IOCPM 2025 Conference

The 1st International Online Conference on Personalized Medicine

29–31 October 2025 | Online

Program and Abstract Book

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The 1st International Online Conference on Personalized Medicine

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Welcome from the Chair

Dear Colleagues,

Please join us at **the 1st International Online Conference on Personalized Medicine** (IOCPM 2025), which will be hosted online from 29 to 31 October 2025.

Personalization to the individual's specific condition has been integral to clinical medicine since ancient times; however, the possibilities of a truly personal approach to diagnosis and therapy have been limited. Now, in the most recent decade, interest in Personalized Medicine has exploded, with over 45,000 publications integrating advances in all biomedical sciences in every branch of medicine, toward the goals of more individualized diagnosis, therapy, and continuing care.

IOCPM 2025 will be a major forum for physicians and scientists, worldwide, to present and discuss advances at the frontier of Personalized Medicine.

IOCPM 2025 is designed to encompass the breadth and depth of topics currently most relevant to Personalized Medicine. Presentations will be channeled into six sessions:

S1. Mechanisms of Diseases;
S2. Personalized Preventive Medicine;
S3. Diagnostics in Personalized Medicine;
S4. Personalized Therapy in Clinical Medicine;
S5. Pharmacogenetics, Omics, and Informatics;
S6. Precision Oncology.

IOCPM 2025 will enable you to share and discuss your most recent research findings in Personalized Medicine with the vibrant global community of scientists and physicians in the field.

IOCPM 2025 will make your presentation accessible to hundreds of researchers worldwide, with the active engagement of the audience in question-and-answer sessions and discussion groups that will take place online.

The conference committee will review all submitted abstracts. The authors of accepted contributions will have their work displayed in an abstract collection. Following the conference, outstanding contributions will be invited to be submitted as a full-length paper for publication in the *Journal of Personalized Medicine.*

IOCPM 2025 promises to be a most exciting conference, which we anticipate will become a transformative landmark in Personalized Medicine. We hope you will join us, present your work, contribute to discussions, and meet new colleagues. Together at IOCPM 2025, we will shape the future of Personalized Medicine.

Best wishes,

Prof. Dr. Kenneth P. H. Pritzker
Conference Chair
Laboratory Medicine and Pathobiology;
Surgery Temerty Faculty of Medicine,
University of Toronto, Toronto, ON,
Canada

Journal of
Clinical Medicine
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Journal of Personalized Medicine (*JPM*; ISSN 2075-4426) is an international, open access journal aimed at bringing all aspects of Personalized Medicine together on one platform. *JPM* reports innovative preclinical and translational scientific research, technological advances, and novel clinical medicine applications that advance the study and implementation of Personalized Medicine, publishing research papers, reviews, editorials, communications, etc. Our aim is to encourage scientists to publish their experimental and theoretical results in as much detail as possible, with their full experimental details provided so that their results can be reproduced.

We provide a forum that brings together academic and clinical researchers, biotechnologists, diagnostic and pharmaceutical companies, health professionals, regulatory and ethical experts, and government and regulatory authorities. By deploying high-quality continuous improvement in all its processes, the *Journal of Personalized Medicine* seeks to be the most relevant and highest quality journal in its field, and aspires to be amongst the best journals across scholarly publishing.

Journal Webpage: https://www.mdpi.com/journal/jpm

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Department of Molecular and Precision Medicine, Pennsylvania State College of Medicine, Hershey, PA, USA

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Invited Speakers

Prof. Dr. Jun Ishihara
Department of Bioengineering, Imperial College London, UK

Dr. Kenneth R. Butler
School of Medicine, University of Mississippi Medical Center, Jackson, MS, USA

Dr. Kazim Yalcin Arga
Department of Bioengineering, Marmara University, Goztepe, Istanbul, Turkey

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Department of Pathology, The University of Hong Kong, Pok Fu Lam, Hong Kong

Dr. Rajan Singh
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Dr. Christopher Farrell
College of Behavioral, Social and Health Sciences, Clemson University, Clemson, SC, USA

Dr. Seeun Ha
Department of Microbiology and Immunology, University of Nevada, School of Medicine, Reno, NV, USA

Dr. Giacomo Fari
Department of Biological and Environmental Science and Technologies (Di.S.Te.B.A.), University of Salento, Lecce, Italy

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Professor Nicola Normanno
IRCCS Istituto Romagnolo per lo Studio dei Tumori (IRST) "Dino Amadori" Meldola, Italy

Program at a Glance

29 Oct Morning	30 Oct Morning	31 Oct Morning
Session 5. Pharmacogenetics, Omics, and Informatics	Session 4. Personalized Therapy in Clinical Medicine	Session 5. Pharmacogenetics, Omics, and Informatics
29 Oct Afternoon	**30 Oct Afternoon**	**31 Oct Afternoon**
Session 1. Mechanisms of Diseases Session 2. Personalized Preventive Medicine	Session 3. Diagnostics in Personalized Medicine	Session 6. Precision Oncology

IOCPM 2025 Program

29 October 2025 (Wednesday)

Session 5. Pharmacogenetics, Omics, and Informatics

Time: 9:00 (CET) | 04:00 (EDT) | 16:00 (CST)

CET	Speaker	Title
09:00-09:10	**Prof. Dr. Kenneth Pritzker** Event Chair	*Opening Speech*
09:10-09:20	**Prof. Stefania Nobili** Session Chair	*Welcome from the Session Chair*
09:20-09:35	**Hala M. Alzeer** Selected Oral Speaker	Artificial Intelligence in Melanoma: Integrating Multi-Omics Data for Precision Oncology and Personalized Gene Therapy
09:35-09:50	**Vy Ong** Selected Oral Speaker	Precision Proteomics for Personalized Medicine: A Unified MS1/MS2 Linear Mixed-Effects Model for Robust Biomarker Identification
09:50- 10:05	**Sakshi Mishra** Selected Oral Speaker	Machine Learning – Driven Identification of Multi-Target Repurposable Drugs for Colorectal Cancer Using Transcriptomics and Network Pharmacology
10:05-10:20	**Ana Carolina Maldonado da Costa e Silva** Selected Oral Speaker	Bioinformatics screening of phenylpropanoids from Pyrostegia venusta for treatment of ER+ Breast Cance
10:20-10:35	**Yao Wei** Selected Oral Speaker	Structural Insights into CYP3A4–P-gp Interactions and Their Role in Personalized Autoimmune Drug Therapy
10:35-11:50	**Makrina Katsanopoulou** Selected Oral Speaker	Anti-Inflammatory and Antiplatelet Effects of NSAIDs and Clopidogrel on PAF and ADP Pathways: In Vitro Assessment Using Human Platelets
11:50-12:05	**Bijak Rabbani** Selected Oral Speaker	Advanced Cardiovascular Risk Stratification through Combined Clinical, Polygenic, and Monogenic Risk Models
12:05-14:00	**BREAK**	

29 October 2025 (Wednesday)

Session 1. Mechanisms of Diseases

Time: 14:00 (CET) | 09:00 (EDT) | 21:00 (CST)

CET	Speaker	Title
14:00–14:10	**Dr. Seungil Ro** Session Chair	*Welcome from the session chair*
14:10–14:35	**Dr. Christopher Farrell** Invited speaker	Drug resistance in chemotherapy-naive colorectal patients
14:35-15:00	**Dr. Seeun Ha** Invited Speaker	Post-surgical adhesions impair colonic transit through cellular remodeling
15:00-15:35	**Dr. Davide Barbagallo** Keynote Speaker	Identification of a new feedforward ceRNA network involving the kinase PIM1 and the circRNA circPIM1, predicted to be responsible for the relapse of WHO grade 2 meningioma
15:35-16:00	**Dr. Rajan Singh** Invited Speaker	Decoding Gastroparesis: A Paradigm Shift to Precision Pathophysiology & Therapy
16:00-16:15	**Kevin Liu** Selected Oral Speaker	Investigating the Role of CD151 in Systemic Breast Cancer Metastasis
16:15-16:30	**Jhon Esterilla-Viafara** Selected Oral Speaker	The pivotal role of structurally divergent but functionally convergent genes in Wilson's Disease: A bioinformatics approach
16:30-17:00	**BREAK**	

29 October 2025 (Wednesday)

Session 2. Personalized Preventive Medicine

Time: 17:00 (CET) | 12:00 (EDT) | 30 Oct 0:00 (CST)

CET	Speaker	Title
17:00–17:10	**Dr. Raghu Sinha** Session Chair	*Opening Speech*
17:10-17:35	**Dr. Raghu Sinha** Keynote Speaker	The Whole Human
17:35-17:50	**Stefan Thottunkal** Selected Oral Speaker	Comparing LLM Output to Physician Notes for Pharmacogenomics
17:50-18:05	**Alisa Pautova** Selected Oral Speaker	Modulation of microbiota metabolism for the prevention of postoperative complications in patients undergoing cardiac surgery: results of a pilot randomized controlled trial
18:05-18:20	**Shahnd Abu Karesh** Selected Oral Speaker	Personalized Preventive Strategies for Non-Communicable Diseases in Primary Care
18:20-18:35	**Swati Rai** Selected Oral Speaker	Integrating Multi-Omics and Machine Learning for Subtype-Specific Risk Stratification in Breast Cancer: A Step Toward Personalized Preventive Medicine

30 October 2025 (Thursday)

Session 4. Personalized Therapy in Clinical Medicine

Time: 9:00 (CET) | 04:00 (EDT) | 16:00 (CST)

CET	Speaker	Title
09:00–09:10	**Dr. Taulant Muka** Session Chair	*Welcome from the session chair*
09:10-09:45	**Dr. Taulant Muka** Keynote Speaker	TBC
09:45-10:10	**Dr. Joshua Li** Invited Speaker	Personalized Biomarkers for Diagnosis and Theragnosis of Malignant Serous Effusions
10:10-10:35	**Dr. Giacomo Fari** Invited Speaker	Sport for People with Disability: A Rehabilitative Approach for Precision Medicine
10:35-11:00	**Dr. Kai-Uwe Lewandrowski** Invited Speaker	Minimally Invasive Spinal Surgery Through the Lens of Personalized Care Models - A Solution To The Musculoskeletal Healthcare Crisis
11:00-11:15	**Yazun Jarrar** Selected Oral Speaker	Genome-Wide Screening of Pharmacogenomic Biomarkers in Jordanian Patients with Genetic Disorders
11:15-11:30	**Qin Xie** Selected Oral Speaker	Specialized Interventional Care for Massive Esophagogastric Variceal Bleeding in Decompensated Cirrhosis: A Midlife Case Study
11:30-14:00	**BREAK**	

30 October 2025 (Thursday)

Session 3. Diagnostics in Personalized Medicine

Time: 14:00 (CET) | 09:00 (EDT) | 21:00 (CST)

CET	Speaker	Title
14:00–14:10	**Prof. Dr. Kenneth Pritzker** Session Chair	*Welcome from the session chair*
14:10-14:45	**Prof. Dr. Kenneth Pritzker** Keynote Speaker	History of Personalized Medicine
14:45-15:20	**Prof. Dr. Weikuan Gu** Keynote Speaker	Exploring the capability of ChatGPT 4.0 in generating innovative research hypotheses to address key challenges in the early diagnosis of colorectal cancer (CRC)
15:20-15:35	**Daniele Bravoco** Selected Oral Speaker	Integrating Patient-Derived Organoids and Natural Compounds for Diagnostic and Therapeutic Innovation in IBD
15:35-15:50	**Ekaterina Sorokina** Selected Oral Speaker	Gut Microbiota and Systemic Inflammation in Post-COVID-19 Patients
15:50-16:05	**Giuseppe D'Albis** Selected Oral Speaker	Personalized Oral Care through Digital Innovation
16:05-16:20	**Anna Maria Anastasiou** Selected Oral Speaker	A Novel TAZ2 Domain Variant in CREBBP Underlines the Need for Personalized Approaches in Menke-Hennekam Syndrome
16:20-16:35	**Yongting Luo** Selected Oral Speaker	Mitochondrial DNA mutations as a candidate risk factor and diagnostic indicator in Marfan Syndrome

31 October 2025 (Friday)

Morning Session 5. Pharmacogenetics, Omics, and Informatics

Time: 9:00 (CET) | 03:00 (EST) | 15:00 (CST Asia)

CET	Speaker	Title
09:00–09:10	**Prof. Enrico Mini** Session Chair	*Welcome from the session chair*
09:10–09:35	**Prof. Nicola Normanno** Invited Speaker	Cancer Somatic Pharmacogenomics
09:35-10:00	**Prof. Stefania Nobili** Invited Speaker	Methodologies and Applications in Pharmacogenetics for Precision Medicine
10:00-10:25	**Dr. Erika Cecchin** Invited Speaker	Germline pharmacogenetics as a tool to prevent cancer drug adverse reactions
10:25-10:50	**Prof. George P. Patrinos** Invited Speaker	Precision Psychiatry
10:50-11:25	**Prof. Dr. Yves. A. Lussier** Keynote Speaker	Case-Control No More? How N-of-1 Omics Redefines Therapeutic Evidence
11:25-11:30	**Prof. Enrico Mini** Session Chair	*Conclusion of Session*
11:25-14:00	**BREAK**	

31 October 2025 (Friday)

Afternoon Session 6. Precision Oncology

Time: 14:00 (CET) | 09:00 (EDT) | 21:00 (CST)

CEST	Speaker	Title
14:00–14:10	**Dr. Masakazu Kamata** Session Chair	*Welcome from the Session Chair*
14:10-14:45	**Dr. Masakazu Kamata** Keynote Speaker	Exploring breast cancer brain metastasis and intervention strategies.
14:45-15:10	**Dr. Jun Ishihara** Invited Speaker	TBC
15:10-15:25	**Dr. Kazim Yalcin Arga** Invited Speaker	Beyond the Genome: Integrative Strategies for Personalized Cancer Therapy
15:25-15:40	**Pellegrino Mazzone** Selected Oral Speaker	A novel molecular mechanism regulates gastric cancer cell homeostasis
15:40-15:55	**Fanlin Gu** Selected Oral Speaker	Polydopamine-Modified Engineered E. coli for Synergistic Cancer Therapy via Glucose Oxidase-Mediated Starvation and Prodrug Delivery
15:55-16:10	**Riad BenGhida** Selected Oral Speaker	Liquid Biopsy Implementation for NSCLC: What Can New Brunswick Learn from Ontario's Experience
16:10-16:25	**Aditya Vayalapalli** Selected Oral Speaker	Pathway Analysis of Chemoresistance in Glioblastoma Multiforme

Session 1. Mechanisms of Diseases

sciforum-132966: 3'UTR Variant rs12245 in *KRAS* and Its Functional Implications in Breast Cancer Susceptibility

Asbiel Felipe Garibaldi-Ríos [1,2,*], Luis E. Figuera [1], Belida Claudia Gómez-Meda [3], Guillermo Moisés Zúñiga-González [4], Irving Alejandro Carrillo-Dávila [1], Ingrid Patricia Dávalos-Rodríguez [1] and Martha Patricia Gallegos-Arreola [1]

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Introduction

The *KRAS* gene plays a key role in oncogenic signaling. Regulatory variants within its 3' untranslated region (3'UTR) can affect microRNA (miRNA) binding, influencing post-transcriptional regulation. This study evaluated the potential association between the rs12245 variant in the 3'UTR of *KRAS* and breast cancer (BC) susceptibility and explored this variant's possible functional relevance through in silico analysis.

Methods

A total of 627 individuals were genotyped for rs12245, including 385 BC patients and 242 individuals forming a reference group. Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated using logistic regression models. Predictions of altered miRNA binding were obtained from miRNASNP-v3 and PolymiRTS. The expression status of the affected miRNAs was examined in dbDEMC. In addition, eQTL analysis was performed using GTEx data for breast mammary tissue.

Results

The AT genotype was associated with a reduced risk of BC (OR = 0.55; 95% CI: 0.40 to 0.77; p = 0.0003), while the TT genotype and recessive model were associated with an increased risk (OR = 1.44; 95% CI: 1.00 to 2.06; p = 0.023). No significant associations were found with clinicopathological variables. In silico analysis suggested that rs12245 may alter the binding of several miRNAs to the *KRAS* 3'UTR, including hsa-miR-543, hsa-miR-544a, hsa-miR-4803, hsa-miR-5580-3p, hsa-miR-4686, hsa-miR-6738-3p, and hsa-miR-5096, which are deregulated in BC. The GTEx data indicated that rs12245 shows eQTL activity in breast tissue (p = 0.00069; slope = –0.094).

Conclusion

The rs12245 variant in *KRAS* may contribute to determining BC susceptibility and shows potential regulatory effects based on eQTL and miRNA binding predictions. These findings warrant further investigation to clarify this variant's biological significance.

sciforum-119518: Acquired Cystic Fibrosis Transmembrane Conductance Regulator dysfunction

Michael Eisenhut

Luton&Dunstable University Hospital, Luton, United Kingdom

Rhinorrhea associated with viral upper respiratory tract infections or reaction to aeroallergens affects all human beings and has been associated with loss of quality of life. Pulmonary fluid accumulation in acute lung injury is a leading cause of hospital admission and death from lower respiratory tract infection and sepsis.

Methods:

In this narrative review, evidence supporting the hypotheses that both rhinorrhea and inflammation-related pulmonary fluid accumulation are due to the dysfunction of the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) is presented, and novel concepts of the patho-mechanisms involved are explained.

Results:

Upper and lower airway as well as alveolar surface liquid volumes are shown to be dependent on CFTR. Its function is regulated directly by cytokines in allergic- and infection-related inflammation and through increased hydrostatic tissue pressure secondary to vasodilatation in enclosed spaces within the upper airway and in heart failure in pulmonary interstitial spaces. The regulation of upper airway fluid secretion manifested in allergic inflammation and viral infections by rhinovirus and respiratory syncytial virus can be explained by CFTR activation and alveolar fluid accumulation by the inactivation of CFTR through cytokine-induced microRNA and Na/K ATPase inhibition. Therapeutic interventions reducing CFTR dysfunction through anti-inflammatory and CFTR modulating strategies are introduced.

Conclusions:

Excessive fluid secretion in the upper respiratory tract induced by viruses and allergy as well as increased lung water in local and systemic inflammation can be explained by CFTR dysfunction opening avenues for supportive treatment.

sciforum-134107: Investigating the Role of CD151 in Systemic Breast Cancer Metastasis

Kevin Liu *, Naoki Hama, Charles J Kuhlmann, Chloe E Jepson, Madison Blucas, Yoshiko Nagaoka-Kamata and Masakazu Kamata

Department of Microbiology, University of Alabama at Birmingham, Birmingham, 35233, United States of America

Background:

While significant advancements have been made in breast cancer treatment, metastasis remains a negative outcome which drastically worsens the patient prognosis. Common metastatic sites include the bones, lungs, and liver, with secondary brain metastases seen in advanced disease. Treatments for disseminated tumor cells often carry risks of systemic toxicity without guaranteeing complete eradication. It is vital that we identify key molecular mechanisms underlying the systemic metastatic cascade so that we can disrupt this process. Our team has created a unique mouse model utilizing the 4T1 murine mammary tumor cell line, generating lung/brain metastases with a 100% success rate. This model will help identify the conditions necessary for the development of primary and secondary breast cancer metastases.

Methods:

4T1 parental cells (4T1-Ps) were genetically labeled with firefly luciferase and EGFP for imaging. A highly brain-metastatic subpopulation (4T1-BR) was then established via serial in vivo passage and isolation from the brains of BALB/C mice following iv 4T1-P administration. Brain metastasis was confirmed through bioluminescent imaging, the examination of neurological symptoms, and light sheet microscopy. Genes selectively upregulated in 4T1-BR cells were identified through RNA transcriptomic analysis. Twenty-eight potential candidates encoding for surface-expressed proteins were selected. Surface expression was evaluated using flow cytometry and immunofluorescent staining. Upregulated candidates were knocked out using CRISPR-Cas9 in 4T1-BR cells. Changes in the metastatic biodistribution and survival were assessed in vivo following iv administration.

Results:

4T1-BR cells demonstrate increased surface CD151 expression, as observed using flow cytometry and immunofluorescent staining. Mice transplanted with CD151-/- 4T1-BR cells demonstrated a decreased total bioluminescent signal but no change in their survival, the brain metastasis incidence, or the lung/brain tumor burden.

Conclusions:

Surface CD151 expression is increased in brain-metastatic 4T1-BR populations compared to 4T1-Ps. While not directly related to survival or the brain metastatis potential, CD151 may play a functional role in altering systemic biodistribution.

sciforum-134290: The pivotal role of structurally divergent but functionally convergent genes in Wilson's Disease: A bioinformatics approach

Jhon Esterilla-Viafara [1,2] and Fabian Tobar-Tosse [2,3]

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Introduction:

Wilson's disease (WD) is an autosomal recessive hereditary disorder caused by mutations in the ATP7B gene, which impair copper homeostasis. The clinical heterogeneity observed in patients suggests the involvement of modifier genes influencing phenotypic expression.

Objective:

We aimed to characterize the structural and functional properties of genes associated with WD through a bioinformatic approach, aiming to identify relevant molecular patterns and potential modifier genes.

Methods:

Genes related to WD were retrieved from the MalaCards database. Structural annotation was performed using the UCSC Genome Browser (GRCh38/hg38), including for the gene architecture, regulatory elements, repeat content, and evolutionary conservation. The data were statistically processed using Python scripts, and functional enrichment analyses (ToppGene) and protein–protein interaction analyses (STRING) were conducted. The genes were grouped based on patterns of functional convergence and structural divergence.

Results:

A total of 21 genes were identified with significant structural divergence in terms of their exon number, transcript variants, and conservation, yet they exhibited convergent biological functions related to key processes such as the homeostasis of metals, particularly copper. Subgroups were observed with compact gene architectures and high conservation, as well as others with greater structural complexity and lower conservation. Notable genes included COMMD1, ABCC2, HFE, ATP7A, SLC11A2, SLC31A2, and MT1E, some of which have previously been described as potential modifiers in WD.

Conclusions:

These findings support the existence of structurally divergent yet functionally convergent genes in the pathophysiology of WD. Their identification highlights their potential as candidates for use in functional studies aimed at understanding clinical variability and developing predictive models of this disease.

Session 2. Personalized Preventive Medicine

sciforum-143948: Comparing LLM Output to Physician Notes for Pharmacogenomics

Stefan Thottunkal [1,*], Guillaume Denis Nicolas Iarghero [2], Claire Spahn [3], Benjamin Wang [3], Nidhi Rohatgi [4], Ivan Lopez [5], Jison Hong [6], Abha Khandelwal [1], Anand Veeravagu [7] and Latha Palaniappan [1]

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Introduction

Pharmacogenomic (PGx)-guided prescribing can reduce adverse drug reactions and improve efficacy, yet clinical uptake is limited. A key barrier is reliance on complicated, text-dense reports, which are incompatible with routine clinical workflows. Large language models (LLMs) show promise in generating concise, context-specific recommendations, but prior work has largely focused on concept-based question-answering rather than realistic case interpretation. In this study, we examine LLMs' efficacy in interpreting PGx reports.

Methods

GPT-4.5 was deployed in Stanford's HIPAA-compliant SecureGPT environment and paired with retrieval-augmented generation to inject CPIC guidance at inference. To create the test dataset, we created a set of synthetic PGx laboratory reports and accompanying medical histories. These cases covered a range of genotypes and clinical contexts. An expert human evaluator interpreted each case and authored a gold-standard consult note. The LLM generated consult notes that were compared against gold-standard notes quantitatively using ROUGE-L and BERTScore. The qualitative evaluation (LLM-as-a-judge and human evaluators) used a 5-point Likert scale across five quality domains (accuracy, clinical relevance, bias, risk-management, and hallucination).

Results:

Human expert ratings achieved overall scores of 0.91 ± 0.16, while the LLM-as-a-judge scoring produced 0.708 ± 0.17. Semantic similarity metrics showed a BERTScore precision of 0.822 ± 0.012, recall of 0.788 ± 0.018, and F1 of 0.805 ± 0.013. The direct lexical overlap was lower, with a ROUGE-L precision of 0.207 ± 0.084 and a recall of 0.270 ± 0.122.

Conclusion:

LLMs can achieve quality PGx outputs compared to those from human experts. However, our findings show variable performance in the metrics. NLP-based evaluations miss nuanced clinical data and lack flexibility in interpretation. This also raises concerns about the efficacy of NLP metrics for reliably evaluating high-impact clinical information and underscores the necessity of human evaluation. Key limitations included an inability to factor in phenoconversion and decisively synthesise information for drugs influenced by multiple pharmacogenes. Further validation with real-world patient data is in progress.

sciforum-132280: Modulation of microbiota metabolism for the prevention of postoperative complications in patients undergoing cardiac surgery: results of a pilot randomized controlled trial

Alisa Pautova [1,*], Marina Grekova [2], Maxim Babaev [3] and Natalia Beloborodova [1]

[1] Federal Research and Clinical Center of Intensive Care Medicine and Rehabilitology, Moscow, 107031 Russia
[2] Petrovsky National Research Centre of Surgery, Moscow, 119991 Russia
[3] Petrovsky Russian Research Center of Surgery, Moscow, 119991 Russia

INTRODUCTION:

The disruption of microbiota metabolism, measured by changes in the serum concentrations of clinically relevant aromatic metabolites, appears to play a crucial role in the occurrence of complications following cardiac surgery [DOI:10.3390/biomedicines11051335].

The aim of this study was to assess the potential of modulating the microbial metabolism using specific antibiotics to prevent infectious and inflammatory complications after cardiac surgery.

MATERIAL AND METHODS:

Patients (n = 58) who underwent cardiac surgeries under artificial circulation were involved in a randomized prospective interventional study [ClinicalTrials.gov identifier: NCT04921436. Registered May 24, 2021].

Patients in group I (n = 30) received modulation of microbial metabolism through antibiotics that inhibited protein synthesis (a combination of semi-synthetic antibiotics from the tetracycline and macrolide groups); the patients in group II did not experience such modulation (n = 28).

Blood serum samples were collected three times, prior to and on the 3rd and 6th days after the surgery, and analyzed for their clinical parameters and concentrations of clinically significant aromatic acids.

RESULTS:

Six and eight patients developed postoperative complications, including zero and five cases of pneumonia, in groups I and II, respectively. The range of identified microorganisms in group II was considerably broader. Group I (compared to group II) exhibited a more pronounced reduction in the concentration of 4-hydroxyphenylacetic acid when comparing the values prior to surgery to those on the third and sixth days ($p = 0.016$ and 0.005, respectively). The total concentration of aromatic metabolites on the third day, as well as 4-hydroxyphenylacetic acid on the sixth day, showed strong predictive value concerning the occurrence of complications (sensitivity of 100% for both parameters; specificity of 82% and 93%, respectively).

CONCLUSIONS:

The preventive administration of antibiotics that inhibit microbial protein synthesis effectively diminishes the severity of microbiota metabolic dysfunction and lowers pneumonia incidence in the early stages following surgery.

sciforum-141859: Integrating Multi-Omics and Machine Learning for Subtype-Specific Risk Stratification in Breast Cancer: A Step Toward Personalized Preventive Medicine

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Introduction:

Advancements in transcriptomic profiling and machine learning are transforming preventive oncology. Triple-Negative Breast Cancer (TNBC), a clinically aggressive and heterogeneous subtype, lacks targeted therapies and presents challenges for early interception. This study investigates the potential of unsupervised learning to reveal molecular subtypes within TNBC, supporting individualized risk assessment strategies.

Methods:

Transcriptomic and clinical data from the TCGA breast cancer cohort were analyzed. TNBC cases were identified based on basal-like classification. Dimensionality reduction was performed using Principal Component Analysis (PCA), followed by k-means clustering to detect latent subgroups. Genes with the highest variance were used to explore inter-sample expression patterns.

Results:

The PCA of TNBC transcriptomic data revealed distinct variance among patient samples, indicating underlying molecular heterogeneity. The first two principal components captured a substantial portion of the variance, allowing for clear visual separation. K-means clustering (k=3) identified three reproducible molecular subgroups with minimal overlap and strong intra-cluster similarity. Analysis of the top 50 most variably expressed genes showed distinct expression patterns across clusters, suggesting differential pathway activation. Several of these genes are linked to cancer progression, immune response, and therapy resistance, highlighting their potential as early biomarkers. These findings demonstrate that unsupervised transcriptomic clustering can uncover clinically relevant TNBC subtypes, supporting subtype-specific risk stratification and preventive strategies.

Conclusions:

This study presents a reproducible framework for uncovering transcriptional heterogeneity in TNBC using unsupervised machine learning. By enabling early subgroup identification, this approach supports the goals of personalized preventive medicine through data-driven stratification and future biomarker discovery.

sciforum-143831: Personalized Preventive Strategies for Non-Communicable Diseases in Primary Care

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Abstract

Introduction:

Non-communicable diseases (such as hypertension, chronic obstructive pulmonary disease, and cardiovascular disease) represent a major cause of morbidity and mortality worldwide. Preventive medicine is the primary care approach to early detection and treatment. Preventive medicine aims to coordinate patient care and interventions based on patient-specific criteria to improve health outcomes and resource utilization. The purpose of this study is to evaluate the feasibility and short-term outcomes of personalized cancer screening in a primary care clinic.

Methods:

A prospective observational study was conducted in a primary care clinic over a three-month period. Patients aged 18–70 years were assessed using a structured assessment tool that included demographic data, current history, and the Meyer's risk profile (blood pressure, body mass index, fasting blood sugar, and advanced risk profile). The average risk category (low, high, and low) was determined by the patient's individualized consultations, personalized lifestyle recommendations, and personalized lessons.

Results:

Of the 150 patients, 38% were classified as high-risk, 42% as moderate-risk, and 20% as very high-risk. After three months of follow-up, 45% of patients with the disease showed improved blood pressure control, and 30% showed improved adherence to normal activity. The high-risk group also showed significant improvements in dietary and weight management.

Conclusion:

With a small number of people in healthcare, it should be feasible and effective to implement a patient-centered approach to health behaviors. This could play a significant role in reducing the long-term burden of involuntary treatment and patient-centered care in similar healthcare settings.

Session 3. Diagnostics in Personalized Medicine

sciforum-125147: Evaluation of the Choroidal Thickness and Retinal Nerve Fiber Layer Thickness in Patients with Vasovagal Syncope

Batur Gonenc Kanar [1,*], Hasan burak isleyen [2], hatice selen kanar [3], mehmet vefik yazicioglu [4,5] and güzide akcau [3,6]

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Aim:

The aim of the study was to evaluate choroidal and peripapillary retinal nerve fiber layer thickness (pRNFLT) in individuals with vasovagal syncope (VVS).

Method:

A total of 67 consecutive patients with VVS and 61 healthy control subjects were enrolled this study. The choroidal thickness (CT) at fovea, nasal to fovea and, temporal to fovea and pRNLFT measurements assessed by swept source optical-coherence tomography (SS-OCT).

Results:

The mean foveal CT (408.7 ± 92.5 μm vs. 342.1 ± 60.2 μm, p 0.01), mean nasal CT (385.2 ± 88.3 μm vs. 329.2 ± 47.6 μm, p 0.001), and mean temporal CT (379.5 ± 51.6 μm vs. 321.48 ± 43.2 μm, p 0.03) were statistically thicker in patients with VVS compared to healthy controls. There was no statistically significant difference in global and all quadrants of pRNFLT measurements between study groups.

Conlusion:

In conclusion, we showed that patients with VVS exhibited greater CT across all measured regions when compared to healthy controls. Conversely, there were no signifi-cant variations observed in the thickness of the pRNFL. These findings imply that the choroidal blood flow could be influenced by changes in local neurotransmitter levels in individuals suffering from VVS. This interplay underscores the connection between car-diovascular health and CT alterations, suggesting a need for monitoring in individuals with frequent syncopal episodes to prevent complications and maintain ocular health. Further investigation into these dynamics may yield insights beneficial for clinical practice regarding VVS and ocular health.

sciforum-128284: A Novel TAZ2 Domain Variant in CREBBP Underlines the Need for Personalized Approaches in Menke-Hennekam Syndrome

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Introduction:

Menke-Hennekam syndrome (MKHK) is an ultra-rare neurodevelopmental disorder first described in 2016 and linked to variants in exons 30-31 of *CREBBP* and *EP300* genes, which are key regulators of chromatin remodeling. Precision genomic diagnosis is essential given MKHK's clinical heterogeneity. We report a 3-year, 2-month-old male with severe global neurodevelopmental delay, feeding difficulties, failure to thrive, hypodontia, hirsutism, hypertonia, and distinctive facial features, with no relevant family history. His complex presentation underscored the need for individualized molecular investigation to guide prognosis and potential personalized interventions.

Methods:

Clinical exome sequencing was performed using the Illumina NextSeq 2000 platform, while Sanger sequencing was used to validate candidate variants. Extensive bioinformatics analysis and a systematic meta-analysis of reported MKHK cases were conducted.

Results:

We identified a novel *de novo* heterozygous variant, **NM_004380.3:c.5368T>C p.(Cys1790Arg)**, in exon 31 of the *CREBBP* gene, located in the TAZ2 domain. This variant was classified as **pathogenic**, according to the ACMG 2015 and ACGS 2020 guidelines, using the criteria PM2 (supporting), PM1 (moderate), PP3 (strong) and PS2 (strong). The variant was absent from gnomAD database, located in a mutational hotspot, while *in silico* predictive tools (including Revel, AlphaMissense, Varity, SIFT, MutationTaster, among others) strongly supported its pathogenicity. Meta-analysis revealed that cysteine substitutions account for over 18% of MKHK cases, particularly clustering within the ZZ and TAZ2 domains.

Conclusions:

This finding enriches the personalized genomic understanding of MKHK, emphasizes the diagnostic importance of domain-specific variants, and highlights the utility of early precision diagnosis. Recognizing domain-specific pathogenic mechanisms may enable tailored management strategies and support the development of targeted therapies in the future.

sciforum-116276: Artificial Intelligence-Assisted Construction and Clinical Application of Precision Tumor Diagnosis Models

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The increasing incidence of tumors underscores the urgent need for precise diagnostic tools to enhance treatment outcomes and improve patient prognosis. Traditional diagnostic methods, often limited by subjectivity and variability, struggle to meet the demands of modern oncology. This study aims to construct an artificial intelligence (AI)-assisted tumor precision diagnosis model and explore its clinical application value. We collected comprehensive multicenter tumor imaging and clinical data, including histopathological features and patient demographics. Using advanced deep learning algorithms, we developed a diagnostic model capable of distinguishing various tumor types with high accuracy. The model was rigorously validated on an independent dataset, demonstrating superior performance compared to traditional diagnostic methods in terms of diagnostic accuracy, sensitivity, and specificity. For example, in ultrasonographic detection of hepatocellular carcinoma (HCC) and cholangiocarcinoma (CCA), the AI model showed a significant improvement in diagnostic sensitivity. Additionally, the model exhibited good generalizability across different tumor types and clinical settings, indicating its potential for widespread application. The conclusion indicates that the AI-assisted diagnostic model can significantly enhance the precision of tumor diagnosis, providing strong support for clinical decision-making and holding important application prospects. Future research will focus on further optimizing the model architecture and expanding its clinical applications to cover a broader range of tumor types and clinical scenarios. The integration of AI into clinical practice holds promise for improving diagnostic efficiency and patient outcomes in oncology, ultimately contributing to the development of precision medicine.

sciforum-132394: Gut Microbiota and Systemic Inflammation in Post-COVID-19 Patients

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Introduction

Post-COVID-19 syndrome (PCS) is a complex multisystem condition marked by prolonged symptoms after acute SARS-CoV-2 infection. This study investigated clinical, biochemical, and gut microbiota alterations in PCS patients (n = 28) before and after a structured 14-day rehabilitation program, compared to healthy controls (n = 48).

Materials and Methods

Comprehensive evaluations included the following: h**ematological, coagulation, and biochemical profiling** using a UniCel DxH800 hematology analyzer (Beckman Coulter, USA) and Cobas e411 system (Roche, Switzerland); s**erum metabolite analysis** via gas chromatography–mass spectrometry (Trace GC 1310 and ISQ LT; Thermo Electron Corporation, USA); and g**ut microbiota assessment** with real-time PCR (CFX 96, BioRad, USA) using Colonoflor-16 kits (AlphaLab, Russia) to quantify bacterial taxa.

Data were compared against reference ranges and age-matched controls.

Results

Post-rehabilitation, patients reported subjective improvements in respiratory function, mood, and overall well-being. However, persistent abnormalities included the following. Elevated metabolic markers: 4-hydroxybenzoic acid, succinic acid, and fumaric acid. Pro-inflammatory mediators: interleukin-6 levels remained 2.1× higher than controls. Microbiota dysbiosis: increased total bacterial load (4.8 log10 CFU/g), reduced *Lactobacillus* spp., and higher pro-inflammatory taxa. Systemic inflammation: 25% of patients showed elevated ESR (>20 mm/h), and 20% had elevated CRP (>5 mg/L).

Conclusion

While rehabilitation alleviated clinical symptoms, residual metabolic dysregulation and inflammation suggest incomplete recovery. ESR and CRP levels may serve as practical biomarkers for monitoring post-COVID-19 interventions. Acute-phase reactants and microbiota profiles could guide personalized management strategies in PCS.

sciforum-141615: INTEGRATING PATIENT-DERIVED ORGANOIDS AND NATURAL COMPOUNDS FOR DIAGNOSTIC AND THERAPEUTIC INNOVATION IN IBD

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Inflammatory Bowel Disease (IBD), including Crohn's disease and ulcerative colitis, presents a major clinical challenge due to its chronic nature and the limitations of existing therapies. In this context, patient-derived organoids (PDOs) have emerged as powerful preclinical models that preserve the cellular complexity, architecture, and molecular features of the original intestinal tissues, making them ideal tools for both disease modeling and drug screening.

In this study, we established intestinal PDOs from both healthy individuals and IBD patients, demonstrating their ability to recapitulate key features of the native tissue, including the expression of lineage-specific markers and pro-inflammatory mediators. Notably, the IBD-derived organoids retained elevated levels of IL-8 and CLDN1, reflecting their inflammatory state and validating them as a faithful in vitro model of the disease.

Leveraging this platform, we investigated the anti-inflammatory potential of an ozonated extra virgin olive oil derivative, using a luciferase reporter system driven by NF-κB response elements. Upon TNFα-induced inflammation, this natural compound significantly reduced the NF-κB activation in both 2D cell lines and 3D organoid systems, showing comparable efficacy to that of standard anti-inflammatory compounds such as dexamethasone. These findings were further supported by immunofluorescence, which revealed decreased nuclear translocation of p65 following treatment.

Importantly, this compound displayed minimal cytotoxicity at effective concentrations in preliminary viability assays.

Overall, this study underscores the critical value of PDOs in faithfully modeling IBD and evaluating novel therapeutic agents. Our results highlight an olive oil derivative as a promising natural compound with strong anti-inflammatory effects and pave the way for PDO-based personalized medicine approaches in chronic intestinal inflammation. This organoid-driven strategy offers a robust and translational platform for screening natural products and developing safer, more targeted treatments for IBD.

sciforum-124009: Mitochondrial DNA mutations as a candidate risk factor and diagnostic indicator in Marfan Syndrome

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Marfan syndrome (MFS) is an autosomal genetic disease caused by *FBN1* mutation. Patients with the same *FBN1* mutation type exhibit different phenotypes, which indicates that there are extra risk factors. Mitochondrial dysfunction was observed in the aorta of both MFS patients and Marfan murine models. Single-nucleotide variants in mitochondrial DNA (mtDNA) may have harmful consequences on a cell. However, the association of mtDNA mutations with MFS has been unclear. Here, we used targeted mtDNA sequencing to detect whole-blood mtDNA mutations from 48 healthy controls and 77 MFS patients, including 7 mother–offspring pedigrees. Three rare mtDNA mutations, m.279T>C, m.2361G>A and m.3316G>A, were filtered in a family whose predominant phenotype was eye lesions. The MFS patients with these mutations had more severe symptoms than family members without the mutation. m.9738G>A was identified in a family whose dominant phenotype was aortic manifestation. A sporadic case with this rare mutation site had aortic aneurysm. We also described the mutation frequency and mutation rate in MFS. The frequency of all solid variants, nonsynonymous variants, pathogenic or likely pathogenic variants and variants of uncertain significance were more abundant in MFS patients compared to the control group. The mutation rate of the coding region, MT-rRNA and MT-tRNA were higher in the MFS group. These data demonstrate frequent mitochondrial mutation in MFS and suggest that the mtDNA mutation might be a potential modifier and diagnostic indicator of MFS phenotypes.

sciforum-132294: Personalized Oral Care through Digital Innovation

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Introduction:

Personalized dental therapies are becoming increasingly achievable through advancements in digital technologies. The integration of patient-specific data and artificial intelligence (AI) is revolutionizing diagnosis, treatment planning, and the execution of oral rehabilitation, allowing for progress toward precision dentistry.

Methods:

This study outlines a digital workflow for individualized dental treatment, starting with the full digitalization of the patient. Intraoral scans, CBCT imaging, and facial scanning were combined to create a virtual patient model. This integrated digital representation enabled comprehensive diagnostic evaluation and esthetic–functional treatment planning. Furthermore, AI-based systems were incorporated for diagnostic support and prosthetic planning.

Results:

The virtual patient model allowed clinicians to simulate various therapeutic scenarios and optimize treatment strategies based on anatomical, functional, and esthetic criteria. The use of AI tools enhanced diagnostic accuracy, facilitated early detection of pathologies, and supported decision-making in complex rehabilitations. Patient-specific digital planning improved communication with both patients and interdisciplinary teams, leading to more predictable outcomes.

Conclusions:

The integration of digital technologies and AI in dentistry enables highly personalized, precise, and efficient treatments. The creation of a virtual patient through comprehensive digitalization, combined with AI-enhanced planning, represents a significant step forward in individualized oral rehabilitation and sets the foundation for the future of precision dental care.

Session 4. Personalized Therapy in Clinical Medicine

sciforum-134173: Genome-Wide Screening of Pharmacogenomic Biomarkers in Jordanian Patients with Genetic Disorders

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Background:

Pharmacogenomics (PGx) testing aims to identify the most appropriate drug and dose for individual patients based on their genetic profiles. In Jordan, patients with genetic disorders often use multiple medications, some of which have clinical guidelines recommending PGx testing. **Aims:** This study aimed to screen the frequency of clinically relevant PGx biomarkers among a sample of Jordanian patients with genetic disorders.

Methods:

A total of 76 patients (average age 13 ± 14 years; 71% under 13 years old) attending Innovia Biobank in Amman between January 2023 and January 2024 participated. Buccal swabs were collected, and DNA was extracted for whole-genome sequencing using Illumina technology. Variant calling and annotation were performed using DRAGEN, Geneyx, and ANNOVAR tools. A PGx panel based on PharmCAT v2.8.3 and Clinical Pharmacogenetics Implementation Consortium v1.30.0, covering 20 pharmacogenes, was applied.

Results:

In Phase I enzymes, *CYP2D6*10 (25%) and CYP2C19*1/*17 (18.4%)* were most common, while *CYP2C9* and *CYP3A4* variants were less frequent. In Phase II enzymes, *UGT1A1*80+2B appeared in 7.9% and multiple *DPYD* variants found in heterozygous forms 925%). Among toxicity-related markers, *G6PD* and *HLA-B*57:01* were detected in 3.9% and 2.6%, respectively. Transporter gene variants in *SLCO1B1* (15%) and *ABCB1* (21.1%) were relatively frequent. For pharmacodynamic genes, *VKORC1 -1639G>A* (52.6%) and *CYP4F2 V433M* (40.8%) were most prevalent. Accordingly, over half of the patients had genetic variants affecting warfarin response, with additional impacts seen on antidepressants (45%), clopidogrel (35%), and anticancers (30%).

Conclusions:

This study demonstrates the presence of key PGx biomarkers among Jordanian patients with genetic diseases and supports the integration of PGx testing to optimize the use of drugs like antidepressants, clopidogrel, and warfarin.

sciforum-129972: Specialized Interventional Care for Massive Esophagogastric Variceal Bleeding in Decompensated Cirrhosis: A Midlife Case Study

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Objective:

We wished to systematically summarize critical peri-procedural nursing strategies for a middle-aged patient with decompensated liver cirrhosis and esophagogastric variceal bleeding (EGVB) undergoing interventional treatments—specifically percutaneous transhepatic variceal embolization (PTVE) and a transjugular intrahepatic portosystemic shunt (TIPS)—and to develop evidence-based nursing protocols aimed at reducing complications and improving outcomes.

Methods:

Nursing interventions were implemented within a multidisciplinary framework, emphasizing 1. Comprehensive preoperative assessment and preparation; 2. Real-time intraoperative coordination and monitoring; and 3. Rigorous postoperative management to prevent rebleeding, hepatic encephalopathy, and infection. Specialized care included precise puncture site management, continuous portal pressure monitoring, individualized nutritional support, psychological counseling, and targeted health education. The nursing plan was dynamically adjusted based on the patient's clinical status.

Results:

Following PTVE and TIPS, bleeding was effectively controlled; hemoglobin levels increased from 39 g/L to 85 g/L; liver function (total protein, albumin) progressively improved; and no severe complications (puncture site hematoma, hepatic encephalopathy, or stent thrombosis) occurred. Patient satisfaction reached 98%. The patient was discharged stably 24 days postoperatively and remained healthy during the 1-year follow-up.

Conclusion:

Effective perioperative nursing for interventional EGVB management requires 1. Precise monitoring and proactive complication prevention; 2. Integrated multidisciplinary collaboration; and 3. Specialized attention to the portal pressure dynamics, coagulation parameters, and psychological well-being . This protocol establishes a replicable nursing model for similar cases.

Session 5. Pharmacogenetics, Omics, and Informatics

sciforum-133509: Molecular Target Prediction and Transcriptomic Analysis of a Copper Complex as an anticancer candidate agent

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Introduction

PC-Cu (1,10-phenanthroline)(cyclobutane-1,1-dicarboxylate) is a copper-based coordination complex proposed as a novel anticancer candidate. Identifying its potential molecular targets and evaluating their expression in cancer may offer valuable insights into its therapeutic potential within the context of precision oncology.

Methods

We used the *SuperPred* and *TargetNet* platforms to predict potential molecular targets of PC-Cu, applying a cutoff of probability and accuracy ≥ 0.8. Subsequently, we analyzed gene expression profiles using *GEPIA3*, which integrates TCGA and GTEx transcriptomic data. Genes were considered significantly deregulated if they exhibited a log2FC > 1 or –1 and a p-value or q-value 0.05.

Results

A total of 34 high-confidence targets were identified. Of these, 21 showed significant differential expression across various cancer types. Strong overexpression was observed for *BCL2A1* in melanoma (log2FC = 6.37), *CTSD* in diffuse large B-cell lymphoma (log2FC = 5.25), *PRKCG* in cholangiocarcinoma (log2FC = 4.37), *GLRA1* in paraganglioma (log2FC = 4.28), and *CDC25B* in sarcoma (log2FC = 2.31). Conversely, significant downregulation was found for *NR3C1* in bladder cancer (log2FC = –0.86), *CYP19A1* in bladder (–0.87), *NR1H4* in prostate (–0.69), *GLRA1* in lung (–0.73), and *APEX1* in paraganglioma (–0.68). These findings suggest that PC-Cu may modulate key molecular processes including apoptosis regulation, hormonal signaling, and tumor metabolism.

Conclusion

PC-Cu interacts with several genes involved in cancer biology and demonstrates a tissue-specific expression in cancer. These results support its potential as a precision oncology agent and justify further experimental validation.

sciforum-143354: Paving the Path to Precision: Leveraging Pharmacogenomic Screening to Optimize Treatment in a Greek Internal Medicine Clinic

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Introduction

Pharmacogenomic testing (PGt) is increasingly incorporated into clinical practice, with multiple tests available to guide drug administration. The application of PGt in routine clinical care varies considerably across healthcare systems. This study focused on assessing the impact of routine PGt implementation at a high patient volume Internal Medicine clinic in Greece.

Methods

A total of 142 patients (98 females and 44 males; range: 24–91 years) were enrolled in a pilot PGt screening program approved by the "Attikon" University Hospital Research Committee, assessing *CYP2C9, CYP2C19, SLCO1B1,* and *VKORC1* gene variants. Inclusion criteria comprised age ≥18 years and the capacity for autonomous decision-making.

Results

In 139/142 (98%) cases, a pharmacogenetically informative variant was identified. In 34/142 cases, official recommendations were available for the optimization of drug selection and dosing for medications used during their hospitalization. Of these, in 4 cases, recommendations were available for >1 of the prescribed drugs. Overall, recommendations related to three major drug classes: alimentary tract (17 cases), cardiovascular (13 cases), and nervous system (4 cases). These included omeprazole (8), pantoprazole (6), lansoprazole (3), atorvastatin (8), rosuvastatin (2), clopidogrel (2), simvastatin (1), escitalopram (2), and amitriptyline/perphenazine (2). In 23/34 cases, they involved CYP2C19, while in 11/34 cases, they were related to SLCO1B1 variants. The strength of these recommendations according to PharmGKB varied between 'strong' (4), 'moderate' (20), and 'optional' (10).

Conclusion

In summary, genotyping of *CYP2C9, CYP2C19, SLCO1B1,* and *VKORC1* led to actionable findings for 98% of the patient population. In 24% of cases recommendations for optimization of currently administered treatments were available – 12% of which were marked as 'strong'. This study provides insights into the distribution of clinically relevant pharmacogenomic variants within the Greek population and highlights the potential clinical utility of integrating targeted PGt into routine care in Internal Medicine clinics. Knowledge of patient-specific allele frequency data, combined with frequently used medications, may inform evidence-based establishment of new policies.

sciforum-134732: Structural Insights into CYP3A4–P-gp Interactions and Their Role in Personalized Autoimmune Drug Therapy

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Cytochrome P450 3A4 (CYP3A4) and P-glycoprotein (P-gp) are critical regulators of drug metabolism and disposition, with significant implications for inter-individual variability in pharmacokinetics and therapeutic outcomes. CYP3A4 is a major hepatic enzyme responsible for the oxidative biotransformation of a wide range of drugs, while P-gp functions as an efflux transporter, actively exporting drugs out of cells and limiting intracellular drug accumulation. Notably, previous studies have demonstrated a functional interplay between CYP3A4 and P-gp, particularly in tissues where they are co-expressed, such as the intestinal epithelium. Alterations in P-gp and CYP3A4 activity—whether due to genetic variation or to co-administered inhibitors or inducers—can significantly affect drug pharmacokinetics (absorption, distribution, metabolism, and excretion—ADME), posing challenges in dose optimization and drug safety.

In this study, we investigated the structural–functional crosstalk between CYP3A4 and P-gp through protein–protein interaction (PPI) modeling using three different tools: Rosetta protein–protein docking, the Schrödinger pipeline for protein–protein docking, and AlphaFold 3. The resulting complexes were refined and validated via molecular dynamics simulations. We further examined the impact of CYP3A4–P-gp interactions on the metabolism and transport of three Janus kinase (JAK) inhibitors—tofacitinib, baricitinib, and ruxolitinib—which are widely used in autoimmune disease therapy. Molecular docking and simulation analyses revealed how the CYP3A4–P-gp interaction may influence the binding behavior and metabolic handling of these drugs. Preliminary results suggest that physical association between the two proteins may alter substrate accessibility and retention, potentially modulating drug bioavailability and the drug clearance profile. Finally, we constructed an in silico pharmacokinetic compartment model to simulate drug disposition under varying enzymatic and transporter activity.

Our findings highlight the importance of integrating PPI, molecular pharmacology, and pharmacokinetics modeling to advance personalized medicine approaches in immunology.

sciforum-134220: Advancing Cardiovascular Risk Stratification through Combined Clinical, Polygenic, and Monogenic Risk Models

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Introduction:

Cardiovascular disease (CVD) remains a leading cause of mortality globally. Although tools like the Pooled Cohort Equation (PCE) are widely used, genetic testing remains rare and typically targets high-penetrance monogenic variants. Using UK Biobank data (18,686 CVD cases and 12,100 controls), this study evaluates the combined use of clinical risk, polygenic risk scores (PRSs), and monogenic variants to improve CVD prediction.

Methods:

Clinical risk is evaluated using the PCE, polygenic risk through a PRS derived from 1.2 million SNPs, and monogenic risk by pathogenic variants in LDLR, APOB, and PCSK9. Combined models are evaluated using categorical rules, logistic regression, and XGBoost to capture non-linearities. We also enhance prediction by adding 26 clinical variables from five established risk models.

Results:

Cross-validation shows that combined risk models outperform individual predictors in terms of the AUC, particularly among younger individuals. The clinical and PRS models alone yield AUCs of 0.677 and 0.621, while the categorical, logistic regression, and XGBoost models achieve 0.669, 0.699, and 0.701, respectively. The categorical model offers the highest net reclassification index (NRI = 0.058) compared to logistic regression (0.007) and XGBoost (0.010). Incorporating an expanded set of clinical variables further boosts performance, with the AUC reaching 0.796 and the NRI increasing to 0.099.

Conclusions:

Our findings underscore the trade-offs among modeling approaches for cardiovascular risk prediction. Combined models outperformed individual predictors, with logistic regression and XGBoost providing better discrimination, especially when enhanced with additional clinical variables, while categorical methods yielded a higher NRI.

sciforum-134345: Anti-Inflammatory and Antiplatelet Effects of NSAIDs and Clopidogrel on PAF and ADP Pathways: In Vitro Assessment Using Human Platelets

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Cardiovascular disease (CVD) remains the leading cause of death worldwide, with underlying mechanisms often involving platelet activation and chronic inflammation. While antiplatelet agents targeting adenosine diphosphate (ADP)-mediated pathways are well established in CVD management, less is known about their effects on the platelet-activating factor (PAF) pathway—a key mediator of inflammation and thrombosis. This study evaluates the antiplatelet and anti-inflammatory profiles of several commonly used cardiovascular and anti-inflammatory drugs through dual-pathway assessment of ADP- and PAF-induced platelet aggregation. Using human platelet-rich plasma (hPRP) from healthy donors, we assessed platelet responses in the presence of clopidogrel and a range of non-steroidal anti-inflammatory drugs (NSAIDs), including lornoxicam, diclofenac, ketoprofen, naproxen, etoricoxib, niflumic acid, allopurinol, and nimesulide. Clopidogrel confirmed its well-established ADP antagonism and also demonstrated inhibitory activity against the PAF pathway, suggesting a broader and underrecognized pharmacodynamic profile. Notably, several NSAIDs—particularly lornoxicam and diclofenac—exhibited strong inhibitory effects on both platelet activation pathways, whereas naproxen showed comparatively weak activity. These results emphasize the potential for pathway-specific pharmacological action among NSAIDs. Our findings highlight the value of evaluating drug effects beyond their conventional targets. By considering both PAF- and ADP-mediated mechanisms, this dual-pathway analysis contributes to a more nuanced understanding of drug function. Such insights may support the development of more comprehensive and personalized therapeutic strategies for cardiovascular, hypertensive, and inflammation-driven diseases.

sciforum-145421: Artificial Intelligence in Melanoma: Integrating Multi-Omics Data for Precision Oncology and Personalized Gene Therapy

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Introduction:

Cutaneous and uveal melanomas present distinct molecular characteristics and therapeutic responses, complicating their clinical management. Artificial intelligence (AI) is increasingly being applied to improve gene therapy and precision oncology strategies, offering promising solutions to overcome treatment resistance and tumor heterogeneity.

Methods:

This work examines peer-reviewed studies from the past five years, focusing on AI integration in melanoma gene therapy, multi-omics analysis, predictive modeling, and immunotherapy response prediction.

Results:

AI has shown potential to improve treatment planning by predicting therapeutic response and progression-free survival through radiomics-based models. A novel disulfidptosis-linked signature enhances survival prediction and treatment sensitivity, while HLA-DQA1 has emerged as a promising therapeutic target. Integration of single-cell and bulk RNA sequencing has uncovered key metastasis-related genes, and MethylMix analysis has identified methylation-altered genes affecting expression. In uveal melanoma, AI-driven data fusion linked 48 genes to metastasis, while hdWGCNA enabled mapping of gene modules to specific cell types for refined risk prediction. Machine learning models further optimize prognostic assessments and therapeutic response prediction. A composite decision index incorporating programmed cell death modes improves prognostic accuracy. The immune response score predicts overall survival in cutaneous melanoma, and the AI-derived Stem.Sig signature links cancer stemness to immunotherapy resistance. Deep learning has also been used to analyze TERT promoter mutations for metastatic potential, while a six-gene panel predicts anti-PD-1 therapy response. CSIRG-based models improve patient stratification, and logistic regression reaffirms AI's prognostic value.

Conclusions:

Despite the growing success of AI in integrating multi-omics data, enhancing survival prediction, and guiding personalized melanoma therapy, challenges remain. These include limited high-quality, melanoma-specific datasets and algorithmic bias, which may compromise clinical reliability. Overcoming these barriers will require robust data governance, ethical AI model development, and stronger institutional policies.

sciforum-134051: Association of the TYMS 2R/3R Variant (rs45445694) with Chemotherapy Response in Breast Cancer Patients

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Introduction

Thymidylate synthase (TYMS) is a key enzyme in DNA synthesis and a primary target of fluoropyrimidine-based chemotherapy. The rs45445694 variant (2R/3R), located in the 5′UTR region of *TYMS*, may affect gene expression and influence treatment response. This study aimed to evaluate the frequency and clinical relevance of rs45445694 in Mexican breast cancer (BC) patients and its association with chemotherapy response.

Materials and Methods

A total of 785 BC patients were genotyped for the 2R/3R polymorphism and categorized according to chemotherapy response: complete response (n=136), no response (NR, n=311), no response due to recurrence (NRR, n=249), and partial response (PR, n=90). Genotypic frequencies were determined, and associations were evaluated using logistic regression to calculate odds ratios (ORs) and 95% confidence intervals (CIs).

Results

The 2R/3R genotype was the most frequent across all groups, especially among responders (68%), compared to 57.7% in NR, 62% in NRR, and 58% in PR. The 3R/3R genotype was more prevalent in NR (29.5%) and PR (41%) than in responders (13%). In contrast, the 2R/2R genotype was relatively uncommon, showing similar frequencies in responders (16%) and NR (12.5%), with slightly lower proportions in NRR (11%) and PR (10%). The 3R/3R genotype was significantly associated with increased risk of NR (OR=2.94; 95% CI: 1.67–5.16; p=0.0002), NRR (OR=2.57; p=0.0014), and PR (OR=4.88; p0.00001). Conversely, the 2R/3R genotype was protective in NR (OR=0.64; p=0.045) and PR (OR=0.45; p=0.005).

Conclusions

The rs45445694 variant of the *TYMS* gene may influence chemotherapy response in BC. The 3R/3R genotype was associated with poorer outcomes, while 2R/3R appeared more frequently in responders, suggesting a possible protective effect.

sciforum-140031: Bioinformatics screening of phenylpropanoids from *Pyrostegia venusta* for treatment of ER+ Breast Cancer

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Introduction:

Breast cancer is the most prevalent malignancy among women worldwide, and the adverse effects of conventional chemotherapy highlight the need for more selective and less toxic therapeutic alternatives. In this context, bioinformatics approaches have emerged as promising tools for preclinical screening of new chemotherapeutics based on natural compounds.

Methodology:

The cytotoxic potential and molecular mechanisms of action of the phenylpropanoids verbascoside and isoverbascoside, isolated from *Pyrostegia venusta*, were evaluated using in silico methods. Cytotoxicity predictions (pIC_{50}) were performed with CLC-Pred 2.0 for the ER-positive tumor cell lines MCF7 and T47D and the non-tumorigenic MCF-10A cell line. Estrogen receptor interactions were assessed using ADMETLab 2.0, and nuclear receptor binding was further evaluated by molecular docking using CB-DOCK2, with tamoxifen used as a reference. Differentially expressed microRNAs were analyzed using CancerMIRNome, including through the creation of ROC curves and Kaplan–Meier survival analyses. Protein–protein interaction networks were constructed to investigate potential molecular mechanisms.

Results:

Verbascoside and isoverbascoside exhibited higher safety profiles in MCF-10A cells compared to tamoxifen. Tamoxifen showed greater cytotoxicity ($pIC_{50} > 5.3$), whereas the natural compounds had lower pIC_{50} values. Verbascoside stood out with higher predicted growth inhibition ($pIG_{50} = 6.0363$), indicating potential antiproliferative effects. Only tamoxifen and isoverbascoside interacted with the nuclear estrogen receptor. The microRNA hsa-miR-21-5p demonstrated high accuracy in tissue discrimination (AUC = 0.97) but no significant prognostic value (HR = 0.99; p = 0.97). Network analysis suggested involvement of PTEN as a molecular target, with isoverbascoside showing a greater binding affinity to the receptor (-8.4 $kcal.mol^{-1}$), comparable to that of tamoxifen (-7.5 $kcal.mol^{-1}$).

Conclusion:

The findings indicate that these phenylpropanoids, particularly isoverbascoside, hold promising potential for use as natural antitumor agents for treating breast cancer, exhibiting favorable cellular selectivity and relevant interactions with hormonal receptors and molecular biomarkers.

sciforum-140061: High-risk genetic profiles for Pharmacoresistant Schizophrenia: Insights from Belarusian Patients

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Despite antipsychotic drugs being a key treatment for schizophrenia, 20–30% of patients show an inadequate response. This may be due to genetic factors affecting drugs' metabolism, side effects, and efficacy. This study explored links between genetic polymorphisms and pharmacoresistant (PR) schizophrenia in Belarusian patients.

A total of 161 participants were included: 104 with PR schizophrenia (no response after 6–8 weeks of treatment) and 57 responders. All were diagnosed according to the ICD-10 (F20), aged 18–60, gave informed consent, and had no acute physical illnesses. The treatments included clozapine (42.1%) or combined atypical and typical antipsychotics (39.5%). We genotyped 19 polymorphic loci across 15 genes (e.g., CYP2D6, COMT, HTR1A, MDR1) using a Real-Time PCR or Sanger sequencing. The data were analyzed in SPSS 20.0 using ORs and 95% CIs to evaluate the genotype–phenotype associations.

Significant associations with PR were found for the following:

The A-allele and AG genotype of CYP2D6*4 (rs3892097) (OR=2.159 and CI=1.018-4.578 and OR=2.975 and CI=1.269-6.977, respectively);The G-allele of COMT (rs4680, V158) (OR=2.786; CI=1.414-5.489);The CC genotype of HTR1A (rs6295) (OR=2.703; CI=1.151-6.348).

Protective effects were noted for the following:

The GG genotype of CYP2D6 (rs3892097) (OR=0.463; CI=0.218-0.928);The G allele of HTR1A (rs6295) (OR=0.367; CI=0.156-0.864);The AA genotype (Met/Met) of COMT (rs4680) (OR=0.359; CI=0.182-0.707).

Combined genotypes showed an even greater PR risk, including the following:

A-/A- (CYP2D6/CYP1A2) (OR = 2.926; 95% CI = 1.206–7.102);A-/A-/T- (CYP2D6/CYP1A2/MDR1) (OR = 4.833; 95% CI = 1.753–13.328)G-/LL (COMT/SLC6A4) (OR = 6.923; 95% CI = 1.900–25.227);CC/T- (HTR1A/MDR1) (OR = 2.564; 95% CI = 1.120–5.873).

In conclusion, variants in CYP2D6, HTR1A, and COMT, especially when combined with variants in CYP1A2, MDR1, and SLC6A4, significantly contribute to the PR schizophrenia risk in Belarus. These findings support the use of pharmacogenetic testing for personalized antipsychotic treatment, already implemented in the Republican Research and Practice Center for Mental Health (Minsk).

sciforum-140328: Machine Learning-Driven Identification of Multi-Target Repurposable Drugs For Colorectal Cancer Using Transcriptomics and Network Pharmacology

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Introduction:

Colorectal cancer (CRC) ranks third as a leading cause of cancer-related death globally. The urgent development of accurate diagnostic and therapeutic strategies is extensively needed. The drug discovery process in oncology remains a critical bottleneck in modern medicine due to its high cost, long timelines, and frequent clinical trial failures. In contrast, **Drug Repurposing**, a subset of Drug Discovery, identifies new therapeutic uses for existing drugs and has emerged as a powerful strategy to accelerate treatment development. This study aims to establish a computational framework integrating **transcriptomic profiling, network pharmacology,** and **machine learning** to identify prognostic biomarkers and prioritize repurposable drugs for **colorectal cancer (CRC).**

Methods:

Publicly available high-throughput RNA-seq data were analyzed to identify differentially expressed genes. A protein–protein interaction (PPI) network was constructed to isolate **hub genes,** of which **three genes** were significantly overexpressed in tumors and strongly correlated with poor patient survival. This process proved them to be key prognostic biomarkers. A **drug–gene interaction network** was built using curated databases. An **unsupervised machine learning pipeline** combining principal component analysis (PCA) and K-means clustering was developed to integrate gene expression data, survival scores, and interaction profiles for drug ranking.

Result:

Among 34 candidate drugs, **Palbociclib, Vorinostat,** and **Methotrexate** were identified as **high-potential multi-target drugs** linked to all three identified potential biomarkers. These findings highlight multi-target repurposing opportunities in CRC.

Conclusion:

This interdisciplinary approach demonstrates how omics data with AI-driven analytics can accelerate the discovery of personalized, multi-target therapies. The proposed framework offers a scalable, data-driven approach to rapidly identify drug candidates in colorectal cancer and other complex diseases.

sciforum-144137: Precision Proteomics for Personalized Medicine: A Unified MS1/MS2 Linear Mixed-Effects Model for Robust Biomarker Identification

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Pancreatic cancer is among the most lethal malignancies, largely due to its asymptomatic progression and the absence of effective early detection methods. Urinary extracellular vesicles (EVs) represent a promising, non-invasive source of disease-specific biomarkers. Data-Independent Acquisition (DIA) mass spectrometry enables comprehensive proteomic profiling; however, independent analyses of precursor (MS1) and fragment (MS2) ion spectra often yield inconsistent results due to differing sources of signal interference and variability. Urine samples from five pancreatic cancer patients and five healthy controls were processed to enrich EVs via ultracentrifugation. DIA-MS was performed using an Orbitrap Eclipse MS with raw data analyzed using Spectronaut 19.1. MS1 and MS2 intensities were normalized to exosome protein markers. We developed a unified linear mixed-effects model (LMM) to concurrently analyze normalized MS1 and MS2 intensities, treating the MS1 and MS2 signals as technical replicates from the same biological sample. This model estimates protein abundance differences between groups while accounting for intra-group variability. Its performance was compared with Spectronaut quantitation by benchmarking against standard MS1 or MS2 methods using both simulated data and pancreatic cancer clinical data. The unified LMM consistently outperformed single-stream analyses, identifying a balanced and accurate set of differentially abundant proteins while avoiding overestimation. Simulations confirmed the model's robustness, achieving higher true positive rates and lower false positive rates across varying sample sizes. The model also provided conservative estimates when MS1 and MS2 data diverged. While the LMM tends to be more powerful, Spectronaut's methods are comparatively more conservative. In clinical data, the LMM further improved pathway enrichment outcomes, offering deeper biological insights. This LMM approach enhances the reliability of differential protein analysis in DIA-based proteomics by integrating MS1 and MS2 data. Applied to urinary EVs, it enables robust biomarker discovery for pancreatic cancer detection. This method holds significant promise for advancing personalized medicine through precise, non-invasive diagnostics.

Session 6. Precision Oncology

sciforum-134061: Association of the rs2234909 variant of the FGFR3 gene with colorectal cancer in a Mexican population.

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Background:

Colorectal cancer (CRC) ranks as the third most common malignancy worldwide and the leading cause of cancer-related mortality in 2024. While previous studies have explored the role of intracellular genes in CRC development, there is limited evidence regarding the involvement of fibroblast growth factor receptors (FGFR), particularly FGFR3. This gene, located on chromosome 4p16.3, consists of 19 exons and plays a key role in cell cycle regulation. Three high-variability regions, or hotspots, have been identified within the gene, with exon 7 being the most significant—accounting for approximately 88% of reported mutations. Exon 7 encodes the IgIII domain, which is essential for the formation of receptor isoforms via alternative splicing, affecting ligand-binding specificity. The synonymous variant rs2234909, located in exon 7 (codon 294), involves a T>C transition (p.Asn294Asn). Although it does not change the amino acid sequence, it may promote disulfide bond formation between adjacent monomer receptors or induce structural changes in the tyrosine kinase domain, leading to ligand-independent dimerization.

Objective:

To analyze the association between the FGFR3 rs2234909 variant and CRC in the Mexican population.

Materials and Methods:

A cross-sectional analytical study was conducted with 472 DNA samples from CRC patients and 395 from healthy donors. The rs2234909 variant was genotyped using real-time PCR (qPCR) with TaqMan® probes on a Bio-Rad CFX96 system. Genotypic and allelic frequencies were calculated by direct counting. Associations between genotypes and CRC risk were assessed using bivariate analysis (odds ratio, 95% CI), with statistical significance set at p 0.05. Data were analyzed using SPSS v24.

Results:

The GG genotype and recessive model of rs2234909 were significantly associated with an increased risk of CRC (OR = 5.34; 95% CI: 3.36–8.47; p 0.05).

Conclusion:

rs2234909 may serve as a potential genetic susceptibility marker for CRC.

sciforum-133634: Liquid Biopsy Implementation for NSCLC: What Can New Brunswick Learn from Ontario's Experience

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Background:

In the evolving landscape of precision oncology for non-small cell lung cancer (NSCLC), timely and comprehensive molecular profiling is essential for identifying biomarker-matched therapies that improve outcomes in advanced stages. However, tissue biopsy, the current gold standard, presents challenges including invasiveness, insufficient tissue (in 5–16% of cases), inadequate DNA, and long turnaround times (for example, median 36.5 days in some Ontario centres), all of which may delay or compromise treatment. Liquid biopsy, a minimally invasive technique analyzing circulating tumour DNA (ctDNA) and RNA (cfRNA), offers a promising alternative.

Objective:

This review evaluates Ontario's experience with liquid biopsy implementation in NSCLC as a case study to inform adoption strategies in New Brunswick, where such programs are emerging.

Methods:

A targeted policy and literature synthesis was conducted, drawing on publicly available health technology assessments (HTAs), multidisciplinary working group reports, peer-reviewed publications, and international guidelines (ASCO, ESMO, IASLC, and NCCN). Key focus areas included eligibility criteria, diagnostic performance, turnaround time, cost-effectiveness, and integration into public healthcare.

Results:

Ontario proposes liquid biopsy as a complementary, not replacement, tool for tissue biopsy. Funding eligibility includes (1) insufficient or failed tissue biopsy; (2) clinically suspected advanced NSCLC where biopsy is not feasible; and (3) high-risk patients likely to deteriorate before tissue results are available. Liquid biopsy offers faster results (7–10 days) compared to tissue (up to 36.5 days), facilitating earlier treatment. Although sensitivity ranges from 63% to 81% (lower for fusions and CNVs), economic modeling suggests that it may reduce downstream costs and improve patient outcomes when used appropriately.

Conclusion:

Ontario's model provides a structured framework for New Brunswick's implementation. Prioritizing high-need patients, investing in diagnostic infrastructure, and ensuring cost-efficiency can enable broader access to precision therapies while minimizing diagnostic delays.

sciforum-116970: Pathway Analysis of Chemoresistance in Glioblastoma Multiforme

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Glioblastoma multiforme (GBM) is the most aggressive and common brain tumor, with an annual incidence of 3.19 per 100,000 people. Chemoresistance is a major issue in the treatment of GBM with therapeutics like temozolomide (TMZ), especially because of the challenges in making chemotherapeutics that can overcome the blood–brain barrier. Cancer stem cells, mechanisms of protein folding, drug pumps, and the tumor microenvironment have been noted as contributing to chemoresistance in GBM, but its precise molecular mechanisms remain unknown. Differential gene expression data from GSE140441 and GSE98126 was extracted from GEO2R, and we investigated the genes differentially expressed at the p0.05 level between a control group of non-resistant subtypes and an experimental group of GBM cells cultured in TMZ to determine which could confer chemoresistance. The differentially expressed genes were identified and compiled using the dplyr package in R. These genes were submitted for DAVID functional annotation clustering. Clusters were analyzed for their significance at p.05. From the differential expression studies, 1,980 genes were identified and used to conduct DAVID functional annotation clustering. From these genes, 101 functional annotation clusters were identified. Notably, many clusters responsible for mRNA regulation, as well as the clusters regulating conjugation of ubiquitin-like protein (p=1.2E-17) and cadherin binding (p=1.9E-5) clusters, were significantly differentially expressed in chemoresistant GBM. Targeting pathways related to conjugation of ubiquitin-like protein and cadherin binding, as well as other mechanisms of protein breakdown, might further our understanding of the mechanism of chemoresistance in GBM while also improving the clinical utility of treatments. Certain FDA-approved drugs that target both the ubiquitin-like protein degradation pathway and DNA synthesis, including mitoxantrone, 6-mercaptopurine, and 6-thioguanine, should be explored for possible use as drugs to sensitize chemoresistant GBM. Inhibition of the cadherin binding pathway may also be a novel method of overcoming adaptive mechanisms in GBM.

sciforum-141961: A novel molecular mechanism regulates gastric cancer cell homeostasis

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Background

Gastric cancer (GC) is one of the most prevalent malignant tumors worldwide, with incidence and mortality rates expected to rise in the coming years. Standard treatments typically involve surgical resection combined with chemotherapy using platinum-based agents, 5-fluorouracil (5-FU), or capecitabine. The discovery of novel biomarkers associated with GC progression is critical to improving therapeutic strategies and enhancing patient outcomes. In this study, we investigated the role of **Hormonally Upregulated Neu tumor-associated Kinase (HUNK)** in driving the progression of gastric cancer.

Methods

To evaluate the functional effects of HUNK overexpression, we conducted a cell viability assay in gastric cancer cell lines stably transfected with HUNK. To confirm the physical interaction between HUNK and p38 MAP kinase, we performed a co-immunoprecipitation assay. Additionally, to investigate the role of HUNK in apoptosis, we employed siRNA-mediated HUNK knockdown and assessed apoptotic activation by measuring the levels of cleaved PARP and cleaved caspase-3 via Western blot. Apoptotic cell populations were further quantified using flow cytometry after staining with Annexin V-FITC and propidium iodide (PI). NGS analysis was performed to identify HUNK-induced genes.

Results

We demonstrate that HUNK promotes gastric cancer cell proliferation through direct interaction and phosphorylation of p38 MAP kinase. Functional depletion of HUNK significantly reduced cell viability in both gastric cancer cell lines and patient-derived organoids, underscoring its role in tumor cell survival. Moreover, HUNK positively regulates the expression of MUC16/CA-125, a glycoprotein linked to tumor progression and poor prognosis, suggesting its potential as both a biomarker and therapeutic target in gastric cancer.

Conclusions

Our results identify a novel HUNK-mediated molecular mechanism in gastric cancer, supporting its potential as a promising target for the development of targeted therapies.

sciforum-125167: Microbial metabolites and biomarkers in differential diagnosis of infection in children with cancer

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Introduction

Metabolomic studies can be used to stratify patients with systemic inflammatory response syndrome and sepsis. Changes in the concentrations of aromatic microbial metabolites and inflammation biomarkers are considered to identify sepsis as a manifestation of the most severe metabolic dysfunction.

Aim

To evaluate the diagnostic value of inflammation biomarkers and aromatic microbial metabolites in children during the treatment of malignant oncological diseases.

Materials and methods

The study included patients with various malignant oncological diseases (leukemia, lymphoma, nephroblastoma, ependymoma, etc.) without complications (n = 40); patients with inflammatory and infectious complications (n = 31); and, as a control group, healthy children who participated in a routine medical examination (n = 18). In all groups, biomarkers associated with inflammation were determined: C-reactive protein (CRP), procalcitonin (PCT), and presepsin (PSP), as well as aromatic metabolites associated with sepsis: phenyllactic (PhLA), hydroxyphenyllactic (*p*-HPhLC), and hydroxyphenylacetic (*p*-HPhA) acids.

Results

Children with malignant oncological diseases had profound metabolic dysfunction compared to healthy children, regardless of the presence of systemic inflammatory response syndrome (SIRS) or sepsis. The sum of sepsis-associated aromatic microbial metabolite concentrations in children was 2.2 (1.5; 2.6) μmol/L in the control group versus 1.5 (1.1; 1.8) μmol/L in cancer patients (p-value=0.001). High diagnostic ability of procalcitonin and presepsin for detecting sepsis was observed: AUROC=0.875, with a cutoff value (Youden index) of 0.913 ng/ml, and AUROC=0.774, with a cutoff value (Youden index) of 526 pg/ml, respectively.

Conclusion

Decreased concentrations of sepsis-associated aromatic microbial metabolites in cancer patients indicate microbiota dysfunction, which may indicate the need for its timely targeted correction. This study also reveals the high diagnostic ability of procalcitonin and presepsin for detecting sepsis.

sciforum-139448: Polydopamine-Modified Engineered E. coli for Synergistic Cancer Therapy via Glucose Oxidase-Mediated Starvation and Prodrug Delivery

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Abstract: this study aims to gather dopamine (PDA) modified engineering bacteria load glucose oxidase (bigger) and former drug taxol, and realize the tumor targeting hungry treatment and the synergy of taxol drug delivery. By taking advantage of the specific tumor-targeting characteristics of Escherichia coli as a carrier, the recognition and endocytosis ability of tumor cells are enhanced through the camouflage properties of its cell membrane. GOx catalyzes the oxidation of glucose within tumor cells to produce hydrogen peroxide (HO_2), thereby inducing a "starvation" state in tumor cells and inhibiting their proliferation and metabolism. Meanwhile, paclitaxel prodrugs are reduced to active paclitaxel in the tumor microenvironment (TME), exerting anti-tumor effects. This system achieves the synergistic treatment of tumors through a dual mechanism.

The results indicate that PDA-modified E. coli co-loaded with GOx and a paclitaxel prodrug exhibits considerable inhibitory effects against various tumor cell lines in vitro, as well as effective tumor suppression in vivo. Compared with the administration of either GOx or paclitaxel alone, this integrated therapeutic system achieves enhanced treatment outcomes in terms of both tumor growth inhibition and survival extension. Moreover, the system demonstrates favorable site-specific drug release behavior, which effectively mitigates tumor hypoxia and consequently improves overall therapeutic performance.

sciforum-134110: Precision in Practice: A Systematic Review and Meta-Analysis of Intraoperative Neurophysiological Monitoring for Optimizing Outcomes in Extramedullary Spinal Cord Tumor Resection

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Background/Objectives:

Intraoperative neurophysiological monitoring (IONM) is used to detect, reduce, and prevent neurological injury during extramedullary spinal cord tumor (EMSCT) resection. This meta-analysis aims to systematically assess the performance of IONM modalities, somatosensory evoked potentials (SSEPs), transcranial motor evoked potentials (TcMEPs), and multimodal approaches in EMSCT surgery, with a particular focus on determining whether a single monitoring modality is sufficient to predict postoperative neurological deficits.

Methods:

Following PRISMA-DTA guidelines, we searched MEDLINE, PubMed, and Ovid (inception to April 2025) for studies on IONM in EMSCT surgeries (PROSPERO: CRD420251047345). Pooled sensitivity, specificity, and reversibility metrics were calculated using bivariate models, with quality assessed via QUADAS-2. Z-test and Bayesian meta-analysis were used for comparisons.

Results:

Across 20 studies (2,672 patients), multimodal IONM showed a log DOR of 4.310 (95% CI: 3.581–5.039) and an AUC of 94.2%, TcMEP monitoring showed a log DOR of 4.457 (95% CI: 3.775–5.139) and an AUC of 92%, while SSEP monitoring showed a log DOR of 3.463 (95% CI: 2.702–4.224) and an AUC of 82%. All modalities demonstrated high specificity (>95%), indicating low false-positive rates. Bayesian analysis revealed >90% probability that TcMEP-based approaches were superior to SSEPs. Reversible TcMEP changes were associated with an 11% (95% CI: 4–24%) postoperative deficit rate, compared to 35% (95% CI: 12–67%) for SSEPs.

Conclusions:

These findings caution against relying solely on SSEPs and support the use of multimodal IONM strategies, which enhance the early detection of impending neurological injury, enable timely surgical interventions, and help prevent permanent neurological damage in EMSCT resections. Although TcMEP and multimodal monitoring showed similar diagnostic accuracy, we continue to recommend multimodal approaches as the current standard of care, pending prospective studies to determine if TcMEP alone can reliably replace multimodal monitoring.

sciforum-133637: The Development of the Regulatory Net of microRNA–mRNA Interactions in General Biological Processes and Signaling Pathways in Breast Cancer

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The biological heterogeneity of breast cancer complicates the choice of an effective treatment. The participation of microRNAs in the regulation of target mRNAs in biological processes and signaling cascades makes them suitable for use as diagnostic and prognostic markers or targets for therapy.

The aim of our work was to analyze the expression of microRNAs in paired samples of tumor and adjacent normal breast tissue and to assess their potential cooperative participation in biological processes and signaling pathways.

The microRNA expression was analyzed using Taq Man MicroRNA Assay Kits. The differences between the groups were assessed using the nonparametric Mann–Whitney U test. Spearman's correlation coefficient was calculated to identify co-expression. Functional annotation and enrichment analysis concerning Gene Ontology terms and KEGG signaling pathways were performed in R (clusterProfiler, org.Hs.eg.db, enrichplot) (adj. p-value0.05 according to Benjamini–Hochberg procedure).

Positive expression correlations were found for seven pairs of microRNAs: miR-127-5p/miR-125b-5p (Rs=0.47), miR-148a-3p/miR-125b-5p (Rs=0.44), miR-148a-3p/miR-132-3p (Rs=0.46), miR-193a-5p/miR-127-5p (Rs=0.51), miR-24-2-5p/miR-127-5p (Rs=0.43), miR-34b-3p/miR-193a-5p (Rs=0.54), and miR-34b-3p/miR-24-2-5p (Rs=0.58). Enrichment analysis revealed overlapping processes for four microRNA pairs: miR-127-5p/miR-125b-5p (28), miR-148a-3p/miR-125b-5p (355), miR-148a-3p/miR-132-3p (195), and miR-34b-3p/miR-193a-5p (three common processes). We constructed a regulatory net of microRNA–mRNA interactions. MiR-125b-5p was the central node in the net; it bound to multiple oncogenic and suppressor genes, including APC, BCL2, STAT3, and LDLR. Coincident targets such as APC and CDKN1A bound by multiple microRNAs suggest coordinated post-transcriptional regulation.

The constructed net demonstrates potentially significant regulatory axes linking microRNAs and their targets, highlighting their possible common roles in breast cancer pathogenesis.

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