMX, PRAMEF8, DNAH12, TSPAN16*) that were present in tumor samples and cfDNA at various disease stages, supporting their role in TGCT development. Conversely, mutations detected exclusively in resistant tumor samples were found in genes associated with DNA repair and epigenetic modifications (*PRDM9* and *ERCC5*), indicating their potential implication in mechanisms of cDDP resistance.

Discussion

We identified multiple novel candidate genes that have not been previously associated with TGCTs. Our results depict the role of epigenetic regulations and aberrant DNA damage pathways in TGCT progression and highlight the value of liquid biopsy. These findings may lay the groundwork for targeted therapies in patients who do not respond to cDDP treatment.

Conclusions

Our results contribute to the understanding of the molecular mechanisms underlying TGCT pathogenesis and the acquisition of cDDP resistance.

Title	**Screening for Anticardiolipin Antibodies in Early Pregnancy: Findings and Implications**
Author	**MUDr. Veronika Viktoria Matraszek**
Co-Authors	prof. MUDr. L. Krofta, CSc., MBA, prof. RNDr. I. Hromadníková, Ph.D.
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Introduction: The aim of the study was to evaluate obstetric outcomes in aCL positive pregnancies with regard to antibody levels and antibody isotype in the first trimester.

Methods: The retrospective cohort study included 3047 singleton pregnancies that underwent first-trimester aCL screening and delivered on site. Obstetric outcomes were compared between groups with negative antibody results (IgM<7 MPL and IgG<10 GPL) and positive antibody results (IgM≥7 MPL and/or IgG≥10 GPL). The aCL positive group was further divided into a high-titer group (≥40 MPL/GPL) and a low-titer group (<40 MPL/GPL). In the low-titer group, pregnancy outcomes were moreover evaluated with regard to the antibody isotype: IgM-positive group (IgM<40 MPL, IgG negative) and IgG-positive group (IgG<40 GPL units, IgM negative or <40 MPL).

Results: Overall, pregnancy-related complications occurred significantly more often in the aCL-positive group (p=0.004). The pregnancy-related complication rate was significant regardless of the aCL levels (low-titer group: p=0.034; high-titer group: p=0.018). However, when antibody isotypes were analyzed separately in the low-titer group, a higher rate of pregnancy-related complications was observed only in the IgG-positive group (p=0.001), but not in the IgM-positive group (p=0.427).

Discussion: Pregnancy-related complications occur more frequently in the aCL positive group, low-titer and high-titer groups alike. However, in the low-titer group, only the IgG-positive group was associated with greater obstetric risks.

Conclusion: The first-trimester screening for aCL has certain prognostic value and its implementation into clinical practice could improve prenatal care.

Title	**Management of Kidney Transplant Outpatients With COVID-19: A Single Center Experience**
Author	**Michaela Matyskova Kubisova[1]**
Co-Authors	Roman Safranek[1], Sylvie Dusilova Sulkova[1]
Affiliation(s)	1.Department of Nephrology, University Hospital in Hradec Kralove and Faculty of Medicine in Hradec Kralove, Charles University

Introduction

Our single-center retrospective analysis evaluated the outcomes of kidney transplant outpatients with COVID-19 who were managed with reduced immunosuppression and treatment with molnupiravir.

Methods

Between January 2022 and May 2023, we included 93 patients (62 men, average age 56 years), serum creatinine 127 (101-153) µmol/L. Molnupiravir was administered, and immunosuppressive therapy was reduced immediately following the confirmation of SARS-CoV-2 infection by PCR, which was 2 (1-3) days after the onset of symptoms.

Results

Only three (3.2%) patients required hospitalization, and one patient died. Acute kidney injury was observed in two patients. During the follow-up period of 19 (15-22) months, there was no significant increase in proteinuria, no acute or new chronic graft rejection, and kidney graft function remained stable; serum creatinine was 124 (106-159) µmol/L post-COVID-19 infection and 128 (101-161) µmol/L at the end of the follow-up period[1].

Discussion

One of the reasons for the favorable clinical outcomes in our study might be attributed to the early initiation of antiviral treatment with molnupiravir. Consistent with other studies, molnupiravir was well tolerated and did not show evidence of nephrotoxicity.

Conclusions

Our results demonstrate that early initiation of molnupiravir treatment combined with a temporary reduction in immunosuppressive therapy results in favorable clinical outcomes in patients with COVID-19, with preservation of good graft function and no episodes of graft rejection.

1. Matyskova Kubisova M. et al. Management of Kidney Transplant Outpatients With COVID-19: A Single Center Experience. Transpl Int. 2024 Sep 26;37:12920. doi: 10.3389/ti.2024.12920. PMID: 39391264; PMCID: PMC11464333.

Title	**Genetic variants of G protein-coupled estrogen receptor (GPER) and their association with prostate cancer susceptibility in Slovak population**
Author	**Martina Mečiaková[1]**
Co-Authors	Ján Kliment[2], Robert Dušenka[2], Daniel Evin[1,3], Martina Knoško Brožová[1], Monika Kmeťová Sivoňová[1], Dušan Dobrota[1], Jana Jurečeková[1]
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Introduction

GPER mediates rapid, non-genomic estrogen signaling that regulates cell proliferation, survival and metabolism. In this study, we evaluate the effect of 3 SNPs (rs3808350, rs3808351 and rs11544331) in the GPER gene on prostate cancer susceptibility and histopathological characteristics.

Methods

Study population included 701 prostate cancer patients and 663 healthy controls. We used tetra-primer ARMS-PCR to achieve allele-specific amplification.

Results

Overall prostate cancer risk was positively associated with the variant G allele and the heterozygous AG genotype of the rs3808350. Variant allele G was significantly associated with the risk of developing prostate cancer with PSA levels < 10 ng/ml, Gleason score ≥ 7, and pT3/pT4 stage. AG genotype was associated with the risk of developing prostate cancer with distant metastasis, while GG genotype was associated with the risk of developing prostate cancer with PSA<10ng/ml, Gleason score ≥ 7, and with lymph node involvement. Neither rs3808351 nor rs11544331 was associated with overall prostate cancer risk, but the heterozygous CT genotype of rs11544331 was less common in prostate cancer patients with distant metastasis than in patients without.

Discussion

This is a pilot study discussing the effect of genetic variants on specifically prostate cancer, however, rs3808350 was previously seen to be linked to a higher risk of testicular cancer.

Conclusions

We observed a significant association between the rs3808350 variant and prostate cancer, which might play a role in prostate cancer predisposition and aggressiveness.

Title	**Effect of exogenous surfactant on contused lung – experimental animal study**
Author	**Tomáš Merkl [1,2,3]**
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Introduction

Surfactant damage plays a significant role in the pathogenesis of acute respiratory failure (ARF) in patients with lung contusion. Our experimental study aimed to determine whether the administration of exogenous surfactant affects the distribution of tidal volume and, subsequently, the gas exchange in the animal model of lung contusion.

Methods

Experimental animals (n=21) with a lung contusion were divided into three equal groups. Contusion was induced in all three groups. Thirty minutes after the contusion the animal-derived surfactant (Curosurf ®) was administered intrabronchially at doses of 10 mg/kg and 5 mg/kg in the first and second groups, respectively. The third group served as a positive control. Vital signs, blood gases, and regional tidal volume distribution assessed by the electrical impedance tomography (EIT) were periodically monitored.

Results

A sustained, dose-dependent improvement in regional ventilation of the contused lung region, was observed in the 10 mg/kg group. This was accompanied by more efficient ventilation, evidenced by a lower ventilatory ratio and $PaCO_2$. A delayed improvement in systemic oxygenation (PaO_2) was also noted in this group at later time points.

Discussion

The primary effect of surfactant appears to be the improvement of lung mechanics by recruiting contused lung regions. This enhancement in ventilation efficiency suggests a potential to reduce the intensity of mechanical ventilation, thereby minimizing the risk of secondary ventilator-induced lung injury (VILI).

Conclusions

In a porcine model of lung contusion, intrabronchially administered exogenous surfactant at the dose of 10 mg/kg effectively improved regional tidal ventilation, ventilation efficiency and systemic oxygenation.

Title	**Unraveling the antiproliferative mechanisms of indole phytoalexin 1-methoxyisobrassinin in cervical cancer cells**
Author	**Viktória Miškufová**
Co-Authors	Radka Michalková, Martina Zigová, Martina Hájiková, Mariana Budovská, Ján Mojžiš
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Introduction

Natural compounds and their synthetic derivatives represent an important reservoir of bioactive agents with promising anticancer properties. The aim of this study is to examine the antiproliferative effects of indole phytoalexin 1-methoxyisobrassinin (MB-591), a synthetic analogue of secondary metabolites derived from cruciferous plants.

Methods

The antiproliferative effects of MB-591 were assessed using MTT and BrdU assays. Flow cytometry, western blot and fluorescence analysis were employed to study its influence on cell cycle progression and apoptosis induction. Furthermore, ROS levels were monitored, and their role in the compound's effects was investigated using N-acetylcysteine.

Results

MB-591 showed strong antiproliferative and proapoptotic effects in cervical cancer cells in vitro (IC_{50} = 6.87±0.56 μM, selectivity index = 3.99), inducing cell cycle arrest in S and G2/M phases with decreased PCNA and activated p53. Apoptosis was associated with mitochondrial dysfunction, cytochrome *c* release, caspase-9 and PARP cleavage, and H2A.X activation. MB-591 also increased ROS levels, and these effects were reduced by N-acetylcysteine.

Discussion

Indole phytoalexins have attracted increasing attention in recent years due to their anticancer properties, emphasizing their therapeutic potential. The antiproliferative and proapoptotic effects of MB-591 likely result from combined modulation of cell cycle progression and intrinsic apoptotic pathways. These results support further evaluation of MB-591 for cervical cancer therapy.

Conclusions

MB-591 demonstrates potent antiproliferative and proapoptotic activity in cervical cancer cells in vitro, acting through cell cycle arrest, activation of intrinsic apoptotic pathways, and modulation of oxidative stress, highlighting its potential for preclinical development in cervical cancer treatment.

Title	**The asymmetry of bone mineral density in human mandibles**
Author	**Alexander Morávek**(1)
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Introduction

Bone mineral density asymmetry in the human mandible may reflect functional lateralization and biomechanical adaptation. While morphological directional asymmetry in the face has been documented (Martiková et al., 2024), less is known about asymmetry in bone mineral radio-density. This study aimed to quantify voxel-wise directional asymmetry (DA) and fluctuation asymmetry in mandibular bone mineral density, controlling for shape variation.

Methods

Sex-specific 3D templates of the mandible were created from computed tomography data of adult males and females. Each mandible was warped to the corresponding sex-specific template using shape registration to remove morphological variability. Hounsfield Unit (HU) values were sampled voxel-wise from the warped models. For each voxel, DA was computed as the difference between mirrored voxel values on the left and right hemimandible. Positive values indicated greater density on the right side. Fluctuation asymmetry was calculated as variance of differences between original and mirrored image.

Results

Both male and female datasets demonstrated a consistent pattern of higher HU values on the right hemimandible. This right-side predominance was statistically significant and corresponds to findings of Martinková et al., 2024.

Discussion

These findings reveal a reproducible directional asymmetry in mandibular bone mineral density favoring the right side, paralleling previously reported right-side bias in facial morphological asymmetry. This suggests a potential shared developmental or functional origin linking shape and tissue density asymmetry in the craniofacial complex

Conclusions

Quantifying voxel-wise density asymmetry provides new insights into skeletal functional adaptation beyond shape analysis. These results may inform future research on the relationship between mandibular biomechanics, functional loading, and craniofacial asymmetry.

Title	**YB-1 regulates PD-L1 and PD-L2 expression in Pleural Mesothelioma**
Author	**Muhammad Hashim**[1]
Co-Authors	Ries, A.[1], Pirker, C.[1,] Pinós, M.[1,3], Koszik, L[1,2]. Hoda, MA.[2], Schelch, K.[1,2], Döme, B.[2], Berger, W.[1] and Grusch, M.[1]
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Introduction

Y box binding protein 1 (YB-1) is a protein with a highly conserved cold shock domain. It mainly localizes to the cytoplasm and nucleus, where it participates in various cellular functions. Studies have shown that YB- 1 promotes tumor progression and invasion in multiple types of tumors. This study aims to investigate how YB-1 regulates the expression of PD-L1/2 in mesothelial and pleural mesothelioma (PM) cell models.

Methods

Mesothelial cells (Met5a and NP2hTERT) as well as PM cells (MSTO-211H and SPC212) were treated with reactive oxygen species (ROS) to evaluate activation of signaling pathways such as MAPK/PI3K/AKT and YB-1. PD-L1/2 expression were analyzed by qPCR. Cell migration and morphological changes were assessed using live-cell imaging microscopy. MEK/AKT and RSK inhibitors were used to test pathway dependency and their effects on PD-L1/2 expression.

Results

We show that YB-1 is a downstream target of the MAPK/PI3K/AKT pathway, and its phosphorylation increases the expression of PD-L1/2. In addition, inhibiting MAPK or YB-1 decreases cell migration and induces a shift in morphology from elongated to more rounded forms in PM cell models.

Discussion

Previous studies have shown that PD-L1 is regulated by MAPK signaling. Our study further demonstrates that YB-1 acts downstream of the MAPK/PI3K/AKT pathway and regulates both PD-L1/2 in PM cell models. Targeting downstream molecules such as YB-1, rather than broad-spectrum targets like MAPK, may have better therapeutic implications.

Conclusion

In conclusion, in addition to regulating cell migration, the MAPK/PI3K/AKT pathway regulates YB-1 phosphorylation, which in turn regulates PD-L1/2 expressions in PM cells.

Title	**The effect of Hyperbaric Environment on the physiological functions of military Divers in the Czech Armed Forces**
Author	kpt. Mgr. Adam Pásler[1]
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Introduction

The aim of this study is to evaluate the effects of simulated hyperbaric conditions on selected physiological and cognitive parameters in professional divers of the Czech Armed Forces. The research addresses the current lack of evidence regarding the health impacts of hyperbaric exposure, especially in connection with highly specific technical work under water.

Methods

Three experimental modalities are compared: normobaric exercise, exercise at 2.5 ATA (15m), and exercise at 3.5 ATA (25m). Physiological monitoring includes continuous recording of ECG, end-tidal CO_2, and pulse oximetry. Laboratory analyses of chosen blood samples, spirometric assessment and cognitive evaluation using FEAST tests are also performed.

Results

The pilot phase demonstrated methodological feasibility and ensured the reproducibility of measurements under controlled hyperbaric conditions. The main phase of data collection is scheduled for 2025–2026.

Discussion

Preliminary findings confirm the technical and logistical feasibility of complex physiological and cognitive testing under hyperbaric exposure. The study will contribute to understanding adaptive and stress-related mechanisms in divers and may inform evidence-based preventive strategies for military and professional diving operations.

Conclusions

The research emphasises the current gap in high-quality evidence concerning the effects of hyperbaric environments on human physiology and cognition. Verification of adverse outcomes may support the development of preventive measures and operational guidelines for personnel exposed to increased ambient pressure.

Title	**Preoperative pregabalin reduces the Cp50 for skin incision during target-controlled propofol infusion: A randomized, placebo-controlled, double-blind clinical trial**
Author	**Roxana Polojintef-Corbu[1]**
Co-Authors	Johannes Müller[1], Stefan Ulbing[1], Alexandra Graf[2], Birgit Reiter[3], Thomas Stimpfl[3], Walter Plöchl[1]
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Introduction

The potency of propofol is measured by its Cp50 value, the plasma concentration required to suppress motor responses in 50% of patients during surgical incisions. Various drugs can influence Cp50. Pregabalin is commonly administered preoperatively because of its mild sedative and anxiolytic properties. Our placebo-controlled, double-blind clinical trial aimed to evaluate the impact of pregabalin on the Cp50 of propofol.

Methods

Eighty female patients undergoing breast surgery were enrolled and randomised to receive either a placebo or 300 mg pregabalin two hours before induction. Anaesthesia was induced and maintained with continuous target-controlled infusion (TCI) of propofol, administered as the sole agent without supplementary analgesics. Participants were assigned to different target effect-site concentrations of propofol, and motor responses to skin incision were recorded.

Results

A substantially lower Cp50 value of propofol was observed in the pregabalin group (5.62 μg/mL, 95% CI: 3.71 – 7.52), in comparison to the placebo group (8.47 μg/mL, 95% CI: 7.55 – 9.39).

Secondary outcome assessments indicated a significant reduction in opioid consumption and pain levels in the recovery area for the pregabalin group.

Discussion

Our study indicates that preoperative administration of 300 mg pregabalin reduces the Cp50 of propofol, allowing adequate anaesthesia at lower target effect-site concentrations during TCI-based maintenance. Additionally, pregabalin also improved postoperative analgesia and reduced opioid consumption.

Conclusions

In summary, pregabalin premedication provides both intraoperative and postoperative benefits by lowering propofol requirements and enhancing recovery profiles, supporting its role as a valuable adjunct in anaesthetic practice.

Title	**New phenotype in SARS2 deficiency**
Author	Hana Ptáčková[1]
Co-Authors	Štufková H.[1], Křížová J.[1], Hanák P.[1], Rodinová M.[1], Volfová N.[1], Hnízda A.[1], Nosková L.[1], Klement P.[1], Zámečník J.[2], Hansíková H.[1], Honzík T.[1], Tesařová M.[1], Krejčová H.[1]
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Introduction: SARS2 encodes mitochondrial seryl-tRNA synthetase. Its dysfunction has been linked to HUPRA syndrome (Hyperuricemia, Pulmonary hypertension, Renal failure, Alkalosis) or a predominantly neurologic phenotype.

Methods: Diagnosis in our patient was established by whole-exome sequencing (WES). Oxidative phosphorylation (OXPHOS) activities were assessed spectrophotometrically, and complex levels by native electrophoresis (BN-PAGE). Skeletal muscle and fibroblast samples were examined histologically and by electron microscopy.

Results: A previously healthy boy presented at 2.5 years with developmental regression, quadriplegia, epilepsy, and recurrent status dystonicus. Laboratory testing showed elevated serum lactate (5.6 mmol/l; N<2.2), alanine (685 µmol/l; N<500), increased CSF lactate (2.12 mmol/l; N<2.10) and alanine (57 µmol/l; N<35), and hyperlactaciduria (59 mmol/mol creatinine; N<40). Brain MRI was normal. WES identified two novel likely pathogenic SARS2 variants: c.1204_1204delC and c.1292G>A. Spectrophotometry revealed markedly reduced complex IV activity in fibroblasts (11.6 nmol/min/mg; N>18) and muscle mitochondria (57.3; N>120), with additional reduction of complex I+III (48.0; N>100). BN-PAGE confirmed decreased levels of all OXPHOS complexes. The patient is now 13.5 years old; his condition has stabilised on antiepileptic and muscle relaxant therapy, though his development remains severely delayed at a 15-month level.

Discussion: The phenotype did not match either described SARS2 presentations. Unlike HUPRA, renal, cardiac, and uric acid abnormalities were absent. Compared with neurologic cases, the course included acute regression, dystonia, and normal MRI. Biochemical and histological studies confirmed mitochondrial dysfunction, indicating overlap with both phenotypes.

Conclusion: We report a novel phenotype and genotype of SARS2 deficiency, broadening the clinical spectrum of this rare mitochondrial disorder.

Title	**Detection of steatotic liver disease in type 2 diabetes mellitus via utilising retinopathy screening pathways**
Author	**Marwan Qasem [1,2]**
Co-Authors	Ondrej Bednar [1,2], Vojtech Prochazka [2], Dominik Hegyi [2], Karel Dvorak [1,2]
Affiliation(s)	1 4th Department of Internal Medicine – Gastroenterology and hepatology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic; 2 Department of gastroenterology and hepatology, Regional Hospital Liberec, Liberec, Czech Republic.

Introduction

Steatotic liver disease (SLD) is a global health burden, particularly prevalent in individuals with type 2 diabetes mellitus (T2DM). Although guidelines recommend non-invasive tests (NITs) to screen high-risk groups, uptake in routine care remains low. This study evaluates the feasibility of incorporating SLD screening into annual diabetic retinopathy examinations (DRE) examinations using vibration-controlled transient elastography (VCTE).

Methods

We prospectively screened consecutive adults with T2DM for SLD during DRE visits. Data included VCTE results, patient history, and lab results. Participants with liver stiffness measurement (LSM)≥8.0 kPa underwent further aetiological workup. Baseline characteristics and NIT performance were analysed.

Results

Among 261 participants with valid LSM, 49 (18.8%) had LSM≥8.0 kPa and 27 (10.3%) had LSM≥12.0 kPa, 147 (56.3%) had CAP≥280 dB/m and 156 (59.8%) were diagnosed with SLD and classified as metabolic dysfunction-associated steatotic liver disease (MASLD; n=125,80.1%), metabolic and alcohol-associated liver disease (MetALD; n=25,16.0%), alcohol-related liver disease (ALD; n=5,3.2%), and miscellaneous (n=1,0.6%). Of those with LSM ≥8.0 kPa, 45 (91.8%) had Fibrosis-4 index (FIB-4) results and of them only 24 (53.3%) would have been referred for VCTE based on current FIB-4-based recommendations.

Discussion

Integrating VCTE into DRE visits is feasible and detects more advanced cases than recommended referral pathways. Proactive case finding led to diagnosing many cases that would have remained undetected using conventional algorithms. However, implementation may be constrained by limited access to VCTE in some settings.

Conclusions

Opportunistic VCTE during DRE, when feasible, is a practical SLD screening strategy and improves detection of insidious cases without additional referrals.

Title	**Tissue Repair Potential of *Agrimonia eupatoria* L. Extract in Advanced 3D Skin Models**
Author	**Jana Sabová[1]**
Co-Authors	Veronika Brindza Lachová[2], Petra Mitrengová[2], Pavel Mučaji[2], Peter Gál[1,2,3], Lucie Bačáková[4]
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Introduction

Impaired wound healing and skin pathologies pose a significant clinical challenge. Advanced 3D models provide microenvironments closer to tissue conditions and are increasingly used to study wound repair and evaluate novel bioactives. This study investigated an aqueous *Agrimonia eupatoria* L. (AE) extract in 2D and 3D systems, focusing on fibroblast activation, keratinocyte response, and angiogenesis.

Methods

Polyphenolic composition was profiled by HPLC-DAD/MS, and cytocompatibility was evaluated in keratinocytes, fibroblasts, and endothelial cells using MTS assay. Functional assays included collagen contraction, scratch migration, immunofluorescence, and Western blotting of signaling proteins. Endothelial angiogenesis was assessed in prevascularized 3D collagen constructs by confocal microscopy with quantitative image analysis of vascular networks.

Results

AE showed good cytocompatibility across all cell types. In fibroblasts, it slightly reduced TGF-β1–induced contraction, decreased fibronectin and α-SMA, and modestly attenuated SMAD2/3 signaling. Keratinocytes preserved epithelial features, stabilized keratins, enhanced E-cadherin, and maintained migration capacity. Endothelial cells maintained VEGFR2/VE-cadherin signaling, increased total AKT, and formed enhanced $CD31^+$ networks in 3D constructs. Quantitative analysis confirmed longer and more branched vascular structures, suggesting active angiogenic sprouting with incomplete maturation.

Discussion

Integration of 3D collagen constructs with fibroblasts, keratinocytes, and endothelial cells enabled evaluation of AE effects in a tissue-relevant context, providing insights beyond conventional 2D assays.

Conclusions

AE extract represents a polyphenol-rich cytocompatible preparation, supporting tissue remodeling, maintenance of keratinocytes function, and angiogenesis. The study underscores the value of advanced 3D models for translating molecular effects into tissue-level outcomes and supports their use for testing novel wound healing agents.

Title	**Morphological features of the lungs of offspring that developed in utero under maternal genitourinary system chronic inflammatory process conditions**
Author	**Liliia Sukharieva**
Co-Authors	Mykhailo Myroshnychenko
Affiliation(s)	Kharkiv National Medical University, Kharkiv, Ukraine

Introduction

Maternal genitourinary chronic inflammation often complicates pregnancy, adversely affecting offspring. The aim was to determine lung morphology in progeny exposed in utero to maternal chronic genitourinary inflammation (CGI) caused by *Streptococcus pyogenes*.

Methods

Study performed on WAG rats. Group 1 included 318 one-week-old, 204 one-month-old and 214 two-month-old rats from physiological pregnancies. Group 2 included 257 one-week-old, 134 one-month-old and 121 two-month-old rats from CGI mothers. Lung fragments were examined histologically (hematoxylin-eosin, Sudan III and Van Gieson's picrofuchsin).

Results

Group 1 demonstrated normal pulmonary structure. Group 2 revealed parenchymal and stromal alterations: foci of dystelactasis, atelectasis and emphysematous changes. Alveolocytes showed focal alterative-desquamative changes, also found in bronchial and bronchiolar epithelium. Interalveolar septa were thickened due to sclerosis; similar modifications occurred in bronchial and vascular walls. Vessels of various calibers were congested with perivascular hemorrhages and occasional acute thrombi. Some showed luminal narrowing due to medial hypertrophy and sclerosis. Interalveolar septa, perivascular and peribronchial zones contained focal-diffuse cellular infiltrates, mainly lymphocytes and macrophages. The intensity of changes in Group 2 increased with age.

Discussion

Morphological analysis revealed significant parenchymal and stromal remodeling in lungs of offspring developing under maternal CGI. These structural changes confirm the damaging transplacental effect of chronic maternal pathology and may predispose to diverse bronchopulmonary diseases throughout ontogenesis.

Conclusions

Prenatal exposure to maternal chronic genitourinary inflammation caused by *Streptococcus pyogenes* results in offspring lungs characterized by parenchymal-stromal alterations: alterative-desquamative and sclerotic changes, vascular disturbances, foci of dystelectasis, atelectasis, emphysematous remodeling and progressive immune-cell infiltration.

Title	**Ultrastructural Changes in the Bloodstream and Anatomical Structures of the Kidney of White Laboratory Rats during Severe Dehydration and Rehydration**
Author	**K. Vakhnovska[1]**
Co-Authors	Supervisor: I. Herasymiuk[2]
Affiliation(s)	[1] State Establishment «Lugansk State Medical University», Rivne, Ukraine [2] I. Horbachevsky Ternopil National Medical University, Ministry of Health of Ukraine, Ternopil, Ukraine

Abstract:
Body fluids mainly consist of water containing electrolytes, metabolites, and proteins. Balance of these components is vital for survival. Severe dehydration (>10 days without water) was modeled in laboratory rats. Two rehydration methods were compared: dosed and non-dosed water.

Introduction:
Main ultrastructural kidney components: glomerular capillaries, basement membrane, podocytes, tubular epithelium. Endothelial cells are fenestrated with centrally located nuclei. Objective: assess dehydration-induced structural changes and the effect of different rehydration strategies.

Methodology:
We used electron microscopy (TEM–125K) used for ultrastructural analysis. Fixation in glutaraldehyde and osmium tetroxide. Ultrathin sections prepared and contrasted by Reynolds' method.

Results:
Day 1 (mild): microcirculatory disturbances, narrowed capillary lumen, endothelial hyperactivity.
Day 6 (midlle): further blood flow reduction, tubular epithelial dystrophy, mitochondrial alterations.
Day 10 (severe): pronounced hemodynamic disorders, endothelial nuclei narrowing lumen, severe dystrophic changes.
Rehydration: With an underdosed water regime persistence and worsening of vascular and epithelial damage (erythrocyte stasis, organelle destruction). With dosed drinking water rapid recovery of capillary and tubular ultrastructure, normalization of mitochondria.

Discussion:
Severity of ultrastructural changes correlates with dehydration duration. Rehydration method critically influences recovery dynamics.

Conclusions:
Dehydration induces progressive ultrastructural kidney damage. Dosed rehydration is the most effective strategy for restoring water-salt balance. After 6–9 days of dosed rehydration, ultrastructure of kidneys approaches that of intact animals.

Title	**A Novel Cellular Model for Investigating Experimental Therapy in Alpha-1-antitrypsin Deficiency**
Author	**Šárka Veselá[1]**
Co-Authors	Veronika Barešová[2], Mariia Lunova[1], Petr Vyleťal[2], Dita Mušálková[2], Pavel Strnad[3], Stanislav Kmoch[2,4], Martina Živná[2,4], Milan Jirsa[1]
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Introduction

Alpha-1-antitrypsin (A1AT) is a liver-secreted plasma serine protease inhibitor encoded by S*ERPINA1*. Mutations in *SERPINA1* lead to alpha-1-antitrypsin deficiency (AATD), a genetic disorder affecting lung and liver. The most prevalent pathogenic allele named Z (c.1096G>A; p.Glu366Lys), causes misfolding and retention of mutated A1AT in endoplasmic reticulum (ER) of hepatocytes, resulting in hepatocellular damage and progressive liver disease. BRD4780, a small molecule shown to promote degradation of misfolded MUC-1 protein through TMED9-positive cargo receptor-containing vesicles, has demonstrated therapeutic potential in proteinopathies. This study investigates its effect on Z-A1AT clearance using a novel cellular model of AATD.

Methods

Conditional *SERPINA1*-transgenic HeLa cell lines were generated using lentiviral transduction with Tet-On-regulated cassettes expressing either wild-type M1V-A1AT or mutant Z-A1AT. A1AT expression was assessed by RT-PCR, SDS-PAGE, and native PAGE. Confocal microscopy compared subcellular A1AT localization in model cells and in liver of Z-A1AT-transgenic mouse and AATD patients.

Results

Inducible *SERPINA1* mRNA and A1AT protein expression was detected. Z-A1AT-transgenic cells retained more and secreted less A1AT than M1V-A1AT-transgenic cells. A1AT aggregates were present only in Z-A1AT-transgenic cells and colocalized with the ER, similarly to the patterns observed in liver tissue of Z-A1AT-transgenic mice and AATD cirrhosis patients. BRD4780 treatment reduced intracellular Z-A1AT.

Discussion

The model recapitulates early AATD pathology. Reduction of aggregates after BRD4780 treatment suggests that modulation of ER quality-control pathways may restore proteostasis.

Conclusions

Our model provides a platform for AATD therapeutic interventions. BRD4780 treatment is promising, further studies are required to confirm the observed effect.

Title	**Genotype Phenotype Evaluation of Statistical Association using PhenoPackets: Advancing the Automated Analysis of Monogenic Disease Phenotypes**
Author	**Ondřej Vladyka[1]**
Co-Authors	Daniel Danis[2], Peter N. Robinson[2,3], Adam Klocperk[1]
Affiliation(s)	[1] Department of Immunology, 2nd Faculty of Medicine, Charles University and University Hospital in Motol, Prague, Czech Republic. [2] Berlin Institute of Health at Charité, Universitätsmedizin Berlin, Germany [3] The Jackson Laboratory for Genomic Medicine, 10 Discovery Drive, Farmington CT 06032, USA

Rare diseases often display highly variable clinical phenotypes, even among individuals with identical monogenic mutations. Progress in understanding the genotype-phenotype correlations (GPCs) and reporting of clinical phenotypes has been constrained by the scarcity of well-characterized cohorts and problematic comparison of phenotypic data between published studies.

To alleviate this issue and streamline the genomic-phenomic research pipelines, as part of an international taskforce of experts in the field of primary immunodeficiencies we updated the Human Phenotype Ontology terminology with descriptors needed for accurate annotation of immunophenotypes.

We then utilized the HPO terminology along with the PhenoPacket data schema, a computationally analyzable data structure encoding geno-phenotypes, in two cohorts of patients with rare IEIs (TBX1 and MAGT1 deficiency), enabling the largest current meta-analysis of the reported cases.

Finally, our data was used to develop and test the Genotype Phenotype Evaluation of Statistical Association (GPSEA), a python-based framework which leverages PhenoPackets for genotype-phenotype correlation analyses. GPSEA enables the discovery and visualization of categorical, continuous, severity-based, and survival-related GPCs. An independent filtering step (IF-HPO) leverages the hierarchical structure of HPO to reduce redundancy and maximize statistical power. Applying GPSEA to 6,613 individuals across 85 cohorts and 122 rare diseases, we identified 241 significant GPCs—confirming known associations and uncovering novel ones.

Our approach enables precise, automated interpretation of GPCs in rare diseases with the potential to uncover more novel correlations as automation enables mass annotation of data from patient records, including patients with variants of unknown significance, which are underrepresented in current datasets.

Title	**IFN-γ drives phenotypic changes in melanoma cells and potentiates cell sensitivity to GLUT1 inhibition**
Author	**Piotr Wawrzyniak**
Co-Authors	Malgorzata Sztiller-Sikorska, Wiktoria Sobolewska, Natalia Chrzan, Malgorzata Czyz, Mariusz L. Hartman
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Introduction

Immunotherapy with immune checkpoint inhibitors (ICIs) is one of the currently approved treatment approaches for melanoma patients. Despite improved survival of ICI-responding patients, a substantial fraction of patients do not respond or develop resistance to ICIs, e.g., due to interferon-gamma (IFN-γ)-dependent signaling. This study aimed to assess the role of IFN-γ in inducing phenotypic changes in melanoma cells and altering the sensitivity of cells to an inhibitor of glucose transporter 1 (GLUT1).

Methods

Melanoma cell lines were exposed to IFN-γ either short-term (up to 48 hours) or long-term to achieve the IFN-γ-adapted state (at least 2 weeks). To evaluate phenotypic changes induced by IFN-γ, qRT-PCR, western blotting, flow cytometry, and senescence assays were conducted. Melanoma cell viability after exposure to the GLUT1 inhibitor was assessed using the propidium iodide staining.

Results

Melanoma cells showed a maximal cellular response to IFN-γ at 6 ng/ml. IFN-γ induced distinct phenotypic changes, including metabolic alterations that varied significantly between the short-term and long-term exposure. Treatment with the GLUT1 inhibitor induced cell death, which was potentiated by the addition of IFN-γ.

Discussion

In addition to previously shown IFN-γ-driven modulation of immunotherapy with ICIs we found time-dependent changes in metabolic phenotype of melanoma cells. Long-term exposure to IFN-γ can lead to the acquisition of resistance to ICIs. Targeting metabolic pathways in ICI-exposed melanoma cells may potentiate the antimelanoma response of immunotherapy.

Conclusions

Alterations in melanoma cell phenotype induced by IFN-γ can be potentially exploited in the context of cell death induced by GLUT1 inhibitor.

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