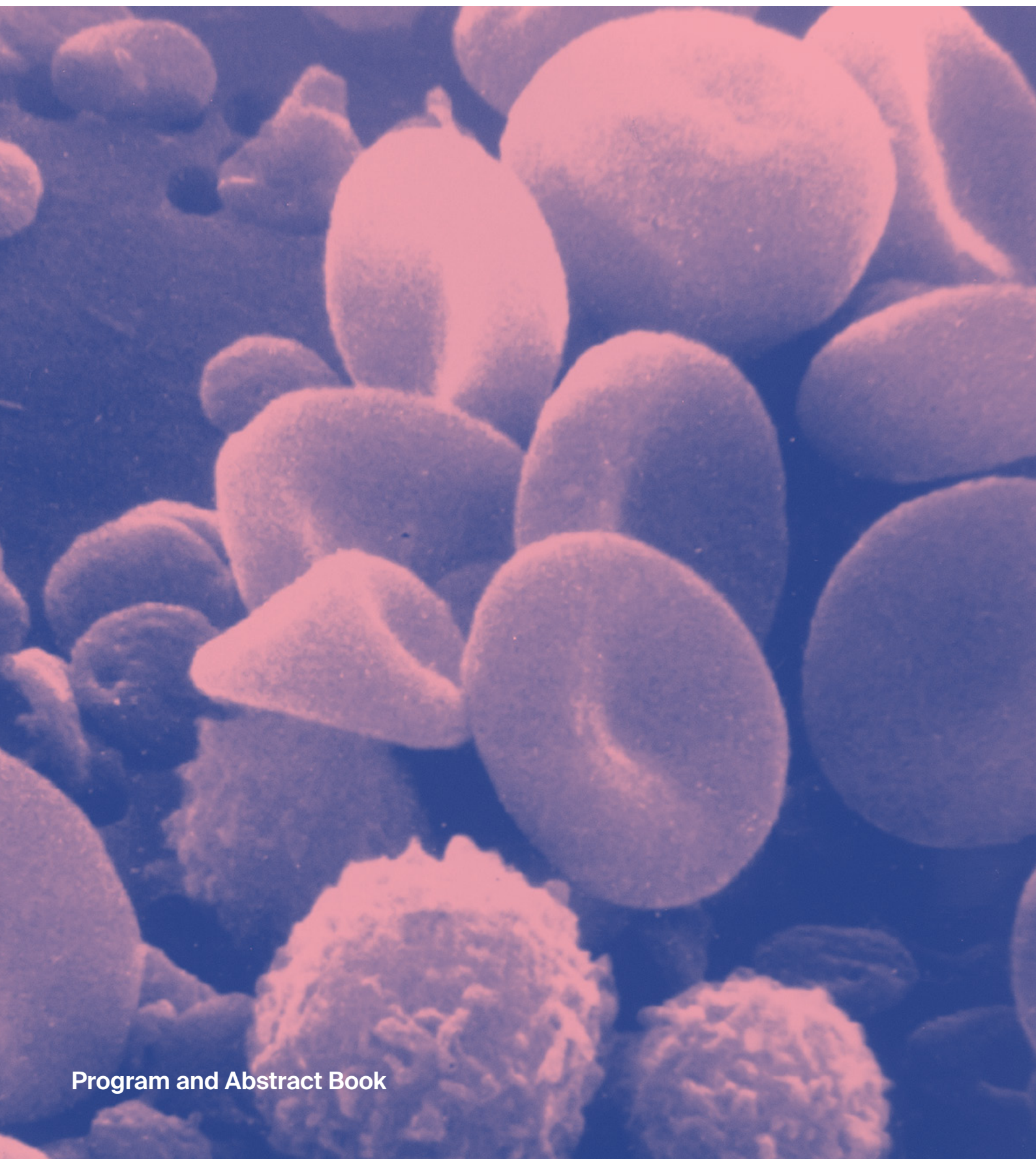




The 5th International Electronic Conference on Cancers

10-12 June 2026 | Online



Program and Abstract Book

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The 5th International Electronic Conference on Cancers

10–12 June 2026 | Online



Organizing Committee

Conference Chair

Prof. Dr. Masaharu Seno

Session Chairs

Dr. Farrukh Aqil
Prof. Nicola Amodio
Prof. Dr. Ajay Pratap Singh
Prof. Dr. Andrew A. Gumbs
Prof. Dr. Angeliki Magklara

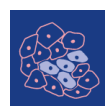
Prof. Dr. Ewa Koscielniak
Prof. Dr. Guo-Min Li
Prof. Dr. Henry H. Heng
Prof. Dr. Sebastiano Mercadante
Prof. Dr. Masaharu Seno

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Conference Secretariat

Email: iecc2026@mdpi.com

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Welcome from the Chair

Dear colleagues,

On behalf of MDPI and *Cancers*, we would like to invite you to participate in the 5th International Electronic Conference on Cancers (IECC 2026) to be held from 10 to 12 June, 2026.

This conference aims to bring together researchers and experts from the wide range of basic to clinical fields of cancer research, academia, and biotech companies to discuss state-of-the-art findings and developments in cancer research, as well as the application of therapeutic strategies to explore further stages.

In this conference, the following sessions will be held:

Session 1. Cancer Stem Cells.

Session 2. Tumor Heterogeneity.

Session 3. Drug Resistance and Anti-cancer Drug Development and Screening.

Session 4. Cancer Survivorship and Quality of Life.

Session 5. Causes, Diagnosis and Treatment of Cancer.

Session 6. Patterns and Treatment Considerations of Childhood Cancer.

Session 7. Novel Methods and Technologies for Research and Treatment.

It is a must-attend conference for anyone interested in these subthemes.

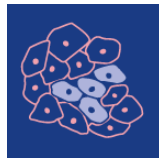
We invite you to participate in this dynamic and interdisciplinary online forum by submitting abstracts for short talks related to the subthemes. IECC 2026 will provide you with a stimulating environment where you can present your research, engage in insightful discussions, and connect with fellow experts.

We look forward to welcoming you to IECC 2026.



Prof. Dr. Masaharu Seno
Conference Chair

Laboratory of Cancer Stem Cell
Engineering, Faculty of
Interdisciplinary Science and
Engineering in Health Systems,
Okayama University, Okayama,
Japan



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Cancers (ISSN 2072-6694) is an international, peer-reviewed open access journal on oncology. It publishes article types including 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. The full experimental details must be provided so that the results can be reproduced.

There is, in addition, a unique feature of this journal: we accept studies showing meaningful but negative results. While there are many journals that focus on cancer studies, none of them actively accepts negative results. As a result, most negative data end up not being in the public domain even if the data were meaningfully negative and the study well designed. By accepting those negative results, our journal encourages scientists to share those data so that they would not need to repeat the experiments that somebody else has already done.

Impact Factor: 4.4 (2024); 5-Year Impact Factor: 4.8 (2024)

Session Chairs



Dr. Farrukh Aqil

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2. Department of Surgery, Otto von Guericke University Magdeburg, Magdeburg, Germany



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1. Laboratory of Clinical Chemistry, Faculty of Medicine, School of Health Sciences, University of Ioannina, Ioannina, Greece;
2. Biomedical Research Institute, Foundation for Research and Technology-Hellas, Ioannina, Greece



Prof. Dr. Ewa Koscielniak

Medical Faculty, University of
Tübingen, Tübingen, Germany



Prof. Dr. Guo-Min Li

Institute for Cancer Research,
Chinese Institutes for Medical
Research, Beijing, China



Prof. Dr. Henry H. Heng

Center for Molecular Medicine
and Genetics, Wayne State
University School of Medicine,
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**Prof. Dr. Sebastiano
Mercadante**

Main Regional Center for Pain
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Prof. Dr. Masaharu Seno

Laboratory of Cancer Stem Cell
Engineering, Faculty of
Interdisciplinary Science and
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Okayama University, Okayama,
Japan

Keynote Speakers



Prof. Dr. Jinsong Liu

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Texas MD Anderson Cancer
Center, Houston, TX, USA



Prof. Dr. Henry H. Heng

Center for Molecular Medicine
and Genetics, Wayne State
University School of Medicine,
Detroit, MI, USA

Invited Speakers



Dr. Enrica Antonia Martino

Unit of Hematology, AO of
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Prof. Dr. Ahmed Elsayem

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Medical University of Lublin,
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Prof. Dr. Kwok-Leung Cheung

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Prof. Dr. Takeaki Ishizawa

Department of Hepatobiliary-
Pancreatic Surgery,
Graduate School of Medicine,
Osaka Metropolitan University,
Osaka, Japan

Program at a Glance

10th June	11th June	12th June
Morning - 9:00 AM CEST	Morning - 9:00 AM CEST	Morning - 9:00 AM CEST
Session 4. Cancer Survivorship and Quality of Life Session 1. Cancer Stem Cells	Session 7. Novel Methods and Technologies for Research and Treatment	Flash Poster Session Session 5. Causes, Diagnosis and Treatment of Cancer
Afternoon - 14:00 PM CEST	Afternoon - 14:00 PM CEST	Afternoon - 14:00 PM CEST
Session 3. Drug Resistance and Anti-cancer Drug Development and Screening	Session 7. Novel Methods and Technologies for Research and Treatment Session 2. Tumor Heterogeneity	Session 5. Causes, Diagnosis and Treatment of Cancer

IECC 2026 Program

10th June 2026 (Wednesday)

Session 4. Cancer Survivorship and Quality of Life

Time: 09:00 (CEST, Basel) | 03:00 (EDT, New York) | 15:00 (CST Asia, Beijing)

CET Time	Speaker	Title
9:00–9:05	<i>Prof. Dr. Masaharu Seno</i> <i>Opening Remark from Conference Chair</i>	
9:05–9:10	<i>Prof. Dr. Sebastiano Mercadante</i> <i>Welcome from the Session Chair</i>	
9:10–9:30	Prof. Dr. Kwok-Leung Cheung Invited Speaker	Quality of life and psychosocial wellbeing in older women with primary breast cancer
9:30–9:50	Prof. Dr. Ahmed Elsayem Invited Speaker	When less is Actually more, Goals of Care for Patients with Advanced Cancer
9:50–10:05	Laia Barrachina-Bonet Selected Speaker	The role of the European Cancer Information System on pancreatic cancer surveillance
10:05–10:20	Ruichen Han Selected Speaker	Decision-making patterns of adjuvant endocrine therapy among women with breast cancer: A qualitative study
10:20–10:35	Elsa Vitale Selected Speaker	Influence of Health Literacy on Quality of Life in oncology patients
10:35–10:50	Qiang Hu Selected Speaker	The Impact of Mobile Health on the Quality of Life of Cancer Patients: An interventional study
10:50–11:05	Alexandru Roșu Selected Speaker	Clinical outcomes of Sacituzumab Govitecan in metastatic breast cancer: evidence of survival and quality of life from a systematic review and meta analysis

Session 1. Cancer Stem Cells

Time: 11:05 (CEST, Basel) | 5:05 (EDT, New York) | 17:05 (CST Asia, Beijing)

CET Time	Speaker	Title
11:05–11:10	<i>Prof. Dr. Masaharu Seno</i> <i>Prof. Dr. Angeliki Magklara</i> <i>Welcome from the Session Chairs</i>	
11:10–11:25	Junyi Lin Selected Speaker	Biomimetic Homotypic Nanoparticles Co-delivering Gemcitabine and IKK β Inhibitor Reverse Gemcitabine induced Stemness for Enhanced Pancreatic Cancer Therapy
11:25–11:40	Gaia Giannitti Selected Speaker	Dissecting the contribution of CD36 to extracellular vesicle-driven metabolic crosstalk between melanoma cells and adipocytes

Session 3. Drug Resistance and Anti-cancer Drug Development and Screening

Time: 14:00 (CEST, Basel) | 8:00 (EDT, New York) | 20:00 (CST Asia, Beijing)

CET Time	Speaker	Title
14:00–14:05	<i>Dr. Farrukh Aqil</i> <i>Welcome from the Session Chair</i>	
14:05–14:20	Alaa Aboushanab Selected Speaker	Synergistic Chemo-Immunomodulation via Nanocarrier Co-Delivery of Doxorubicin and Pexidartinib
14:20–14:35	Mariana Sousa Selected Speaker	Functional reactivation of p53 as a promising therapeutic strategy in the treatment of ovarian cancer
14:35–14:50	Inês Mota Selected Speaker	Combination of BBIT20 and Immunotherapy Enhances Antitumor Activity in Pancreatic Cancer
14:50–15:05	Ana Catarina Matos Selected Speaker	Restoring therapeutic vulnerability in Multidrug-Resistant Ovarian Cancer with a first-in-class disruptor of the BRCA1-BARD1 interaction

15:05–15:20	SYLWIA AMMOUN Selected Speaker	Cellular Prion Protein (PrPC) as a Therapeutic Target in Meningioma and Schwannoma Development and Multidrug Resistance
15:20–15:35	Wioletta Rozpędek-Kamińska Selected Speaker	Selective PERK inhibition as a strategy to overcome hypoxia-induced survival in colorectal cancer cells
15:35–15:50	Alexander A. Shtil Selected Speaker	Electrochemical Reduction of Copper (II) As a Potent and Versatile Approach for Tumor Cell Eradication
15:50–16:05	Martyna Natalia Muskała Selected Speaker	Induction of apoptosis by extracts from transformed hairy roots of <i>Plectranthus venterii</i> in an in vitro cancer model
16:05–16:20	farnaz mohammadi Selected Speaker	Targeting EPS8 by CRISPR/Cas9 Genome Editing Reduces Gemcitabine Resistance in Pancreatic Cancer Cells
16:20–16:40	Prof. Dr. Axel H. Schönthal Invited Speaker	Development of Novel Drug Delivery Pathways Enabled by Perillyl Alcohol (NEO100), a Monoterpene with Multifaceted Biomedical Applications

11th June 2026 (Thursday)**Session 7. Novel Methods and Technologies for Research and Treatment****Time: 09:00 (CEST, Basel) | 03:00 (EDT, New York) | 15:00 (CST Asia, Beijing)**

CET Time	Speaker	Title
9:00–9:05	<i>Prof. Dr. Guomin Li</i> <i>Welcome from the Session Chair</i>	
9:05–9:20	Olga Tselousova Selected Speaker	CIRCULATING TUMOR DNA AS A BIOMARKER OF GENOMIC INSTABILITY AND CLONAL EVOLUTION IN BREAST CANCER
9:20–9:35	Ekaterina Lindunen Selected Speaker	Bioinformatic Identification of ACTN4 as a Candidate Master Regulator of Local Invasion in Glioblastoma
9:35–9:50	Yuzhe Wang Selected Speaker	A Novel CAM-Based Dual-Reporter Imaging Platform to Study Secretome-Driven Vascular Remodeling in Sarcoma
9:50–10:05	Michael Laurence Langsen Selected Speaker	Validation and Clinical Translation of Non-Invasive Imaging Biomarkers for the Classification of Gliomas
10:05–10:20	Anna Shorina Selected Speaker	Machine Learning-Based Association of Copy Number Alterations in a Mechanobiological Gene Panel with Metastatic Status Across Cancer Types
10:20–10:35	Olga Kamaeva Selected Speaker	Investigation of the Protein Corona on Polyvinyl Alcohol-Stabilized Polymeric Nanoparticles
10:35–10:50	Elizaveta Kontareva Selected Speaker	High-nitrogen artificial gas mixture-induced hypoxia decreases nanoparticle uptake in breast tumor cells with varying malignancy
10:50–11:05	Nikhil Gudivada Selected Speaker	An analysis of RCTs using PARP inhibitors in the treatment of breast cancer
11:05–11:20	Maryem Mahfoud Selected Speaker	Exploration of genes identified in antitumor resistance in triple-negative breast
11:20–11:35	Omar Hamad Selected Speaker	Digital Pathology Approach to Mapping Collagen VI Tumor Spatial Arrangement in COVID-19 Tissue Slides Using ImageJ

Session 7. Novel Methods and Technologies for Research and Treatment**Time: 14:00 (CEST, Basel) | 08:00 (EDT, New York) | 20:00 (CST Asia, Beijing)**

CET Time	Speaker	Title
14:00–14:05	<i>Prof. Dr. Andrew A. Gumbs</i> <i>Welcome from the Session Chair</i>	
14:05–14:25	Prof. Dr. Takeaki Ishizawa Invited Speaker	Intraoperative fluorescence imaging for cancer surgery
14:25–14:45	Prof. Dr. Karol Rawicz-Pruszyński Invited Speaker	AI in Gastric Cancer
14:45–15:00	Anastasia Frolova Selected Speaker	A systematic LC-HRMS urinary metabolomics framework for identifying urothelial malignancy biomarkers within a comparative multi-cancer study
15:00–15:15	Taufeeque Ali Selected Speaker	A Self-Amplifying Redox-Based Combination Therapy Using an ROS-Responsive Prodrug and Pharmacologic Ascorbate for Targeted Triple-Negative Breast Cancer Treatment
15:15–15:30	Nosimot Buhari Selected Speaker	Comprehensive Computational Profiling of MSH3 Missense Mutations and Stability Effects in Cancers and Neurodegenerative Disorders

Session 2. Tumor Heterogeneity**Time: 15:30 (CEST, Basel) | 9:30 (EDT, New York) | 21:30 (CST Asia, Beijing)**

CET Time	Speaker	Title
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15:30–15:35	<i>Prof. Dr. Henry H. Heng</i> <i>Welcome from the Session Chair</i>	
15:35–16:05	Prof. Dr. Henry H. Heng Keynote Speaker	Cancer as a Supersystem: Chromosomal Instability Drives Multiscale Heterogeneity Through Two-Phased Evolution
16:05–16:35	Prof. Dr. Jinsong Liu Keynote Speaker	Polyploid Giant Cancer Cells as a Window into Tumor Heterogeneity
16:35–16:50	Paula De Juan-Maciá Selected Speaker	The hypertrophic adipocyte niche fuels metabolic plasticity and invasive signaling in colorectal cancer
16:50–17:05	Fei Yang Selected Speaker	Intratumoral Metabolic Heterogeneity Predicts Treatment Response in High-Risk Hodgkin Lymphoma: Evidence from the AHOD0831 Trial
17:05–17:20	Elena Filippova Selected Speaker	SNHG6-centered RNA regulatory network links epithelial plasticity and apoptosis signaling in breast cancer
17:20–17:35	Fabrizio Fontana Selected Speaker	Unraveling the role of extracellular vesicle-mediated interleukin-8 signaling in melanoma invasion

12th June 2026 (Friday)**Flash Poster Session****Time: 09:00 (CEST, Basel) | 03:00 (EDT, New York) | 15:00 (CST Asia, Beijing)**

Session	Poster Presenter	Title
Session 1		
9:00–9:05	Olga Pershina Selected Speaker	Age-related features of cancer stem cell and T-cell response to therapy in a lung cancer model in aged mice
Session 2		
9:05–9:10	Alexey M. Burdenny Selected Speaker	Tumor-associated miR-124 and miR-137 in post-transcriptional regulation of ovarian cancer
9:10–9:15	Meryem Aarab Selected Speaker	Phenotypic Heterogeneity of Circulating Tumor Cells in Lung Cancer Revealed by Immunocytochemical Profiling
9:15–9:20	Maria Francesca Fiorita Selected Speaker	Adipocyte-Derived Conditioned Medium Influences the Malignant Phenotype of Human Breast Cancer-Associated Fibroblasts
Session 3		
9:20–9:25	Mariarosa Fava Selected Speaker	Lamotrigine Inhibits Breast Cancer Progression Through FoxO3a/TXNIP axis
9:25–9:30	Yueyang Zhang Selected Speaker	Evaluation of Lobaplatin Chemosensitivity and Mechanistic Insights Using a 3D Bioprinted Primary Colorectal Cancer Model
9:30–9:35	Ye Yuan Selected Speaker	Vimentin facilitates ubiquitination and degradation of NCOA4 to promote resistance to olaparib-induced ferroptosis in glioblastoma
9:35–9:40	Souandaou ATHOUMANI ALI Selected Speaker	An RNA Sequencing approach for the identification of anticancer effects of Docetaxel in cervical cancer
Session 4		
9:40–9:45	Ioannis Adamopoulos Selected Speaker	Survival impact of surgery and radiotherapy in malignant phyllodes tumors: Meta-Analysis of cohort studies
9:45–9:50	Marzia Sichetti Selected Speaker	MIND–BODY INTERVENTION FOR SYMPTOM MANAGEMENT IN BREAST CANCER SURVIVORSHIP: A FEASIBILITY QIGONG PILOT STUDY
Session 5		
9:50–9:55	Linda Manna Selected Speaker	Serum from Subjects with High Body Mass Index Modulates Multiple Myeloma Cell Phenotype
9:55–10:00	Ionela Codruta Bubuianu Selected Speaker	Decoding Therapy-induced Senescence EVs: Proteomic and miRNomic Clues to NSCLC Chemoresistance
10:00–10:05	Erina Iwabuchi Selected Speaker	Significance of HER2-related factor in HER2-low breast cancer
10:05–10:10	Lisa Elm Selected Speaker	Distinct YAP-TEAD signaling states revealed by integrated mRNA and protein analysis in thymic epithelial neoplasms
Session 7		
10:10–10:15	Sofia Kleimenova Selected Speaker	Development of novel drug delivery systems based on extracellular vesicles and cell membranes for cancer therapy
10:15–10:20	Michaila Akathi Pantelaoui Selected Speaker	Smart nanocarriers encapsulating chemotherapeutic agents
10:20–10:25	Daria Prilutskaya Selected Speaker	Extracellular vesicles as a targeted drug delivery platform for cancer treatment
10:25–10:30	Anastasia Dubrovina Selected Speaker	Development Omnipose Neural Network-Based Analytical Module for Morphometric Analysis of Metastatic Cancer Cells

Session 5. Causes, Diagnosis and Treatment of Cancer

Time: 10:30 (CEST, Basel) | 04:30 (EDT, New York) | 16:30 (CST Asia, Beijing)

CET Time	Speaker	Title
10:30–10:45	Daniele Viavattene Selected Speaker	Guilty by association: calcium-mediated apoptosis regulated at the ER by a newly discovered mTOR-STAT3 pathway
10:45–11:00	Wenyu Xue Selected Speaker	Integrated Clinical and Functional Analysis Identifies miR-16-1-3p as an Active Passenger Strand Associated with Osteosarcoma Progression and Chemoresistance
11:00–11:15	Nemany A.N. Hanafy Selected Speaker	Hyaluronic acid-functionalized CaCO ₃ crystals as novel polyelectrolyte multilayer reservoirs for CPT-RB (Chemotherapy and Photodynamic therapy) targeting multiple myeloma
11:15–11:30	Ladislav Görög Selected Speaker	Ratiometric TGF-β–MMP Biomarkers Capture Pathway Imbalance and Stratify Colorectal Cancer Progression
11:30–11:45	Imane SAIF Selected Speaker	Evaluation of the epigenetic signatures of BRCA1 and TP53 as tools for metastatic prognosis: Translational study on a cohort of Moroccan women

Session 5. Causes, Diagnosis and Treatment of Cancer

Time: 14:00 (CEST, Basel) | 08:00 (EDT, New York) | 20:00 (CST Asia, Beijing)

CET Time	Speaker	Title
14:00–14:05	<i>Prof. Nicola Amodio Welcome from the Session Chair</i>	
14:05–14:25	Dr. Enrica Antonia Martino Invited Speaker	Diagnosis and treatment of Multiple Myeloma
14:25–14:40	Ilenia Valentino Selected Speaker	MARCH5-Driven MFN2 Degradation Sustains Mitochondrial Fission and Drug Resistance in Multiple Myeloma
14:40–14:55	Valeria Abril Pelayo-Ramírez Selected Speaker	In Silico Transcriptomic Identification of Recurrent Transmembrane Receptors Across 12 Major Cancers for Targeted Non-Viral Gene Therapy
14:55–15:10	Oloche Celestine Eije Selected Speaker	Brain Cancer Gene Expression Analysis for Subtype Classification and Biomarker Discovery Using Machine Learning
15:10–15:25	Wei-Hsiung Yang Selected Speaker	Transcription factor NR5A1 enhances wild-type p53 transactivation
15:25–15:40	Francesca Gualtieri Selected Speaker	Heparan Sulfate-Mediated Mechanotransduction Promotes EMT and Aggressiveness in Ovarian Cancer
15:40–15:55	Kaoutar ANOUAR TADLAOUI Selected Speaker	miR-200c and PRR11: A Diagnostic Duo in HPV-Driven Cervical Cancer—Unraveling Their Inverse Regulation for Early Detection
15:55–16:10	Elena Marusich Selected Speaker	Iron Oxide Nanoparticles as Potential Agents for Combined Radiotherapy
16:10–16:25	Xiaoke Wang Selected Speaker	Stem Cell Exhaustion Defines an Immunogenic Niche and a Circulating Biomarker for Nasopharyngeal Carcinoma
16:25–16:40	Xiaohong Li Selected Speaker	Pralsetinib for RET Fusion-Positive Advanced Ascending Colon Cancer with Liver Metastasis: A Case Report and Literature Review

Poster List

Submission ID	Author	Title
sciforum-141251	Yashi Mahendra, Anuj Kumar	Genetic Factors Affecting Tobacco Cessation
sciforum-154893	Yujing TAN, Cheng Zeng, Lin Zhu, Jiani Wang, Fei Ma	Transcriptome differences revealed by high-plex digital spatial profiling associated with endocrine sensitivity for hormone receptor-positive/human epidermal growth factor receptor 2-negative (HR+/HER2-) early breast cancer (EBC)
sciforum-157598	Leila Hosseinzadeh Anvar, Esmaeil Babaei, Mitra Rezaei, Mortaza Bonyadi	KRAS activity improves overall survival and fosters an anti-tumor microenvironment in colorectal cancer
sciforum-158108	Ioannis Adamopoulos, Aida Vafae Eslahi, Niki Syrou, George Mpourazanis, Panagiotis Tsirkas, Moustafa Younis	Survival impact of surgery and radiotherapy in malignant phyllodes tumors: Meta-Analysis of cohort studies
sciforum-162465	Olga Pershina, Angelina Pakhomova, Lubov Sandrikina, Lena Kogai	Age-related features of cancer stem cell and T-cell response to therapy in a lung cancer model in aged mice
sciforum-166356	Michaila Akathi Pantelaiou, Stergios Pispas	Smart nanocarriers encapsulating chemotherapeutic agents
sciforum-168193	Alina Badlaeva, Anna Tregubova, Natalia Arzhanukhina, Alevtina Chamorovskaya, Vladimir Borzunov, Aleksandra Asaturova	Evaluation of Interobserver Agreement in the Classification of Peritoneal Implants in Ovarian Serous Borderline Tumors and Low-Grade Serous Carcinomas: A Multi-Reviewer Study
sciforum-169030	Marek Pająk, Jakub Włodarczyk, Magdalena Woźniczka, Jakub Fichna	The effect of the degree of oxidation and the molecular structure of cobalt complexes with imidazole on the metabolic profiles of CCD 841 CoN and HT-29 cells
sciforum-169131	Erina Iwabuchi, Yasuhiro Miki, Minoru Miyashita, Takashi Suzuki	Significance of HER2-related factor in HER2-low breast cancer
sciforum-169390	Lisa Elm, Nadja Gerlitz, Jens Neumann, Georgia Levidou	Distinct YAP-TEAD signaling states revealed by integrated mRNA and protein analysis in thymic epithelial neoplasms
sciforum-169576	Riddhi Shah, Davide Pradella, Ashley Sullivan, Ana Marie Perea, Daniel Heller, Robert E Schwartz, Robert Benezra	Exploring the mechanism of ID1-dependent liver inflammation induced by dietary fat and a therapeutic approach to target IDs in cancer
sciforum-169648	Jaydeep Jadhav, Yuktha G, Subhash Kudhale, Mugdha Nilesh Harmalkar	"Exploring the Antioxidant and Anticancer Activity of Clematis heynei, an Endemic Medicinal Plant of the Western Ghats"
sciforum-170432	Sofia Kleimenova, Mariia Mollaeva, Daria Prilutskaya, Nikita Yabbarov, Maria Sokol, Margarita Chirkina, Maksim Klimenko, Ivan Gulyaev, Elena Nikolskaya	Development of novel drug delivery systems based on extracellular vesicles and cell membranes for cancer therapy
sciforum-170770	Irina Valerievna Pronina, Inna Ganshina, Tatiana Zavarykina, Irina Kolyadina	PLASMA MICRORNAS IN ASSESSING THE RISK OF RECURRENCE IN TRIPLE-NEGATIVE BREAST CANCER
sciforum-170842	Tinashe Adrian Mazhindu, Anna Mary Nyakabau, Webster Kadzatsa	A Cross-Sectional Evaluation of Guideline-Adherent Screening Eligibility Among Zimbabwean Patients Diagnosed with Lung Cancer
sciforum-170867	Anastasia Dubrovina, Margarita Pustovalova, Sergey Leonov, Yulia Merkher	Development Omnipose Neural Network-Based Analytical Module for Morphometric Analysis of Metastatic Cancer Cells
sciforum-170890	Mohammed El Magroud, mohammed meziane, Anass Haloui, Nassira Karich, Amal Bennani	SUBEPENDYMAL GIANT CELL ASTROCYTOMA: A RARE CENTRAL NERVOUS SYSTEM TUMOUR WITH A COMPLEX HISTOLOGY
sciforum-170956	Muhammad Zurgham Akram, Mehwish Majeed	NDS: A Novel Deep Learning-Based Systems Biology Framework for Identifying Prognostic Biomarkers in Hepatocellular Carcinoma
sciforum-171015	Priti Chatterjee	A comprehensive study of HMG-CoA reductase in Uterine cancer with an in silico perspective
sciforum-171060	Manal KHARKHACH, asmae AISSAOUI, Anass HALOUI, Nassira KARICH, Amal BENNANI	Endometrioid Adenocarcinoma of the Endometrium with Mucinous Differentiation: An Anatomopathological Case Report

Submission ID	Author	Title
sciforum-171077	Daria Prilutskaya, Maria Mollaeva, Sofia Kleimenova, Nikita Yabbarov, Maria Sokol, Margarita Chirkina, Maksim Klimenko, Ivan Gulyaev, Yulia Bortnevskaya, Natal'ya Bragina, Kseniya Zhdanova, Elena Nikolskaya	Extracellular vesicles as a targeted drug delivery platform for cancer treatment
sciforum-171108	Linda Manna, Giuseppina Augimeri, Luca Gelsomino, Cinzia Giordano, Massimo Gentile, Enrica Antonia Martino, Ennio Avolio, Catia Morelli, Diego Sisci, Daniela Bonofiglio, Ines Barone, Stefania Catalano	Serum from Subjects with High Body Mass Index Modulates Multiple Myeloma Cell Phenotype
sciforum-171155	Mouna Aqerrou, Imane Mharrach, Imane Ouariagli, Abdelilah Laraoui, Khalid Ennibi, Moulay Mustapha Ennaji	Urinary Dual OncomiR Signature of miR-21 and miR-155: A Non-Invasive Approach for Bladder Cancer Detection in a Moroccan Cohort
sciforum-171178	Qingmei Yang, Yiwei Xu, Xinjia Wang	Analysis of Screening Results for Upper Gastrointestinal Cancer and Precancerous Lesions among High-Risk Individuals Aged 40-69 in the Chaoshan Region, Guangdong Province, China
sciforum-171251	Amal El Masri, Firas Haddad, Karim Bachir, Nicole Charbel, Ali Awada, Aya Tamim, Nada Assaf, Firas Kreidieh	Retrospective Registry for Uveal Melanoma in Lebanon: 10-year Single-Center Experience of a Major Referral Center in the Middle East and North Africa
sciforum-171252	Maria Francesca Fiorita, Giuseppina Augimeri, Luca Gelsomino, Cinzia Giordano, Daniela Bonofiglio, Ines Barone, Stefania Catalano	Adipocyte-Derived Conditioned Medium Influences the Malignant Phenotype of Human Breast Cancer-Associated Fibroblasts
sciforum-171288	Martina Pallone, Francesca Gualtieri, Valentina Rocca, Giuseppe Viglietto, Carmela De Marco	Heparan Sulfates Regulate Angiogenic Signaling and Drug Response in Aggressive Ovarian Cancer
sciforum-171346	Mikhail Karpushin, Nikita Shelepin, Elena Komarova, Irina Balalaeva	Specific expression profile of genes associated with extracellular matrix and phenotypic plasticity in triple-negative breast cancer
sciforum-171464	Maria Fernanda Barrientos Nava, Fabiola Estefanía Tristán-Flores, Guillermo Antonio Silva-Martínez	Molecular Docking and Molecular Dynamics Approaches to Evaluate the Specificity of the AS1411-Lapatinib Aptamer Complex in HER2-Positive Breast Cancer
sciforum-171523	Toshihiro Ona, Junko Johzuka	Anti-cancer Drug Development by Rapid and Synchronized Dormancy-Breaking Kyoho Grape Seed Endosperm
sciforum-171608	Sarah Allegra, Francesco Chiara, Valeria Ballero, Giuliana Abbadessa, Maura Caudana, Silvia De Francia	Clinical Pharmacokinetics of Imatinib: Evidence of Sex-Related Differences in Drug Exposure
sciforum-171632	Marvah Qanoot, Amjad Hussain	Synthesis and Pharmacological Evaluation of N-(2-Bromoethyl) Phthalimide-Based Hybrid Compounds
sciforum-171661	Onochie Peter Eze, Lubov V Krylova, Elizaveta Mikhailovna Pnachina, Vasilii F Otvagin, Natalia S Kuzmina, Alexander V Nyuchev, Alexey Yu Fedorov, Irina V Balalaeva	Bioorthogonally Activatable Chlorin e6 Photosensitizer for Targeted Photodynamic Therapy: Photophysical and Biological Properties in vitro
sciforum-171678	FRANCESCO CHIARA, Sarah Allegra, Federico Itri, Valeria Ballero, Silvia De Francia, Marco De Gobbi	Intracellular and Erythrocyte Partitioning of Venetoclax and its Metabolites: A Multi-Compartmental Pharmacokinetic Model Derived from Paired Patient Samples using High-Resolution Mass Spectrometry
sciforum-171695	Maram Mokhtar	The correlation between estrogen level and microbial interaction in breast cancer

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sciforum-171742	Maria Karpova, Artur Bozhenko, Alexey Dolinin, Fedor Sarafanov, Nikolay Ilin, Evgeny Mareev, Irina Balalaeva	COMPARISON OF THE SENSITIVITY OF CANCER AND NORMAL HUMAN CELLS TO CHANGES IN BACKGROUND MAGNETIC FIELD
sciforum-171745	Mariarosa Fava, Sofia Spadafora, Marianna Strumbo, Antonella Galati, Ivan Casaburi, Rosa Sirianni, Marilena Lanzino, Diego Sisci, Ines Barone, Catia Morelli	Lamotrigine Inhibits Breast Cancer Progression Through FoxO3a/TXNIP axis
sciforum-171757	Imene DERARDJA, Redouane REBAI, Luc Jasmin, Abdennacer Boudah	Network pharmacology-based elucidation of the multi-target mechanisms of piperlongumine targeting oncogenic survival and immune-evasive pathways in pancreatic cancer
sciforum-171776	Antonella Galati, Camilla Longobucco, Marzia De Santo, Rocco Marinaro, Natascia De Cicco, Laura De Lellis, Alessandro Cama, Rosalba Florio, Serena Veschi, Mariarosa Fava, Sofia Spadafora, Diego Sisci, Luigi Pasqua, Antonella Leggio, Catia Morelli	FOLATE-FUNCTIONALIZED MESOPOROUS SILICA NANOPARTICLES FOR TARGETED DELIVERY OF MEBENDAZOLE IN FR+ BREAST CANCER CELLS
sciforum-171780	Samia BENMALI, ANASS HALOUI, nassira karich, AMAL BENNANI	Giant Gastric Gastrointestinal Stromal Tumor with Schwannian-Like Features: A Diagnostic Pitfall
sciforum-171789	Meryem Aarab, Salma Saadi, Imane Tabyaoui, Nadia Tahiri Jouti	Phenotypic Heterogeneity of Circulating Tumor Cells in Lung Cancer Revealed by Immunocytochemical Profiling
sciforum-171915	Yueyang Zhang, Haitao Zhou	Evaluation of Lobaplatin Chemosensitivity and Mechanistic Insights Using a 3D Bioprinted Primary Colorectal Cancer Model
sciforum-172100	Ali Moghimi-Khorasgani, Naeimeh Rezaei, Abbas Kiani-Isfahani, Kianoush Dormiani	Reprogramming T Cells via Minicircle DNA Platforms: A Novel Nonviral Strategy for CD19-Directed CAR-T Therapy in Leukemia
sciforum-172151	Emmanuel C. Okoro, Amara A. Nwose, Chikaodili S. Ugwuanyi, Chizelum C. Mgbe, Paul C. Onwuasoanya, Sandra I. Abana, James E. Sunday, Blessing E. Ugwuodo, Lilian I. Nweke, Charles O. Nnadi, Wilfred O. Obonga	Exploring the anticancer mechanism of isolated compounds from endophytic fungi of the Meliaceae family by a network pharmacological analysis
sciforum-172859	farnaz mohammadi, Mahboobeh Forozanfar, Ali Valipour, Kianoush Dormiani	Targeting EPS8 by CRISPR/Cas9 Genome Editing Reduces Gemcitabine Resistance in Pancreatic Cancer Cells
sciforum-173856	Marzia Sichetti, Eugenia Giglio, Giovanni Pace, Marisabel Mecca, Graziella Marino	MIND-BODY INTERVENTION FOR SYMPTOM MANAGEMENT IN BREAST CANCER SURVIVORSHIP: A FEASIBILITY QIGONG PILOT STUDY
sciforum-177486	Omar Hamad, Helen Naim Zarwi, Sarah Aldoseri, Moayed Al Abdul Wahed, Paul G. Murray	Digital Pathology Approach to Mapping Collagen VI Tumor Spatial Arrangement in COVID-19 Tissue Slides Using ImageJ
sciforum-177853	Eva González-Cantó, Laia Barrachina-Bonet, Guillermo Bagues-Navarro, Clara Cervero-Carbonell, Carmen Martos	Geographical and temporal incidence patterns of childhood central nervous system tumours in Europe: Insights from the European Cancer Information System
sciforum-178005	Rajaram Vishnupriya, Janu P, Anandha Jothi S, Sara Ayisha Imthiaz Pasha, Arun Dharmarajan	Breast Cancer in South India: Clinical Patterns and Lifestyle Associations in the Tiruchirappalli district
sciforum-178158	Zain Nofal, Margarita Pustovalova, Sergey Leonov	Confined migration-derived breast cancer sublines reveal subtype-specific responses to Arp2/3 inhibition
sciforum-178239	Daniel Regassa, Marat S. Babaev, Evgeniya Y. Shabalina, Philipp Y. Maximov, Elena V. Petersen	A Statistically Rigorous Multi-Scale Texture Analysis Framework for 3D Spheroid Characterization: Temporal Autocorrelation Correction and Molecular Validation
sciforum-178243	Ionela Codruta Bubuianu, Giulia Canarutto, Simona Arena, Luca Triboli, Lucia Bertuccini, Silvano Piazza, Isabella Parolini, Giulia Antoniali	Decoding Therapy-induced Senescence EVs: Proteomic and miRNomic Clues to NSCLC Chemoresistance

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sciforum-178266	Asmat Ullah, Somia Shehzadi	Evodiamine Illuminating New Horizons in Colorectal Cancer Therapy by Disrupting Hypoxia-Driven Angiogenesis via the HIF-1 α /VEGF Axis
sciforum-178317	Luciano Ferrando, Evelio Alonso Alonso, Marina Manzanera Diaz, José Felipe Reoyo Pascual, Miguel Angel Alvarez Rico	Diagnostic Performance of High-Resolution Anoscopy in Detecting High-Grade Anal Lesions in an Anal Cancer Screening Programme
sciforum-178329	Luciano Ferrando, Marina Manzanera Diaz, Adel Eldabe Mikhail, José Felipe Reoyo Pascual, Miguel Angel Alvarez Rico	Retrorectal Hamartoma Presenting as a Presacral Mass: Surgical Management and Diagnostic Challenges
sciforum-178332	Luciano Ferrando, Evelio Alonso Alonso, Marina Manzanera Diaz, José Felipe Reoyo Pascual, Miguel Angel Alvarez Rico	Predictive Value of Visual Assessment During High-Resolution Anoscopy in Anal Cancer Screening
sciforum-178369	Charu Verma, Praveen Kumar Verma	IN SILICO PHARMACOKINETIC PROFILING AND MOLECULAR DOCKING OF MARGOLONONE AGAINST THE ONCOGENIC IDH1-R132H MUTANT
sciforum-178371	Mahmoud Aberkane, Anass Haloui, Chaimae Daoudi, Manal Derkaoui, Nassira Karich, Amal Bennani	Rare Palatal Cribriform Adenocarcinoma of the Salivary Glands: a Case Report
sciforum-178387	Sara Munir, yasir Riaz	Emerging Strategies in Cancer Detection and Treatment: A Systematic Review of Immunotherapy, Gene Editing, and Artificial Intelligence
sciforum-178401	Abdullah Muhammad Saied Assad Hamdan, Ola Hamdan	Evaluating Agentic AI for Autonomous Hypothesis Generation in Clinical Datasets
sciforum-178422	Inês Mota, Tatiana Q. Aguiar, Lucília Domingues, Lucília Saraiva	Elucidating BBIT20's disruption of the BRCA1/BARD1 interaction: A new therapeutic avenue in pancreatic cancer
sciforum-178433	Liubov Zelena, Galina Baranova, Nataliia Tkachuk, Svitlana Zahorodnia	Impact of AgNPs on LLC cells

Session 1. Cancer Stem Cells

sciforum-162465: Age-related features of cancer stem cell and T-cell response to therapy in a lung cancer model in aged mice

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Metastasis and tumor recurrence are closely linked to highly resistant cancer stem cells (CSCs). It is unclear how the content of CSCs changes with age in cancer development and whether these changes correlate with a higher incidence of tumors in elderly individuals. Previously, we demonstrated the positive effect of reprogrammed CD8⁺ T-cells (rCD8-T) derived from the bone marrow of young mice with Lewis lung carcinomas (LLCs) on CSCs.

Lung cancer was modeled by injecting LLC cells into C57/BL6 mice (aged 80–82 weeks). On day 7, morphological and histological examinations of the lungs were conducted, along with cytometric analyses to quantify populations of CSCs, CD4, and CD8 T-cells in blood and lungs.

In aged mice receiving rCD8-T therapy, there was a significant reduction in lung tumor growth activity. However, notable histopathological changes were observed, characterized by extensive patchy necrosis within the livers of treated animals. Additionally, rCD8-T therapy led to a marked expansion of various CD4⁺ and CD8⁺ T-cell subsets in blood (up to 1,000-fold increases) and lung tissues (approximately 2–4-fold increases) compared to tumor-bearing mice without treatment. Notably, while untreated mice exhibited reduced numbers of circulating CD4⁺ and CD8⁺ T-cells, the population of CSCs expressing the Sox2 marker - associated with more aggressive tumor phenotypes increased substantially. After treatment, however, the frequency of Sox2-positive CSCs in circulation declined compared to those in untreated animals. In contrast, CSCs in the lungs showed little change.

Therefore, rCD8-T therapy in aged mice, although beneficial for reducing tumor growth and eliminating CSCs, induces hyperactivation of the immune system. To enhance therapeutic efficacy and ensure safety in elderly patients with lung cancer, targeted approaches against Sox2 expressing CSCs may prove effective. Combining these strategies with conventional chemotherapeutic regimens holds promise for improving overall survival outcomes in this patient population.



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sciforum-177016: Biomimetic Homotypic Nanoparticles Co-delivering Gemcitabine and IKK β Inhibitor Reverse Gemcitabine induced Stemness for Enhanced Pancreatic Cancer Therapy

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Pancreatic ductal adenocarcinoma (PDAC) is highly aggressive, with early metastasis, poor prognosis, and limited surgical eligibility. Chemotherapy, primarily gemcitabine (GEM), remains the standard treatment, but rapid development of GEM resistance partly driven by the induction of cancer stem cell (CSC)-like properties severely limits its efficacy. Aberrant activation of the IKK β /NF- κ B signaling pathway promotes CSC maintenance, tumor progression, and chemoresistance, suggesting that targeted inhibition could enhance GEM sensitivity. In this study, we developed a biomimetic nanoparticle system (84/PGEM@KPC) by loading the IKK β inhibitor Analog 84 into GEM-based polymeric prodrug nanoparticles, followed by coating with KPC pancreatic cancer cell membranes to achieve homotypic targeting and immune evasion. The 84/PGEM@KPC nanoparticles exhibited a uniform size of about 20nm, a zeta potential around -20mV, and high drug loading and stability, achieving more efficient tumor penetration and accumulation than 84/PGEM. In vitro, these nanoparticles effectively reversed GEM induced stemness, suppressed NF- κ B activation, and synergistically promoted apoptosis of pancreatic cancer cells. In vivo, treatment with 84/PGEM@KPC markedly inhibited PDAC growth, increased the infiltration of IFN- γ ⁺ and Granzyme B⁺ CD8⁺ T cells, and reduced immunosuppressive regulatory T cells, demonstrating both potent antitumor efficacy and favorable immune modulation. Collectively, this dual functional nanoplatform integrates GEM prodrug delivery, IKK β inhibition, and homotypic targeting to overcome chemoresistance and remodel the immune microenvironment, providing a promising strategy for enhanced pancreatic cancer therapy.



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sciforum-170334: Dissecting the contribution of CD36 to extracellular vesicle-driven metabolic crosstalk between melanoma cells and adipocytes

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Introduction Melanoma is a highly aggressive malignancy characterized by a strong metastatic potential, underscoring the need to elucidate the mechanisms driving its progression in order to improve clinical outcomes. Increasing evidence points to a tumor-promoting interaction between melanoma cells and subcutaneous adipose tissue; however, the contribution of extracellular vesicles (EVs) to this intercellular crosstalk remains largely undefined.

Methods We investigated the impact of melanoma-derived EVs on adipocyte phenotype and lipid metabolism, as well as the functional consequences on melanoma cells. Activation of the cAMP/PKA/HSL signaling pathway, induction of lipolysis, and release of free fatty acids (FFAs) were analyzed in adipocytes exposed to melanoma EVs. FFA uptake and tumor-associated behaviors in melanoma cells were assessed, together with the role of the fatty acid transporter CD36 using pharmacological inhibitors, including sulfo-N-succinimidyl oleate (SSO) and SMS121.

Results Melanoma-derived EVs reprogram adipocytes toward a cancer-associated state by activating the cAMP/PKA/HSL signaling pathway, resulting in enhanced lipolysis and increased FFA release. These FFAs are subsequently taken up by melanoma cells, where they promote a stem-like phenotype characterized by increased proliferation, clonogenic capacity, survival, migration, invasion, and resistance to anoikis. Importantly, CD36 was identified as a critical mediator of this metabolic crosstalk, as pharmacological inhibition of CD36 effectively abolished the pro-tumorigenic effects induced by adipocyte-derived FFAs.

Conclusions Collectively, our findings support a model in which melanoma-derived EVs establish a metabolic feedback loop with adipocytes that enhances tumor aggressiveness. Targeting CD36 may therefore represent a promising therapeutic strategy to disrupt this pathogenic intercellular communication.



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Session 2. Tumor Heterogeneity

sciforum-171266: Dynamics of Tumor Heterogeneity: Molecular Mechanisms and Implications for Therapeutic Resistance—A Literature Review

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Introduction: Cancer is no longer viewed as a monolithic cellular mass but as a complex, evolving ecosystem. Tumor heterogeneity, encompassing both inter-tumoral and intra-tumoral diversity, represents the primary barrier to therapeutic success, driving divergent clinical responses and unpredictable relapses. This review explores the underlying clonal architecture of tumors and its profound impact on disease progression and management.

Methods: A systematic analysis was conducted using the literature indexed in PubMed and Web of Science between 2016 and 2025. The selection prioritized high-impact studies involving multi-region genomic sequencing, single-cell transcriptomics, and longitudinal clonal tracking. Data from over 50 peer-reviewed articles were synthesized to correlate cellular diversity with patient prognosis and therapy escape mechanisms.

Results: Findings indicate that heterogeneity is driven by a combination of inherent genomic instability and selective pressures within the tumor microenvironment. Evidence highlights that rare subclonal populations, often undetectable through conventional bulk biopsies, frequently harbor pre-existing mutations that confer resistance to chemotherapy and targeted inhibitors. Furthermore, this review identifies significant phenotypic plasticity, where tumor cells undergo reversible state transitions to bypass metabolic and therapeutic stress.

Conclusions: Deciphering the complexities of heterogeneity necessitates a shift from static treatment protocols to dynamic, adaptive strategies. The clinical integration of liquid biopsies and single-cell diagnostics is vital for monitoring clonal shifts in real-time, facilitating the transition toward genuine precision oncology.



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sciforum-178371: Rare Palatal Cribriform Adenocarcinoma of the Salivary Glands: a Case Report

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Introduction:

Cribriform adenocarcinoma of the salivary glands (CASG) is a rare tumor (1% of salivary gland tumors). It typically affects patients in their fifth to sixth decades of life, with no gender predilection. The tongue is the most common site, although other locations such as the palate, tonsil, retromolar region and upper lip have been reported. CASG mainly metastasizes to regional lymph nodes.

Case report:

A 64-year-old patient with a history of ischemic heart disease presented with a progressively enlarging palatal swelling over two years.

Oral examination revealed a well-circumscribed 3 cm mass of the soft palate. Cervical computed tomography showed a palatal mass measuring 18 × 14 mm, without local invasion or cervical lymphadenopathy. A biopsy was performed.

Results:

Histologically, the lesion showed a lobulated carcinomatous proliferation composed of solid nests and cribriform structures separated by fibrous septa.

Tumor cells displayed moderate atypia, with vesicular, optically clear nuclei, peripheral nucleoli, minimal mitotic activity and eosinophilic cytoplasm. Immunohistochemistry revealed positivity for CK7 and S100, focal CK5/6 expression, and negativity for CK20 and p63.

These findings were consistent with CASG. The patient subsequently underwent surgical excision.

Discussion:

CASG is currently considered a variant of polymorphous adenocarcinoma (WHO 5th edition). Histologically, it shows cribriform or solid architecture, sometimes with glomeruloid features. Cellular atypia is usually mild, with nuclei resembling those of papillary thyroid carcinoma.

The differential diagnosis includes polymorphous adenocarcinoma, papillary thyroid carcinoma and adenoid cystic carcinoma.

Treatment of CASG is primarily surgical excision, with optional cervical lymph node dissection or radiotherapy. Despite regional metastasis, prognosis remains excellent.

Conclusion :

CASG is a rare, low-grade malignancy, considered a variant of polymorphous adenocarcinoma. Palatal localization is less common, and tumor shares cytological features with papillary thyroid carcinoma. Prognosis remains favorable, even in the presence of cervical lymph node metastasis.



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sciforum-171252: Adipocyte-Derived Conditioned Medium Influences the Malignant Phenotype of Human Breast Cancer-Associated Fibroblasts

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Introduction: Obesity represents a global health concern, leading to the development of several types of malignancy, including breast cancer (BC). In the obese state, adipocytes become hypertrophic, releasing elevated amounts of fatty acids, adipokines and pro-inflammatory cytokines, which support BC progression. The secreted factors from adipocytes establish paracrine network with BC cells and the components of the tumor microenvironment (TME), creating a pro-tumoral milieu. Cancer-associated fibroblasts (CAFs) represent the main population within the TME. However, whether their phenotype might be influenced by the secreted factors from adipocytes is not fully understood. Here, we aimed to investigate whether the conditioned medium of mature 3T3-L1 adipocytes (3T3-L1A) influences human breast CAF phenotype.

Methods: CAFs were isolated from breast tumor biopsies. Conditioned medium (CM) from adipocytes was collected incubating mature murine adipocytes (3T3-L1A) in 3% charcoal-stripped fetal bovine serum for 36–48 hours and used in co-culture systems with CAFs. MTT, Boyden Chamber Migration, Contraction, Phalloidin Staining Assays and Multiplex Bead-Based Immunoassay were performed to assess the phenotypic features of 3T3-L1A CM-treated CAFs.

Results: CM from 3T3-L1A enhanced CAF viability and migration compared to untreated control. CAF contractility was markedly increased after incubation with 3T3-L1A CM for 48 h and 72 h. Consistent with this result, the stress fiber formation was higher in 3T3-L1A CM-treated CAFs. Multiplex analysis revealed that 3T3-L1A CM induced the upregulation of several pro-tumoral secreted factors in CAFs, with RANTES among the most markedly upregulated.

Conclusion: Our findings demonstrated that the secreted factors from adipocytes affect the phenotypic features of human breast CAFs, highlighting the relevance of paracrine interactions within the TME.



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sciforum-171742: Comparison of the Sensitivity of Cancer and Normal Human Cells to Changes in Background Magnetic Field

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Weak magnetic fields (WMFs) with intensities up to 1 mT remain poorly studied, and the combined effects of magnetic fields (MFs) and other stress factors have received little attention.

The aim of this study was to investigate the effects of WMFs of different intensities on the growth of normal and cancer human cells, both as an independent factor and in combination with serum deprivation. The study used immortalized human embryonic kidney HEK-293T cells, cervical adenocarcinoma HeLa cells, and epidermoid carcinoma A-431 cells.

To generate the required magnetic conditions, a system of three-axis Helmholtz coils producing a gradient of a quasi-static MF with intensities from 6.5 to 115 μ T was placed inside a CO₂ incubator. A 96-well plate containing the cells was positioned at the center of the setup.

Cells were exposed to the WMF for 72 hours, after which cell viability was assessed using the MTT assay. To evaluate the effect of serum deprivation on cellular sensitivity to WMFs, fetal bovine serum (FBS) concentration was reduced from 10% to 3% for HEK-293T cells and completely removed for HeLa and A-431 cells, resulting in a 50% decrease in viability in HEK-293T and HeLa cells and a 30% decrease in A-431 cells.

Proliferation of HEK-293T cells was dependent on MF intensity, and this effect was enhanced under stress conditions. No significant effects were observed in HeLa and A-431 cell lines, and this pattern persisted under serum deprivation. Tumor cells are known to exhibit pronounced metabolic and redox heterogeneity. It is suggested that MFs influence the cellular redox balance. The lack of effect in HeLa and A-431 may reflect the predominance of subpopulations in these lines that are adapted to oxidative stress.

This work was supported by a grant from Russian Science Foundation (RSF, project no. 25-24-00505, <https://rscf.ru/project/25-24-00505/>).



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sciforum-171060: Endometrioid Adenocarcinoma of the Endometrium with Mucinous Differentiation: An Anatomopathological Case Report

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Endometrioid adenocarcinoma is the most common histological subtype of endometrial carcinoma. The presence of mucinous differentiation may represent a diagnostic challenge, particularly in distinguishing it from primary mucinous carcinoma of the endometrium or mixed epithelial tumors, entities that may carry different prognostic and therapeutic implications.

We report the case of a 63-year-old woman who underwent total hysterectomy with bilateral salpingo-oophorectomy for endometrial carcinoma. Histopathological examination revealed a FIGO grade 2 endometrioid adenocarcinoma with deep myometrial invasion exceeding 50% of the myometrial thickness. The tumor displayed predominantly glandular and papillary architecture, with tumor cells showing abundant cytoplasm containing intracytoplasmic mucin. Mucinous differentiation was confirmed by Alcian blue staining, which highlighted both intracytoplasmic and luminal mucin deposits. No serous or clear cell component was identified.

Immunohistochemical analysis demonstrated a wild-type p53 staining pattern and a deficient mismatch repair (dMMR) phenotype, characterized by loss of PMS2 expression with weak and heterogeneous MLH1 staining, while MSH2 and MSH6 were retained. The tumor cells showed diffuse positivity for CK7 and progesterone receptors, supporting an endometrial origin and excluding a high-grade serous carcinoma.

This case highlights the morphological and immunohistochemical features of endometrioid adenocarcinoma with mucinous differentiation and emphasizes the importance of an integrated diagnostic approach. Accurate recognition of this variant is essential to avoid misclassification and to ensure appropriate prognostic stratification and therapeutic management in accordance with current FIGO and ESGO/ESTRO/ESP recommendations.



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sciforum-171849: Extracellular Matrix-Driven Signaling Heterogeneity in Head and Neck Squamous Cell Carcinoma Revealed by Single-Cell Transcriptomics

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Introduction:

Intratumoral heterogeneity is a major determinant of progression and treatment failure in Head and Neck Squamous Cell Carcinoma (HNSCC). While genetic diversity has been extensively characterized, the contribution of extracellular matrix (ECM)-mediated signaling to functional heterogeneity remains less well defined. Given the central role of the tumor microenvironment in shaping cellular behavior, we sought to examine how ECM ligands influence pathway activity across distinct cellular compartments at single-cell resolution.

Methods:

Single-cell RNA sequencing data from HNSCC tumors were analyzed using a curated NABA core matrixome gene set. The Matrix Influence Scoring Algorithm (MASC) was applied to quantify the regulatory influence of ECM ligands on hallmark cancer pathways, including epithelial-mesenchymal transition (EMT), angiogenesis, and hypoxia. Influence scores were computed per cell and subsequently aggregated by annotated cell types to evaluate compartment-specific signaling patterns.

Results:

TGFBI, PAPLN, and MFGE8 consistently emerged as the most influential ECM ligands across pathways. Their regulatory impact varied markedly between cellular populations. Cancer-associated fibroblasts and myofibroblasts exhibited elevated ECM-associated EMT influence scores, endothelial cells displayed higher angiogenesis-related ECM influence, and malignant epithelial cells showed variable hypoxia-associated signaling patterns across pathways. Correlation analyses revealed substantial cross-pathway consistency in ligand influence, suggesting coordinated upstream regulation. Importantly, ECM-driven signaling was spatially and functionally restricted rather than uniformly distributed across the tumor ecosystem.

Conclusions:

These findings highlight the ECM as a critical contributor to functional heterogeneity in HNSCC. Single-cell influence modeling uncovers compartment-specific signaling programs that may shape tumor plasticity and therapeutic response, underscoring the potential of targeting microenvironmental signaling networks in precision oncology.



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sciforum-171780: Giant Gastric Gastrointestinal Stromal Tumor with Schwannian-Like Features: A Diagnostic Pitfall

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Introduction

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal neoplasms of the gastrointestinal tract and originate from the interstitial cells of Cajal. They usually display spindle cell or epithelioid morphology and characteristically express KIT (CD117) and/or DOG1. Unusual histological patterns, including schwannian-like features, may be encountered and represent a diagnostic challenge, particularly in gastric tumors.

Methods

We report a clinicopathological study of a surgically resected gastric mass in a 64-year-old patient. Gross examination and routine histological analysis using hematoxylin and eosin staining were performed. Mitotic activity was assessed in high-power fields. Immunohistochemical studies included DOG1, CD117, CD34, S100 protein, desmin, and smooth muscle actin (SMA).

Results

The tumor arose from the greater curvature of the stomach and measured 21 cm in greatest dimension. Histologically, the lesion was ulcerated at the surface and composed of spindle cells arranged in a nodular architecture, with nodules separated by fibrous septa. Tumor cells showed nuclear palisading, creating a schwannian-like appearance. The stroma was predominantly fibrous with focal myxoid areas, and tumor necrosis was present. A high mitotic rate was identified, estimated at 25 mitoses per 21 high-power fields. Immunohistochemically, the tumor cells showed diffuse positivity for DOG1, CD117, and CD34, while S100 protein, desmin, and smooth muscle actin were negative.

Conclusions

This case highlights a giant gastric GIST with schwannian-like features that may closely mimic a gastric schwannoma. Recognition of this morphological pitfall is crucial to avoid misdiagnosis. Immunohistochemistry remains indispensable for accurate diagnosis and prognostic assessment.



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sciforum-170624: Intratumoral Metabolic Heterogeneity Predicts Treatment Response in High-Risk Hodgkin Lymphoma: Evidence from the AHOD0831 Trial

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Background: Conventional imaging biomarkers for high-risk Hodgkin lymphoma—such as metabolic tumor volume (MTV) and maximum standardized uptake value (SUVmax)—do not account for intratumoral metabolic heterogeneity (IMH). This study evaluates the predictive value of baseline IMH quantified by Image Biomarker Standardization Initiative (IBSI)-compliant radiomics relative to these conventional metrics in pediatric patients with high-risk Hodgkin lymphoma.

Methods: The current study analyzed 110 pretreatment FDG-PET/CT scans from high-risk Hodgkin lymphoma patients enrolled in AHOD0831. Radiomics texture features (GLCM: 24; GLRLM/GLSZM: 16 each; GLDM: 14; NGTDM: 5) were extracted from predefined metabolic tumor volumes following IBSI guidelines. Complete response (CR) vs. non-complete response (nCR) served as the primary endpoint. Binary logistic regression models (BLRMs) were built using features most strongly associated with the endpoint, with performance evaluated by receiver operating characteristic (ROC) analysis against benchmarks using MTV and SUVmax.

Results: BLRM using the top radiomics feature (IBSI: glcm_LMC1) achieved an AUC of 0.68, outperforming MTV alone (AUC 0.62; DeLong p 0.001) and SUVmax alone (AUC 0.50; p 0.001). Incorporating the second-best feature (IBSI: ngtdm_Coarseness) further improved AUC to 0.70, surpassing the combined MTV and SUVmax model (AUC 0.62; p 0.001).

Conclusion: Radiomics-derived IMH captures tumor metabolic heterogeneity overlooked by conventional metrics, demonstrating superior predictive performance for treatment response. These findings position IMH as a promising biomarker to guide risk-adaptive therapies in high-risk Hodgkin lymphoma.



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sciforum-171789: Phenotypic Heterogeneity of Circulating Tumor Cells in Lung Cancer Revealed by Immunocytochemical Profiling

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Tumor heterogeneity is a key determinant of progression, metastasis, and therapeutic resistance in lung cancer. Circulating tumor cells (CTCs) provide a minimally invasive means to explore this heterogeneity beyond primary tumor biopsies. In this study, we investigated the phenotypic diversity of circulating cells with tumor-associated features using a cytoBlock-based enrichment approach followed by immunocytochemical analysis.

Peripheral blood samples from one hundred newly diagnosed lung cancer patients were enriched and processed to preserve rare circulating cells and stained with a panel of epithelial (pan-cytokeratins, EpCAM), organ-specific (TTF-1), and hematopoietic (CD45) markers. Typical CTCs were defined as nucleated epithelial marker-positive and CD45-negative cells. Circulating hybrid cells (CHCs) were identified based on co-expression of epithelial markers and CD45. In addition, rare nucleated cells lacking immunocytochemical staining but displaying atypical cytomorphology were documented as potential undifferentiated tumor cells, without definitive lineage attribution.

Overall, potential CTCs were morphologically detected in 98% of patients, with a subset exhibiting pronounced phenotypic heterogeneity. Non-epithelial phenotypes, including CHCs and marker-negative atypical cells, were frequently observed, particularly in patients with clinically advanced disease. These findings indicate that circulating tumor-associated cells in lung cancer extend beyond classical epithelial definitions and that epithelial-restricted detection strategies may underestimate this diversity. In conclusion, integrating morphological assessment with multiparametric immunocytochemical profiling allows a more comprehensive characterization of circulating tumor heterogeneity and may enhance the biological relevance of liquid biopsy approaches in lung cancer.



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sciforum-177490: Renal Oncocytoma : The Great Mimicker of Chromophobe Renal Cell Carcinoma – A Case Report

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Introduction

Renal oncocytoma is a benign epithelial neoplasm arising from the intercalated cells of the distal renal tubules. Despite its benign nature, it may represent a diagnostic challenge because of its close morphological resemblance to certain malignant renal tumors, particularly the eosinophilic variant of chromophobe renal cell carcinoma. Accurate diagnosis therefore requires careful correlation between clinical presentation, imaging findings, histopathological examination, and immunohistochemical analysis.

Methods

We report the case of a 43-year-old woman with no significant past medical history who presented with intermittent right-sided lumbar pain evolving for approximately one year. Physical examination revealed a hemodynamically stable and afebrile patient with a soft abdomen and mild diffuse tenderness.

Results

Abdominal computed tomography initially revealed a small indeterminate lesion in the mid-portion of the right kidney. Subsequent magnetic resonance imaging demonstrated a well-circumscribed cortico-medullary mass located at the upper pole of the right kidney, confined to the renal parenchyma without vascular invasion, extrarenal extension, or regional lymphadenopathy. A partial right nephrectomy was therefore performed.

Macroscopic examination showed a surgical specimen measuring 2.4 × 2 cm containing a well-defined, firm, brownish nodule measuring 2 × 1.4 × 0.9 cm, located 2 mm from the nearest surgical margin. The renal capsule was intact with focal hemorrhagic areas.

Microscopically, the tumor consisted of large eosinophilic cells with finely granular cytoplasm arranged in nests and trabeculae. No significant nuclear atypia, mitotic activity, or necrosis was observed. Immunohistochemistry revealed diffuse CD117 and cyclin D1 expression, with negative AMACR and absent or focal CK7 staining, supporting the diagnosis of renal oncocytoma.

Conclusion

Renal oncocytoma is a benign tumor with an excellent prognosis; however, its close resemblance to malignant renal neoplasms may complicate diagnosis. Careful histopathological evaluation supported by immunohistochemistry is essential for accurate classification and appropriate clinical management.



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sciforum-178432: SNHG6-centered RNA regulatory network links epithelial plasticity and apoptosis signaling in breast cancer

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Introduction

Regulatory interactions among long non-coding RNAs (lncRNAs), microRNAs (miRNAs), and mRNAs play an important role in epithelial plasticity and tumor progression in breast cancer. However, the network-level organization of these RNA-mediated regulatory interactions remains insufficiently characterized.

Methods

Candidate EMT-associated regulators were identified through integrative bioinformatic screening of GEO and TCGA-BRCA datasets together with curated interaction databases. Expression of selected coding and non-coding RNAs was quantified in 40 paired primary breast tumors and adjacent normal tissues using RT-qPCR. Correlation and partial-correlation analyses were applied to identify candidate lncRNA-miRNA-mRNA regulatory modules consistent with the competing endogenous RNA (ceRNA) framework. Network reconstruction and functional enrichment analyses were performed to characterize the regulatory architecture of the identified interactions.

Results

Correlation-based analysis identified several candidate ceRNA modules centered on the lncRNA SNHG6, including SNHG6-miR-200c-3p-CDH1 and SNHG6-miR-16-5p-CDH1 axes. In addition, a SNHG6-miR-16-5p-BCL2L1 module linked EMT-associated regulatory circuits with apoptosis signaling. Network reconstruction revealed a compact regulatory network in which SNHG6 connected two key miRNA regulators (miR-200c-3p and miR-16-5p) with EMT- and stemness-associated genes including CDH1, SOX4, BMI1, and BCL2L1. Functional enrichment analysis highlighted biological processes related to epithelial differentiation and stem cell regulation and identified cancer-associated pathways including Hippo signaling, cadherin signaling, and apoptosis-related pathways.

Conclusions

These findings identify an SNHG6-centered RNA regulatory network linking epithelial plasticity, stemness-associated transcriptional programs, and apoptosis-related signaling in breast cancer and suggest candidate regulatory axes for future functional validation.

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sciforum-178431: Targeting the USP8-PTK7-PIK3CB Axis: A Novel Mechanism Accelerating Malignant Progression in Pancreatic Cancer

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Introduction: Protein tyrosine kinase 7 (PTK7) is significantly upregulated in pancreatic cancer (PC), yet its precise molecular mechanisms in driving tumor progression remain elusive. This study investigates the regulatory interplay between PTK7, USP8, and PIK3CB in PC pathogenesis.

Methods: PTK7 mRNA and protein levels in PC cell lines were assessed using PCR and WB, respectively. Macrophage M2 polarization was evaluated by co-culturing THP-1-derived macrophages with PC cell-conditioned medium, followed by flow cytometric analysis of CD206+ cells. Co-immunoprecipitation (CoIP) assays were conducted to determine PTK7 interactions with USP8 and PIK3CB. *In vivo* xenograft models were utilized to assess PTK7 knockdown and PIK3CB overexpression on PC tumorigenesis.

Results: PTK7 expression was markedly elevated in PC tumor tissues and cell lines, correlating with aggressive disease phenotypes. Silencing PTK7 significantly reduced PC cell proliferation, invasion, and macrophage M2 polarization, while concurrently promoting apoptosis, indicating its critical role in tumor progression and immune evasion. Mechanistically, USP8 was identified as a key regulator of PTK7 stability through deubiquitination. Knockdown of USP8 suppressed PC cell growth and invasion, effects reversed by PTK7 overexpression, highlighting the dependence of PC cells on the USP8-PTK7 axis. CoIP assays confirmed a direct interaction between PTK7 and PIK3CB, with PIK3CB overexpression abrogating the tumor-suppressive effects of PTK7 silencing. This suggests that PTK7 exerts its oncogenic effects, at least in part, by activating PIK3CB. Further investigation revealed that USP8 positively regulates PIK3CB expression via PTK7, thereby activating the PI3K/AKT pathway a well-established driver of cell survival, proliferation, and metastasis. *In vivo* studies corroborated these findings, demonstrating that PTK7 knockdown significantly impaired tumorigenesis by downregulating PIK3CB, thereby inhibiting the PI3K/AKT signaling cascade.

Conclusion: The USP8-PTK7-PIK3CB axis promotes PC progression, presenting a novel and actionable therapeutic target for intervention.



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sciforum-178156: The hypertrophic adipocyte niche fuels metabolic plasticity and invasive signaling in colorectal cancer

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Background

Obesity is a major risk factor for aggressive colorectal cancer (CRC), yet how dysfunctional adipose tissue shapes tumor behavior remains unclear. In particular, the role of obesity-associated adipocytes in driving tumor metabolic heterogeneity and phenotypic plasticity is poorly defined. Here, we investigated whether hypertrophic adipocytes establish a metabolic niche that promotes distinct metabolic states and invasive phenotypes in CRC cells through direct cell-cell communication.

Methods

HCT-116 CRC cells were co-cultured with SGBS human adipocytes differentiated into mature or hypertrophic (obese) phenotypes. Untargeted LC-MS metabolomics was conducted on tumor lysates, adipocyte lysates, and conditioned media. Multivariate (PCA, PLS-DA) and univariate statistical approaches (Welch's ANOVA with Games-Howell post-hoc correction) identified differential metabolites and pathway alterations. Western blotting assessed ECM components (fibronectin, integrin $\alpha 5$), fatty acid oxidation (CPT1A), lipogenesis (FASN), and oncogenic signaling (Akt/mTOR).

Results

Adipocyte-tumor interaction induced profound metabolic reprogramming, evidenced by elevated glycolytic intermediates, altered TCA cycle flux (increased citrate and α -ketoglutarate; decreased malate), and enhanced glutaminolysis (glutamate/glutamine accumulation). Metabolic exchange was pronounced in supernatants, showing glucose depletion alongside elevated lactate, succinate, methionine, and purine metabolites. Notably, hypertrophic adipocytes specifically upregulated fibronectin, integrin $\alpha 5$, CPT1A, and FASN expression, concomitant with Akt/mTOR activation, linking lipid-rich microenvironments to invasive signaling.

Conclusions

These findings demonstrate that obesity-associated adipocytes actively reshape the tumour microenvironment by promoting metabolic heterogeneity in CRC, characterized by enhanced glycolysis, glutaminolysis, and ECM remodeling. This adipocyte-tumour metabolic axis drives invasive phenotypes and highlights actionable metabolic vulnerabilities for therapeutic intervention.



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sciforum-154893: Transcriptome differences revealed by high-plex digital spatial profiling associated with endocrine sensitivity for hormone receptor-positive/human epidermal growth factor receptor 2-negative (HR+/HER2-) early breast cancer (EBC)

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Objective: This study aims to explore the spatial and transcriptome differences associated with endocrine sensitivity in HR+/HER2- EBC.

Methods: Postoperative FFPE samples of patients with HR+/HER2- EBC were collected. All patients received adjuvant tamoxifen after surgery. The follow-up period was ten years. Based on disease-free survival, patients were stratified into the ET-resistant and ET-sensitive groups. A total of 111 spatially resolved regions in three tissue compartments defined by morphology markers [tumor (PANCK+), leucocytes (CD45+), and nonimmune stroma (CD45-/PANCK-)] were assessed based on GeoMx digital spatial profiling. ET-associated genes were collected from over 5,000 published articles. Enrichment analyses were performed using multiple bioinformatics approaches.

Results: A specific panel comprising 235 ET-related genes was constructed. In PANCK+ regions, 11 upregulated and 7 downregulated differentially expressed genes (DEGs) were identified when comparing the ET-resistant with the ET-sensitive group, with GATA3 showing the most differential expression. A total of 44 KEGG pathways were enriched, among which Th1 and Th2 cell differentiation had the greatest significance ($p=6.25E-4$). GO functions were mainly enriched in the nucleus, nucleoplasm, and negative regulation of transcription. In CD45+ regions, 14 upregulated DEGs were found, with most enriched in the HER signaling pathway ($p=5.57E-08$). Cellular activities, including protein serine/threonine kinase activity, protein phosphorylation, and protein kinase activity, were profoundly enriched. In CD45-/PANCK- regions, 21 upregulated and 6 downregulated DEGs were detected in the ET-resistant group versus the ET-sensitive group. Proteoglycans in cancer ($p=3.98E-07$) and signaling pathways regulating the pluripotency of stem cells ($p=8.70E-07$) showed higher statistical significance. GO functions were mainly enriched in the nucleus, nucleoplasm, and positive regulation of transcription by RNA polymerase II.

Conclusion: Our study first shows transcriptome heterogeneity among patients with different responses to ET across three PANCK+ (CD45+ and CD45-/PANCK-) regions. This may provide a reference for exploring molecular mechanisms of endocrine resistance.



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sciforum-178434: Tumor-associated miR-124 and miR-137 in post-transcriptional regulation of ovarian cancer

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Introduction: Ovarian cancer (OvCa) exhibits high mortality due to asymptomatic progression and early metastasis. Long noncoding RNAs (lncRNAs) and miRNAs are vital regulators and potential therapeutic targets. We investigated the ceRNA (lncRNA/miRNA/mRNA) mechanisms involving miR-124 and miR-137 in OvCa.

Methods: Bioinformatics screening of targets for miR-124 and miR-137 used GSE211669 and GSE119055 datasets (NCBI GEO). SKOV3 and OVCAR3 cells were transfected with miR-124-3p and miR-137-3p mimics, followed by Affymetrix HTA 2.0 microarray analysis. Expression of lncRNAs and mRNAs was validated via RT-qPCR in 56 paired (T/N) clinical OvCa samples using TaqMan assays.

Results: Bioinformatics identified lncRNAs *GAS5*, *MEG3*, *ZNF667-AS1*, and 15 mRNA targets (r -0.6, 7-8mer sites). Experimental validation in cell cultures and clinical samples confirmed the following regulatory axes:

GAS5
/ miR-124-3p, -5p /
ANAPC1, *HLTF*, *IL15*, *PARP14*, *TRAF3*, *ZEB1*
;
GAS5, *MEG3*, *ZNF667-AS1*
/ miR-137-3p /
ANAPC1, *HLTF*, *RNF169*, *TRAF3*, *VIM*, *ZEB1*
.

Strong positive correlations between lncRNAs and target mRNAs (p 0.05) support the ceRNA sponging mechanism.

Conclusions: The observed findings may reflect intratumoral heterogeneity in ovarian cancer. The identified ceRNA axes exhibit variability in both expression levels and the strength of correlation patterns across clinical samples, which may be attributed to differences in molecular subtypes, cellular composition, and the extent of epithelial-mesenchymal transition. Regulation of key genes, including *ZEB1*, *VIM*, and *TRAF3*, through lncRNA/miRNA/mRNA networks likely contributes to the emergence of functionally distinct tumor cell subpopulations, including those with increased metastatic and immunosuppressive potential. Collectively, these findings suggest that the identified ceRNA networks may act not only as regulatory frameworks but also as indicators of tumor molecular heterogeneity, with potential implications for patient stratification and the development of personalized therapeutic strategies.



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sciforum-170326: Unraveling the role of extracellular vesicle-mediated interleukin-8 signaling in melanoma invasion

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Introduction

Metastasis is a critical step in tumor progression and represents the main cause of melanoma-related mortality. This process is sustained by dynamic intercellular communication among heterogeneous tumor cell populations within the tumor microenvironment. Tumor-derived extracellular vesicles (EVs) have emerged as key mediators of this crosstalk, as they shuttle bioactive molecules capable of reprogramming recipient cells. However, the contribution of EVs to the horizontal transfer of metastatic traits within melanoma cell populations remains incompletely understood.

Methods

We investigated the effects of EVs released by aggressive melanoma cell lines (A375M and SM) on poorly invasive A375P cells. EVs were isolated and characterized, and phenotypic as well as functional changes in recipient cells were assessed following EV exposure. Molecular mechanisms were explored by analyzing EV cargo composition, neutralizing IL-8 activity, inhibiting NF- κ B signaling, and stimulating cells with recombinant IL-8.

Results

EVs derived from aggressive melanoma cells induced marked phenotypic and functional changes in A375P cells, including elongated morphology, increased migratory and invasive capacity, resistance to anoikis, anchorage-independent growth, enhanced re-adhesion, and increased clonogenic potential. Mechanistically, these effects were driven by IL-8 enrichment in aggressive melanoma-derived EVs. Neutralization of IL-8 or pharmacological inhibition of the NF- κ B pathway completely abolished EV-induced phenotypes, whereas stimulation with recombinant IL-8 was sufficient to recapitulate them.

Conclusions

These findings demonstrate that melanoma-derived EVs promote invasive and metastatic traits in recipient cells through activation of the IL-8/NF- κ B axis, highlighting this signaling pathway as a potential therapeutic target in advanced melanoma.



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Session 3. Drug Resistance and Anti-cancer Drug Development and Screening

sciforum-169648: “Exploring the Antioxidant and Anticancer Activity of *Clematis heynei*, an Endemic Medicinal Plant of the Western Ghats”

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Introduction

Clematis heynei (CH) is a medicinal plant endemic to the Western Ghats of Maharashtra and is traditionally used in indigenous healthcare practices. Despite its ethnomedicinal relevance, scientific validation of its bioactive potential remains limited. This study aimed to evaluate the antioxidant properties and *in vitro* anticancer activity of ethanolic leaf extracts of *C. heynei*.

Methods

Ethanolic extracts of *C. heynei* leaves were subjected to phytochemical analysis to determine total phenolic and flavonoid contents, along with ferric reducing antioxidant power (FRAP). Antioxidant activity was assessed using DPPH and ABTS radical scavenging assays. Anticancer potential was evaluated in HeLa cervical cancer cells through cell viability assays, morphological observation, wound healing, clonogenic assays, and cytological staining, including Hoechst nuclear staining.

Results

Phytochemical analysis revealed a higher flavonoid content compared to total phenolic content, accompanied by notable ferric reducing capacity. Antioxidant assays showed strong ABTS radical scavenging activity, while DPPH scavenging was comparatively moderate. In HeLa cells, the CH extract induced concentration-dependent reductions in cell viability, with evident morphological changes such as cell rounding and structural disruption. Wound healing and clonogenic assays demonstrated significant inhibition of cell migration and colony formation, even at lower extract concentrations. Cytological staining revealed dose-dependent cytoplasmic granulation, membrane blebbing, and loss of membrane integrity, while Hoechst staining indicated increased apoptotic cell populations at higher doses.

Conclusion

Overall, *C. heynei* exhibits significant antioxidant and *in vitro* anticancer potential, supporting its traditional medicinal use and highlighting the need for further phytochemical characterization and mechanistic studies.



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sciforum-177243: Induction of apoptosis by extracts from transformed hairy roots of *Plectranthus venteri* in an in vitro cancer model

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Introduction

Plectranthus venteri Van Jaarsv. & Hankey, an endemic species of the Lamiaceae family, is a potential source of biologically active secondary metabolites. There are no studies on the anticancer activity of extracts from transformed roots of this species. The aim of this study was to evaluate the cytotoxic and proapoptotic effects of extracts from *P. venteri* hairy roots in an in vitro cell model and to provide a preliminary characterization of their mechanism of action.

Methods

Transformed roots were cultured in vitro and then freeze-dried, ground, and extracted with methanol and acetone. The extracts were profiled using HPLC-ESI-QTOF-MS/MS. Cytotoxicity was assessed using the MTT assay in breast cancer cell lines (MCF-7). The mechanism of action was analyzed by determining caspase 3/7 activity, mitochondrial membrane potential ($\Delta\Psi_m$), and the expression of pro- and antiapoptotic genes using RT-qPCR.

Results

The MTT assay demonstrated a cytotoxic effect of the extract from transformed *Plectranthus venteri* roots on MCF-7 breast cancer cells, with an insignificant influence on normal human fibroblast HGF-1 cells. A dose-dependent loss of $\Delta\Psi_m$ and activation of caspases 3/7 were observed. Molecular analysis indicated an increase in BAX/CASP3/CASP9 and a decrease in BCL2/TP53 expression, suggesting the involvement of the mitochondrial pathway in the induction of apoptosis.

Conclusions

Extracts from transformed roots of *P. venteri* may represent a potential source of anticancer activity. These studies constitute the first data on the biological activity of this species and provide a basis for further phytochemical and biological analyses.



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sciforum-171776: Folate-Functionalized Mesoporous Silica Nanoparticles for Targeted Delivery of Mebendazole in FR+ BREAST Cancer Cells

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Breast cancer is the most frequently diagnosed cancer among women worldwide. In recent years, mebendazole (MBZ), an orally available FDA-approved anthelmintic drug, has gained attention as a repurposing candidate in oncology due to its anticancer activity across multiple tumor types, including breast cancer; however, its clinical translation is limited by low oral bioavailability. To overcome this limitation and enhance tumor targeting, we developed a folate-functionalized mesoporous silica nanoparticle system (FOL-MSN-MBZ) for the delivery of MBZ to folate receptor-positive (FR⁺) breast cancer cells, including tamoxifen-resistant and triple-negative breast cancer (TNBC) models.

FOL-MSN-MBZ was synthesized by covalently grafting folic acid (FOL) onto the surface of MSNs, followed by MBZ loading through a two-step impregnation process (drug loading: 8.80%). The cytotoxic activity of free MBZ was evaluated using MTT assays. The selective efficacy of FOL-MSN-MBZ was assessed in FR⁺ breast cancer cell lines—MCF-7, tamoxifen-resistant MCF-7 (TamR), TamR T47D, MDA-MB-231, and MDA-MB-468—and in FR[−] normal 3T3-L1 fibroblasts, using cell proliferation and clonogenic assays. The efficacy of the nanosystem was further evaluated in 3D breast cancer models.

Our data demonstrate that FOL-MSN-MBZ effectively induces selective cell death in all FR⁺ breast cancer cell lines, while sparing normal FR[−] 3T3-L1 fibroblasts. The nanosystem also inhibits clonogenic potential in tumor cells and reduces spheroid size and viability in 3D breast cancer models. In contrast, free MBZ demonstrated cytotoxic effects across all tested cell lines, including the non-cancerous ones.

Our results indicate that FOL-MSN-MBZ enables targeted delivery of MBZ, inducing cytotoxicity specifically in FR⁺ tumor cells while sparing normal cells, suggesting that the nanosystem can reproduce the antitumoral effects of the free drug with enhanced tumor specificity. This study was supported by NextGenerationEU-PNRR e PRIN—Project Title “Drug repositioning as a safer and sustainable way to fight hard-to-treat cancer”—P2022T7FXB.



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sciforum-178449: Functional reactivation of p53 as a promising therapeutic strategy in the treatment of ovarian cancer

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Introduction: Ovarian cancer (OC) is the eighth leading cause of cancer-related death among women worldwide, with over 300,000 new cases and 200,000 deaths annually. It is characterized by late diagnosis, molecular heterogeneity, and poor survival (~40% at 5 years). Inactivation of the tumour suppressor p53, mainly caused by *TP53* mutations, occurs in more than 90% of high-grade serous carcinomas. Beyond loss of tumour-suppressive activity, mutant p53 (mutp53) frequently acquires oncogenic gain-of-function properties that promote tumour progression, immune evasion, and therapy resistance. Pharmacological reactivation of p53 therefore represents a promising therapeutic strategy. MANIO is a p53 activator capable of restoring wild-type-like activity to mutant p53. This study evaluated the anticancer potential of MANIO in OC.

Material and Methods: The anticancer effects of MANIO were evaluated as a single agent and combined with standard therapies using OC cell lines and patient-derived OC organoids. In vivo antitumor activity was assessed in xenograft mouse models harbouring mutant p53 by tumour volume measurements and immunohistochemical analyses. Statistical significance was determined using Student's t-test or ANOVA (*p* 0.05).

Results: MANIO showed selective antiproliferative activity in OC cells expressing wild-type or mutant p53, whereas p53-deficient cells were less sensitive. Cell-cycle analysis revealed G2/M arrest and increased sub-G1 population, consistent with apoptosis. In patient-derived OC organoids with different p53 statuses, MANIO induced dose-dependent growth inhibition, with IC50 values correlating with p53 status. MANIO also showed synergistic effects with oxaliplatin, paclitaxel, and olaparib. In vivo, it significantly inhibited tumour growth without evident toxicity. Immunohistochemical analyses revealed decreased proliferation, increased apoptosis, reduced angiogenesis, and downregulation of epithelial-mesenchymal transition markers.

Conclusion: MANIO demonstrates selective p53-dependent antitumor activity across OC models, including patient-derived organoids and xenografts, and enhances the efficacy of standard therapies. These findings support MANIO as a promising therapeutic strategy for ovarian cancer, particularly in tumours harbouring mutant p53.

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sciforum-178433: Impact of AgNPs on LLC cells

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Introduction. Silver nanoparticles (AgNPs) are widely applied in various fields: medicine, pharmaceuticals, agriculture and others. They are suggested to exhibit antibacterial, antifungal, antiviral and anticancer activities. However, their effects depend on particle size, shape, physicochemical properties, synthesis method and target biological system. Lewis Lung Carcinoma (LLC) cells are an aggressive tumor model characterized by high oncogenicity and relative resistance to a range of anticancer drugs. The purpose of this study was to assess the influence of AgNPs on LLC cells in terms of cytotoxicity, apoptotic gene expression and potential genotoxicity.

Methods. LLC cells were obtained from the Cell Bank of the R.E.Kavetsky Institute of Experimental Pathology, Oncology and Radiobiology of the NAS of Ukraine and were cultured according to standard methods. Colloidal silver concentrate coated with natural resin was manufactured by Noble Elements LLC (USA). Nominal particle size was 10 ± 2 nm and a silver concentration of 20000 ppm was used. Cytotoxicity of AgNPs was determined using the MTT assay. The studied concentration of NPs was 10-1000 ppm. Evaluation of apoptosis-associated gene expression was carried out with RT-qPCR analysis and amplification with primers to short nucleotide repeats was performed to determine the genotoxicity effect.

Results. The results indicated that the IC_{50} value of AgNPs was 750 ppm; concentrations of 320 and 640 ppm were selected for the subsequent research. Analysis of apoptosis-related gene transcriptional activity showed slight changes in p53 and caspase 3 and 8 expression in treated LLC cells. The comparative analysis of PCR product patterns revealed differences between control and treated samples. The most prominent differences, characterized by the absence of some amplicons in the banding profile, were observed in LLC cells treated at 640 ppm.

Conclusions. The data suggest that the inhibitory effect of investigated AgNPs on LLC cell viability is more likely to involve oxidative stress response mechanisms rather than the apoptotic pathway.



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sciforum-171346: Specific expression profile of genes associated with extracellular matrix and phenotypic plasticity in triple-negative breast cancer

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The tumor extracellular matrix (ECM) promotes the phenotypic plasticity of tumor cells, a key mechanism of metastasis and therapeutic resistance. Therefore, ECM is considered a promising therapeutic target for various cancer subtypes.

The aim of the study was to determine the expression profile of genes associated with ECM and phenotypic plasticity specific to triple-negative breast cancer (TNBC), and to evaluate its prognostic relevance.

To identify differentially expressed genes (DEG), we analyzed datasets (GSE65194, GSE45827) from the NCBI GEO. Both datasets have identical composition: 155 samples in total, of which 41 are TNBC samples and 11 are samples of normal breast tissue. The list of genes of interest was compiled based on data from MatrisomeDB and MSigDB. DEG analysis ($|\log_2FC| > 1$, $p > 0.05$) was performed using a software tool, which was developed using Python (pandas, numpy, matplotlib) and R. The prognostic significance ($HR \neq 1$, $p > 0.05$) was assessed by overall survival (OS) in basal-like cohorts using the KM-Plotter, comparing the first and fourth quartiles.

The analysis covered 1,027 genes. 31 genes with differential expression specific for TNBC compared to normal tissue and other BC subtypes were identified (14 elevated, 17 decreased). A significant relationship was found between the level of gene expression and OS for genes: CLEC4A, CLEC7A, IFNG, COL22A1, CRLF3, HPSE, CXCL12, OMD, and HTRA1. High expression of upregulated genes and low expression of downregulated genes were both associated with improved survival. Except for CXCL12 and OMD, which were downregulated, their high expression was associated with improved survival.

Our findings indicate that TNBC exhibits a specific expression profile of genes associated with ECM and phenotypic plasticity. We assume that some of these genes may be promising candidates for therapeutic targeting, as has also been reported by other researchers.

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sciforum-178429: Synergistic Chemo-Immunomodulation via Nanocarrier Co-Delivery of Doxorubicin and Pexidartinib

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Introduction: Despite the widespread use of doxorubicin (DOX) as a chemotherapeutic agent, its effectiveness is often limited by the development of resistance in various cancers. Therefore, combination therapy has gained increasing attention as an effective strategy to enhance doxorubicin's efficacy and overcome resistance in cancer cells. Pexidartinib (PLX), a colony-stimulating factor 1 receptor inhibitor, decreases immunosuppressive tumor-associated macrophages and reprograms the functions of the remaining macrophages, which may help reverse chemoresistance. Consequently, developing a nanosystem capable of efficiently co-delivering PLX and DOX while addressing the challenges associated with dual drug delivery is expected to overcome resistance mechanisms and improve therapeutic outcomes. **Methods:** We designed and characterized a crosslinked nanoparticle based on β -cyclodextrin (β -CD) for effective co-delivery of DOX and PLX. The physicochemical properties of the nanoparticles were characterized, and their therapeutic efficacy was evaluated in vitro and in vivo. **Results:** The nanoparticles exhibited an average particle size of ~ 100 nm and a zeta potential of around +2 mV, indicating excellent stability. The entrapment efficiency exceeded 90% for both drugs. The release profile of DOX from the nanoparticles showed a pH-dependent pattern, with preferential release at pH 5 compared to physiological pH. Synergistic effects between DOX and PLX were observed in colorectal and breast cancer cell lines, with combination index (CI) values consistently below 1 across multiple drug ratios. Biodistribution and deep tissue penetration studies demonstrated preferential accumulation in tumor tissue over normal tissue. Moreover, the co-loaded nanoparticles significantly improved therapeutic efficacy compared with single-drug treatments in a subcutaneous MC38 tumor model. Flow cytometry analysis revealed increased CD8⁺ and decreased exhausted CD4⁺ cells after combination therapy. **Conclusion:** These results demonstrate that the co-delivery of DOX and PLX using a crosslinked nanoparticle system provides a promising strategy to enhance anticancer efficacy and overcome chemoresistance.



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sciforum-176650: A Tetramethylpyrazine-Releasing Hydrogel Potentiates CAR-T Cell Therapy Against Triple Negative Breast Cancer by Reprogramming Tumor Vasculatures

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Background and Purpose:

Chimeric antigen receptor T (CAR-T) cell therapy has shown limited efficacy in solid tumors like triple-negative breast cancer (TNBC), largely due to the immunosuppressive tumor microenvironment characterized by hypoxia resulting from abnormal vasculature. Tetramethylpyrazine (TMP), an active component of the traditional Chinese medicine *Ligusticum wallichii*, possesses vasomodulatory properties, yet its potential to enhance CAR-T therapy via vascular remodeling remains unexplored. This study aims to investigate whether sustained intratumoral release of TMP can reprogram tumor vasculature to potentiate HER1-CAR-T cell therapy against TNBC.

Experimental Approach:

An injectable, hydrogen peroxide-responsive hydrogel (PEGDMA/FeCl₂) was developed for sustained intratumoral delivery of TMP (TMP@PEGgel). Its effects on vascular endothelial cells were assessed by evaluating VEGF expression, eNOS phosphorylation, and NO production. In TNBC-bearing mice, TMP@PEGgel was intratumorally injected, followed by intravenous administration of HER1-CAR-T cells. Tumor vascular normalization, hypoxia relief, CAR-T cell infiltration, survival, effector function, and therapeutic efficacy were comprehensively evaluated.

Results:

TMP treatment activated VEGF expression and the eNOS/NO axis in endothelial cells, promoting angiogenesis and vascular maturation. TMP@PEGgel enabled sustained intratumoral release of TMP, leading to prolonged vascular remodeling and significant alleviation of tumor hypoxia. This improved tumor microenvironment facilitated enhanced infiltration, prolonged survival, and augmented effector cytokine secretion (IL-2, TNF- α , IFN- γ) of HER1-CAR-T cells. Consequently, TMP@PEGgel-assisted HER1-CAR-T therapy synergistically suppressed TNBC tumor growth, achieving complete regression in some cases, without notable toxicity.

Conclusions and Implications:

TMP@PEGgel-mediated tumor vascular reprogramming effectively relieves hypoxia and enhances the therapeutic potency of HER1-CAR-T cells against TNBC. This study presents a novel and translatable strategy to potentiate adoptive cell therapy by remodeling the tumor vasculature using a traditional medicine-derived agent.



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sciforum-171550: An RNA Sequencing approach for the identification of anticancer effects of Docetaxel in cervical cancer

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This study aims to systematically elucidate the molecular basis of the response to chemotherapeutic agents in cervical cancer cells using an RNA-sequencing-based comprehensive screening approach. The main focus of the research is to characterize cellular responses and resistance mechanisms to docetaxel, a widely used microtubule inhibitor, at the transcriptomic level.

In this context, human cervical cancer-derived HeLa and C-4 I cell lines were treated with six different doses of docetaxel (25–800 nM). An MTT assay based on mitochondrial dehydrogenase activity was performed to determine cytotoxic effects and IC₅₀ values. Subsequently, treatment-induced gene expression changes were examined using high-resolution RNA sequencing, and signaling pathways associated with differential gene expression were analyzed using bioinformatics methods.

The findings revealed that docetaxel exhibited a clear antiproliferative effect in both cell lines and that this effect was primarily mediated through the apoptosis and necroptosis cell death mechanisms. RNA-seq analyses showed that key signaling pathways such as MAPK, TNF, NF-κB, and JAK-STAT play an active role in the response to treatment. Apoptosis in HeLa cells was associated with the *BIRC3*, *TRAF1*, *TUBAL3*, and *ERN1* genes, while necroptosis was associated with the *BIRC3*, *PYGL*, *TNFAIP3*, and *CHMP6* genes. In C-4 I cells, numerous genes associated with apoptosis (*BIRC3*, *TRAF1*, *BBC3*, *GADD45A*, *CTSL*, *PMAIP1*, *TUBA1A*, *FOS*, *DDIT3*, and *ERN1*) were identified; additionally, the cell cycle was found to be suppressed via genes such as *ORC1*, *MCM5*, *CCND3*, *CDKN1A*, and *KIF2C*.

In conclusion, this study is one of the pioneering studies that reveals the antiproliferative effects of docetaxel in cervical cancer cell lines and the underlying molecular mechanisms using a comprehensive RNA sequencing-based approach. The findings contribute to the identification of molecular markers of chemotherapy response and provide an important scientific basis for understanding resistance mechanisms and developing targeted treatment strategies.



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sciforum-171523: Anti-cancer Drug Development by Rapid and Synchronized Dormancy-Breaking Kyoho Grape Seed Endosperm

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[Background/Aims] We evaluated the direct cytotoxic effects and toxicity of a dried powder sample derived from Japanese Kyoho grapes. This sample utilized a digestive and absorption treatment process designed for oral administration, without extraction or concentration. The sample rapidly and synchronously broke seed dormancy and promoted phase transitions in its constituents. We assessed the effects on human pancreatic cancer, breast cancer, and liver cancer cells, as well as on fibroblasts as normal cells. Furthermore, we investigated the immune-activating effects using human natural killer cells. Evaluation methods employed a novel, proprietary 1h phenotypic screening method—high-precision surface plasmon resonance (HP-SPR-3D)—used as an in vivo-like drug sensitivity test, along with cell assays.

[Results] For all cancers, concentration-dependent efficacy was observed, with effects noted at 2.5 mg/ml or higher and maximum efficacy at 5.0 mg/ml. Higher concentrations exhibited toxicity consistent with mitochondria shutdown, distinct from typical necrosis. In pancreatic cancer, efficacy equivalent to or exceeding that of doxorubicin, paclitaxel, and gemcitabine was achieved despite oral administration. Immune activation was observed from at least 3.75 mg/ml up to 5.0 mg/ml. At these concentrations, normal cells showed almost no effect. These findings indicate that the anti-cancer effects of rapidly and synchronously dormancy-breaking Kyoho grape seed endosperm result from both direct cancer cell killing and indirect immune-mediated effects, both occurring at the same physiologically active concentration. Based on the above, it is anticipated that synergistic effects, such as those achieved by combining two types of anti-cancer drugs, can be obtained simultaneously without side effects.



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sciforum-169854: Antiproliferative and apoptotic activity of Zedoary turmeric oil in human gastric carcinoma cells

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Antiproliferative and apoptotic activity of Zedoary turmeric oil in human gastric carcinoma cells

Abstract:

Gastric cancer remains a leading cause of cancer-related mortality worldwide, underscoring the urgent need for novel therapeutic strategies that combine efficacy with reduced systemic toxicity. Here, we report a comprehensive cellular and mechanistic investigation of the anticancer activity of Zedoary turmeric oil in the human gastric carcinoma cell line SGC-7901. Quantitative viability analyses demonstrate that Zedoary turmeric oil suppresses cancer cell proliferation in a dose- and time-dependent manner, with an IC_{50} of $104.96 \mu\text{g mL}^{-1}$ at 48 h. Morphological assessment reveals hallmark apoptotic features, including cell shrinkage, cytoplasmic condensation, and membrane blebbing, indicating activation of programmed cell death pathways.

Mechanistically, Zedoary turmeric oil induces a pronounced loss of mitochondrial membrane potential, identifying mitochondrial dysfunction as an early and central event in its anticancer action. This mitochondrial perturbation is accompanied by internucleosomal DNA fragmentation and a substantial increase in apoptotic cell populations, as confirmed by agarose gel electrophoresis and flow cytometry, respectively. Cell-cycle analysis further reveals a marked accumulation of cells in the sub-G1 phase, suggesting coordinated cell-cycle arrest and apoptosis induction. The convergence of mitochondrial depolarization, DNA fragmentation, and cell-cycle dysregulation supports a multi-level mechanism of action rather than nonspecific cytotoxicity.

Together, these findings establish Zedoary turmeric oil as a potent inducer of intrinsic apoptosis in gastric cancer cells and provide mechanistic insight into its therapeutic potential, laying a foundation for future translational and in vivo investigations.

Keywords

Zedoary turmeric oil; gastric cancer; SGC-7901; mitochondrial apoptosis; cell-cycle regulation



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sciforum-146470: Azadirachta indica PLGA nanoparticles potentiate antitumor activity, induce apoptosis, and suppress metastasis in murine breast cancer models

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Background: *Azadirachta indica* (Neem) contains bioactive triterpenoids such as nimbolide with anticancer potential, but poor solubility and bioavailability limit its use. We developed PLGA-based Neem extract nanoparticles (NE-PLGA NPs) to improve delivery, cytotoxicity, and in vivo efficacy against breast cancer.

Methods: Neem leaves were extracted with 80% ethanol, and NE-PLGA NPs were prepared by nanoprecipitation (extract:polymer 1:5 w/w). Nanoparticles averaged 128 ± 9 nm with 78% encapsulation efficiency and sustained release over 72 h. Cytotoxicity was assessed in MCF-7, 4T1, and A549 cells versus human dermal fibroblasts. In vivo efficacy was tested in BALB/c mice bearing orthotopic 4T1 tumors ($n = 10/\text{group}$), comparing vehicle, crude extract, NE-PLGA NPs, doxorubicin, and combination therapy. Tumor growth, metastasis, survival, and histological markers of proliferation, apoptosis, and angiogenesis were evaluated.

Results: NE-PLGA NPs significantly improved in vitro potency with IC₅₀ values of 4.8–8.5 $\mu\text{g/mL}$ compared to 22–34 $\mu\text{g/mL}$ for crude extract, while maintaining >85% fibroblast viability at 50 $\mu\text{g/mL}$. Synergy with doxorubicin (CI 0.44–0.67) enhanced cytotoxicity. In vivo, NE-PLGA NPs reduced tumor volume by 68% and prolonged median survival from 28 to 46 days ($p = 0.01$). Combination therapy achieved 89% tumor inhibition, suppressed lung metastasis by 94%, and yielded 80% long-term survival beyond 60 days. Immunohistochemistry confirmed marked apoptosis ($\uparrow$ caspase-3, $\uparrow$ TUNEL), reduced proliferation ($\downarrow$ Ki-67), and suppressed angiogenesis ($\downarrow$ VEGF). No hepatotoxicity, nephrotoxicity, or body weight loss was observed.

Conclusion: Neem-derived PLGA nanoparticles significantly potentiate antitumor activity, overcome resistance, and synergize with doxorubicin while remaining safe in vivo. NE-PLGA NPs represent a promising nanomedicine platform for future preclinical and translational anticancer development.



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sciforum-171661: Bioorthogonally Activatable Chlorin e6 Photosensitizer for Targeted Photodynamic Therapy: Photophysical and Biological Properties in vitro

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The application of photodynamic therapy is limited by the lack of selectivity of photosensitisers (PS) to tumour cells. This study employed bioorthogonal chemistry to enhance photosensitiser selectivity and improve tumour accumulation, using Chl-BCN, a chlorin e6 derivative with a carbohydrate moiety conjugated to cyclooctyne paired with tetrazine-containing targeting moieties YPB374 and YPB254 that selectively bind to biotin receptors on tumour cell surfaces. The two components interact via the inverse electron demand Diels–Alder reaction. The study aims to demonstrate that this bioorthogonal approach can enhance the selectivity of photosensitisers and improve tumour accumulation

The photophysical properties of conjugated and unconjugated photosensitisers were characterised by absorption and fluorescence spectroscopy following irradiation. The assessment of reactive oxygen species (ROS) generation quantum yield ($\Phi\Delta$) was conducted using ROS-sensitive chemical traps. We used a 1,3-diphenylisobenzofuran trap for dimethyl sulfoxide solutions and an anthracene-9,10-diylbis-methylmalonate trap to study singlet oxygen generation in phosphate-buffered saline solutions, with Photoditazine as standard. Photostability assessment was done by monitoring the fluorescence under increasing irradiation power.

In vitro cytotoxicity evaluation was done using the 3-(4,5-dimethyl thiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay in MDA-MB-231 breast cancer cells and non-malignant CHO cells following photodynamic activation at 20 J/cm² (655–675 nm).

The results showed intensive Soret (416 nm) and Q-band (640 nm) absorption with 644 nm fluorescence emission ($\Phi\Delta \sim 3\%$). Chl-BCN showed high photostability. Activation with YPB254/YPB374 significantly enhanced the quantum yield of ROS generation, up to 38.6% (3-fold compared to Chl-BCN alone); however, it reduced photostability by 10-fold. ROS generation was significantly more efficient in hydrophobic environments.

Chl-BCN showed minimal dark toxicity and photodynamic activity (IC₅₀ ~18.4 μ M) against cancer cells. Importantly, CHO cells maintained >80% viability at equivalent doses.

Chl-BCN demonstrates favourable spectra, potent ROS generation, and high stability. Its ability to selectively reduce tumor cell viability while sparing non-tumor cells shows its promising tumor-targeting potential



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sciforum-170524: Cellular Prion Protein (PrP^C) as a Therapeutic Target in Meningioma and Schwannoma Development and Multidrug Resistance

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Meningioma and schwannoma are common tumours of the nervous system that occur either sporadically or as part of NF2-related schwannomatosis (formerly neurofibromatosis type 2), a hereditary tumour predisposition syndrome. Despite their largely benign nature, recurrence rates approaching 50% and treatment options limited to surgery and radiotherapy highlight the urgent need for effective medical therapies and new therapeutic targets.

Our findings identify that the cellular prion protein (PrP^C) is consistently overexpressed in patient tissues and primary cells compared with normal controls and contributes to increased tumour cell proliferation, making it a novel therapeutic target in schwannoma [1] and meningioma tumours.

In both tumour types, PrP^C expression was driven by NFκB signalling, and pharmacological inhibition of NFκB using the clinically tested agent edasalonexent or the FDA-approved drug bortezomib significantly reduced proliferation in patient-derived 2D and 3D *in vitro* tumour models. Notably, these effects were observed at concentrations below those reported in the plasma of patients treated for other cancers.

Mechanistically, PrP^C promoted schwannoma [1] and meningioma cell survival and proliferation through interaction with the laminin receptor (LR/37/67 kDa) and activation of downstream AKT, FAK, and ERK signalling pathways. Disruption of the PrP^C-LR/37/67 kDa interaction effectively suppressed activation of these oncogenic pathways.

In addition, PrP^C knockdown significantly reduced the expression of multidrug resistance (MDR)-associated ABC transporters, MDR1 and MRP1, in patient-derived meningioma and schwannoma cells. PrP^C was expressed by both tumour cells and tumour-associated macrophages. Furthermore, radiation exposure increased PrP^C and MDR1 expression, suggesting that radiotherapy may promote multidrug resistance via PrP^C. Collectively, these results identify PrP^C as a central regulator of tumour signalling and drug resistance, making it a promising therapeutic target in sporadic and NF2-related meningiomas and schwannoma tumours.

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sciforum-178410: Combination of BBIT20 and Immunotherapy Enhances Antitumor Activity in Pancreatic Cancer

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Introduction: Pancreatic cancer (PC) is a hard-to-treat malignancy characterized by its highly aggressive tumor biology and a strongly immunosuppressive tumor microenvironment. Due to its characteristics, immune checkpoint inhibitors, such as anti-PD-1 antibodies, have yielded limited outcomes in this disease. Targeting DNA damage repair pathways has shown to improve tumor immunogenicity, potentiating immunotherapy efficacy. BBIT20, a monoterpene indole alkaloid derivative, is a first-in-class inhibitor of the homologous recombination DNA damage repair pathway. This work used a syngeneic model of PC to explore the potential of BBIT20 to inhibit tumor growth by promoting immune-mediated responses, alone or in combination with anti-PD-1 immunotherapy. **Methods:** KPC cells were injected subcutaneously into C57BL/6J mice, which were then treated with a vehicle, BBIT20 (2 mg/kg), anti-PD-1 (100 µg/animal), or both. Tumor progression was monitored by caliper measurements, and tumors were collected at the experimental endpoint. PD-L1 expression and levels of inflammatory mediators and immune cell populations, including cytotoxic T lymphocytes and macrophage subsets were assessed by immunohistochemistry. **Results:** BBIT20 reduced disease progression while anti-PD-1 alone produced only a modest inhibitory effect, when compared with vehicle-treated animals. The combination of both agents significantly enhanced the antitumor response, indicating a synergistic effect relative to each treatment alone. Immunohistochemical analyses are currently being conducted to investigate treatment-associated alterations in immune cell activation and infiltration within PC tumors. Quantification of PD-L1, CD8, and CD206, and additional markers is in progress, with BBIT20-treated tumors exhibiting decreased PD-L1 expression. **Conclusions:** BBIT20 revealed a synergistic effect with anti-PD-1 in PC, potentiating tumor growth inhibition and reducing PD-L1 expression. These findings support the ability of BBIT20 to improve immunotherapy efficacy in PC through immune-stimulating activity. **Acknowledgments:** This work received support from the PT national funds (FCT/MECI) through the project 2024.13556.PEX (<https://doi.org/10.54499/2024.13556.PEX>).



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sciforum-178158: Confined migration-derived breast cancer sublines reveal subtype-specific responses to Arp2/3 inhibition

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Introduction: Cancer cell migration through confined tissue spaces (CM) leads to the development of a pro-migratory phenotype. The Arp2/3 complex aids in cell movement, creating branched actin networks, and can be blocked by CK-666. We examined how CM-derived sublines of low-metastatic MCF7 and high-metastatic MDA-MB-231 change their mechanics, proliferation, and collective migration in response to CK-666.

Methods: Parental and CM sublines of MDA-MB-231 and MCF7 were generated by three rounds of CM through 8 μm pores. Young's modulus was measured by scanning ion-conductance microscopy. Proliferation, fraction of DNA-replicating cells and collective migration were detected by SRB, Ki67 immunofluorescence and wound healing assays, respectively, at 24 h after treatment.

Results: CM-derived MDA-MB-231 and MCF7 sublines were significantly softer compared to parental counterparts (1051 ± 624.2 vs. 786.4 ± 531 Pa and 2446 ± 1391 vs. 1614 ± 1198 Pa, respectively, all $p < 0.05$). CM-derived MCF7 cells showed 17.5% ($p = 0.0097$) increased viability relative to parental cells after CK-666 treatment, while MDA-MB-231 cells remained unaffected. CK-666 treatment reduced DNA-replicating fraction in MDA-MB-231 CM cells to $23.0 \pm 2.4\%$ ($p = 0.0018$) vs. $39.9 \pm 1.54\%$ in controls. No significant change was observed in parental cells or in MCF7 cells. CK-666 markedly decreased the migration of parental MDA-MB-231 cells ($17.8 \pm 5.25\%$ vs. $34.3 \pm 6.3\%$) and stopped the migration of CM MDA-MB-231 cells (no closure vs. $25.4 \pm 11.0\%$ in controls). CK-666 treatment also diminished collective migration of parental MCF7 cells ($5.28 \pm 3.8\%$ vs. control $18.3 \pm 1.1\%$), while CM MCF7 cells retained substantial wound closure ($10.9 \pm 1.37\%$ vs. control $22.9 \pm 3.2\%$).

Conclusions: CM-related softening is accompanied by subtype-specific functional responses to Arp2/3 inhibition. In high-metastatic MDA-MB-231, CM and Arp2/3 blockade together shift cells into a viable but low-proliferation, migration-defective state. In contrast, in low-metastatic MCF7, the softened CM subline preserves higher proliferation and substantial motility under CK-666, suggesting more Arp2/3-independent, mechanically adapted migration and a more drug-tolerant phenotype.



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sciforum-172868: CRISPR/Cas9-mediated knockout of c-Met reduces gemcitabine resistance in pancreatic cancer

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Background

Pancreatic cancer is one of the most lethal malignancies, and resistance to gemcitabine remains a major obstacle to effective treatment. The receptor tyrosine kinase c-Met has been widely associated with tumor progression and the development of chemoresistance. In this study, we explored whether CRISPR/Cas9-mediated knockout of c-Met could reduce gemcitabine resistance in pancreatic cancer cells.

Methods

c-Met expression was first examined in PANC-1 and AsPC-1 cell lines using RT-qPCR. The sensitivity of these cells to gemcitabine was then evaluated by determining IC₅₀ values using the MTS assay. A CRISPR/Cas9 vector carrying two guide RNAs targeting c-Met was constructed and introduced into the cell line showing higher c-Met expression. After puromycin selection, single-cell clones were isolated, and successful gene knockout was verified by genomic PCR and Sanger sequencing.

Results

AsPC-1 cells exhibited higher c-Met expression and were therefore selected for further experiments. Genomic PCR and Sanger sequencing confirmed efficient disruption of the c-Met gene in selected clones. c-Met knockout led to reduced cell growth and proliferation. Notably, gemcitabine IC₅₀ values were significantly lower in c-Met-deficient clones compared with control cells.

Conclusions

Knockout of the c-Met gene in ASPC-1 cells using the CRISPR/Cas9 system significantly decreased drug resistance to gemcitabine. This research underscores the potential therapeutic advantage of targeting c-Met to overcome chemoresistance in pancreatic cancer, offering a hopeful path for enhancing gemcitabine treatment results.



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sciforum-176945: Decreased susceptibility to death and proliferation inhibition with buthionine sulfoximine by oncogenic *RAS* transformation

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The relationship between intracellular glutathione (GSH) content and tumor growth remains an important area of research, and *RAS* genes are among the most mutated proto-oncogenes in cancer. Using optical microscopy and flow cytometry techniques, we have examined the effect of the glutathione (GSH) synthesis inhibitor buthionine sulfoximine (BSO) on cell growth and death in mouse embryonic and *RAS*-transformed 3T3 fibroblasts. Regarding 3T3 cells and in normal culture conditions, we observe that *RAS* cells reach higher cell densities as they gradually approach quiescence, are smaller in size, exhibit changes in morphology and distribution (a marked reticular structure with abundant cells at the nodes), and are less attached to the substrate. Our data show that 48 and 72 hours after plating the 3T3 cells, there is: (i) a decrease (directly proportional to the concentration of BSO (25, 50 and 100 μ M) in the number of adherent cells and (ii) also cell death with 100 μ M of BSO. However, in *RAS* cells, there is no: (i) decrease in growth at 48 hours, only at 72 hours and with 50 and 100 μ M of BSO, or (ii) cell death for any condition. Furthermore, after 48 and 72 hours of incubation with BSO, *RAS* cells reach cell densities higher than 3T3 cells. And similar results are obtained whether BSO is incubated when the cells are plated or 6 hours later. Finally, preliminary experiments also suggest a shift in the localization of the active growth phase and GSH peak for *RAS* cells compared to 3T3 cells. In conclusion, 3T3 cells transformed by the *RAS* proto-oncogene become more resistant to cell death and their growth is less inhibited by BSO. Our detailed analysis of growth under conditions of BSO-induced GSH synthesis inhibition suggests a central role for GSH metabolism and cellular redox homeostasis in *RAS* protein-mediated tumor development.



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sciforum-167538: Development of Novel Drug Delivery Pathways Enabled by Perillyl Alcohol (NEO100), a Monoterpene with Multifaceted Biomedical Applications

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Perillyl alcohol is a naturally occurring monoterpene related to limonene. We have synthesized a clinical-grade version, called NEO100 (NeOnc Technologies, Inc., Los Angeles, California), which has revealed a variety of highly promising characteristics that we are exploring toward the development of improved cancer-therapeutic regimens. (i) NEO100 can be delivered via intranasal applications, which exploits direct nose-to-brain transport, and an ongoing Phase 2a clinical trial with recurrent malignant glioma patients is generating intriguingly positive results. (ii) In preclinical brain cancer models, we have shown that intranasal NEO100 can act as a carrier to enable nose-to-brain delivery of other cancer drugs directly to the malignant lesions in the brain. (iii) When given via intra-arterial injection, NEO100 was shown to safely and reversibly open the blood-brain barrier (BBB) of mice, which enabled other cancer drugs circulating in the bloodstream to effectively enter the brain and kill brain cancer cells; in the absence of NEO100, these drugs were unable to cross the BBB and did not exert brain-targeted activity. (iv) In further applications, we covalently conjugated NEO100 to other, already established drugs. For example, conjugation of NEO100 to temozolomide, an alkylating agent, resulted in a novel fusion compound called NEO212 (NeOnc Technologies). Our studies in diverse preclinical tumor models established that NEO212 is well-tolerated and highly effective against different cancer types, and a Phase I clinical trial has begun. — This talk will provide an overview of the multifaceted applications of NEO100 toward the development and improved delivery of more effective cancer treatments.



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sciforum-177802: Electrochemical Reduction of Copper (II) As a Potent and Versatile Approach for Tumor Cell Eradication

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At the advanced stages of the disease, tumor cells acquire pleiotropic resistance to a variety of treatment modalities. In these situations, targeted therapies become no longer efficient. Inactivation of non-apoptotic mechanisms of cell survival remains a strategy of choice. Pursuing the role of oxidative damage in killing pleiotropically resistant tumor cells, we developed a series of copper(II) containing inorganic and organic compounds with an idea of Cu²⁺-to-Cu¹⁺ electrochemical transition in the presence of physiological reducing agents cysteine and ascorbate. Rapid generation of reactive oxygen species (ROS) as a result of Cu(II) reduction triggered multiple mechanisms of cell death including direct damage of the plasma membrane and mitochondria. This effect was specific for copper but not for other transition metals; however, the organic ligand may negatively influence the availability of the metal cation to the reducing agent. In cell-based experiments, the combinations of Cu (II)-organic complexes and cysteine potently killed mammalian tumor cells regardless of tissue origin, including multidrug resistant variants. This effect was achievable at non-toxic concentrations of each component of the combination. To attenuate general toxicity, we focused on the delivery of copper to the sites of potential metastasis, e.g., the bone. Our new Cu(II) complex of zoledronic acid, an FDA-approved drug for prevention of bone destruction, represented a ratio of oligomers/monomers in which two organic moieties were coordinated by three metal cations. Combinations of water-soluble Cu-zoledronate formulations and cysteine (at sub-toxic concentrations) triggered a non-apoptotic death of chronic myelogenous leukemia cell line otherwise resistant to the 3rd generation Bcr-Abl inhibitor vamorinib in the medium conditioned by bone marrow-derived fibroblasts. Overall, local oxidative burst upon Cu(II) reduction emerges as a promising approach to eradicate tumor cells, alone and in the microenvironment.



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sciforum-178422: Elucidating BBIT20's disruption of the BRCA1/BARD1 interaction: A new therapeutic avenue in pancreatic cancer

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Introduction: Pancreatic cancer (PC) is highly resistant to treatment, remaining one of the deadliest malignancies worldwide [1]. Deficiency in the homologous recombination (HR) DNA damage repair pathway renders tumours more sensitive to therapeutic approaches [2,3]. However, because only a minority of PCs exhibit deficiencies in this pathway, effective treatment alternatives are essential [4]. BBIT20 was recently developed as a first-in-class molecule that inhibits the BRCA1/BARD1 interaction, a crucial complex in HR. In vitro and in vivo data revealed its potent antitumor activity, both as a monotherapy and combined with chemotherapy, in PC [5]. In silico analyses indicated that the BRCA1 RING domain is the preferential target of BBIT20. Nonetheless, the exact interaction site and mode of action of BBIT20 still require in vitro validation.

Methods: A recombinant BRCA1 RING domain was produced and purified from *Escherichia coli* BL21 (DE3). The interaction between BBIT20 and BRCA1 was assessed by fluorescent quenching and far-UV circular dichroism.

Results: Fluorescent quenching confirmed that BBIT20 induced a dose-dependent quenching effect in the BRCA1 RING domain ($K_{sv} = 3,97 \times 10^4 \text{ M}^{-1}$). Circular dichroism further revealed dose-dependent alterations in the protein's secondary structure, indicating an interaction with BBIT20.

Conclusions: This study indicated that BBIT20 directly interacts with BRCA1 RING domain, inducing structural alterations that hinder formation of the BRCA1/BARD1 heterodimer and ultimately disrupt the HR pathway. Nuclear magnetic resonance (NMR) will be performed to gain deeper insight into the molecular dynamics of this interaction, which will support the rational design of improved BBIT20 derivatives.

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sciforum-171915: Evaluation of Lobaplatin Chemosensitivity and Mechanistic Insights Using a 3D Bioprinted Primary Colorectal Cancer Model

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Aim: To evaluate the chemosensitivity of lobaplatin in primary colorectal cancer using a bioprinted tumor model and to explore its effects on the tumor.

Methods: Primary CRC cells derived from 20 patients were used to establish 3D bioprinted tumor models. After stabilization, constructs were treated with increasing concentrations of lobaplatin. Cell viability was assessed using the CellTiter-Glo 3D assay to determine IC_{50} values and inter-patient variability. Chemosensitivity of lobaplatin was compared with 5-fluorouracil, oxaliplatin, raltitrexed, and TNF- α . In parallel, SW480 and SW620 cell lines were evaluated under both 2D and 3D culture conditions. Low-dose lobaplatin (IC_{20} and IC_{50}) was applied to assess migration and invasion using wound-healing and 3D invasion assays. ELISA was used to detect invasion-related secreted factors, and RNA sequencing was performed to identify differentially expressed genes and enriched signaling pathways.

Results: Lobaplatin demonstrated a clear dose-dependent inhibitory effect in all 20 primary CRC models, with a mean IC_{50} of 21.40 μ M (range: 0.67–74 μ M), indicating marked inter-patient heterogeneity. At clinically relevant concentrations, lobaplatin significantly reduced tumor cell viability and exhibited stronger cytotoxicity than comparator drugs at high doses. In cell line experiments, IC_{50} values were consistently higher in 3D cultures than in 2D cultures. Functional assays revealed that low-dose lobaplatin significantly suppressed migration and invasion in metastatic SW620 cells but showed minimal effects in SW480 cells. Transcriptomic analysis showed upregulation of genes involved in drug metabolism, oxidative stress, and differentiation, and downregulation of pathways related to cell migration, inflammation, immune regulation, and extracellular matrix remodeling.

Conclusion: The 3D bioprinted primary colorectal cancer model effectively captures individual chemosensitivity to lobaplatin and reveals its inhibitory effects on tumor proliferation and metastatic behavior. Lobaplatin may exert antitumor activity by modulating stress-response pathways and suppressing pro-migratory and pro-inflammatory signaling. This model represents a promising platform for individualized chemotherapy evaluation and mechanistic studies in colorectal cancer.



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sciforum-178266: Evodiamine Illuminating New Horizons in Colorectal Cancer Therapy by Disrupting Hypoxia-Driven Angiogenesis via the HIF-1 α /VEGF Axis

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Introduction: Colorectal cancer (CRC) remains the second leading cause of cancer-related deaths worldwide, with over 1.9 million new cases and 900,000 deaths reported in 2020. Tumor hypoxia, a hallmark of solid tumors, promotes angiogenesis, metastasis, and therapeutic resistance by upregulating angiogenic factors such as VEGF and HIF-1 α . Targeting hypoxia presents a promising strategy for CRC treatment. Natural products, known for their safety and efficacy, offer valuable leads for drug development. Evodiamine (EVD), an alkaloid derived from *Evodia fructus*, has demonstrated anti-cancer potential across various malignancies.

Methods: SW480 and HUVEC cells were cultured under hypoxic conditions to evaluate EVD's effects. Cell viability was assessed using MTT assays, while tube formation assays evaluated angiogenesis. Western blotting and RT-qPCR analyzed VEGF and HIF-1 α expression. In vivo studies involved xenograft models in nude mice, with tumor growth and molecular responses monitored following EVD treatment. Statistical analysis was performed using GraphPad Prism 5.0, with significance determined by one-way ANOVA and Tukey's test (p < 0.05).

Results: EVD significantly inhibited CRC cell proliferation (IC₅₀: 8.342 μ M) and reduced hypoxia-induced VEGF and HIF-1 α expression in a dose-dependent manner. Under hypoxic conditions, EVD suppressed tube formation in HUVECs (p > 0.05) and impeded tumor growth in xenograft models without inducing toxicity. In vivo, EVD administration reduced tumor volume and weight, confirming its anti-tumor efficacy. Molecular analyses revealed EVD's potential to disrupt HIF-1 α accumulation and activity, highlighting its dual mechanism of action.

Conclusion: EVD emerges as a potent anti-angiogenic and anti-tumor agent for CRC, particularly in hypoxic microenvironments. By targeting HIF-1 α degradation and transcriptional suppression, EVD disrupts critical pathways driving tumor progression. These findings position EVD as a novel therapeutic candidate for advanced CRC, warranting further exploration of its clinical potential and structural optimization.



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sciforum-172151: Exploring the anticancer mechanism of isolated compounds from endophytic fungi of the Meliaceae family by a network pharmacological analysis

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Traditional single-target drug discovery misses the multi-target complexity of cancer and underexplores fungal endophytes as sources of bioactive compounds. Endophytic fungi from the Meliaceae family produce diverse secondary metabolites, but their molecular targets and systemic mechanisms in cancer remain poorly understood. This study applied a network pharmacology approach to understand the mechanisms of the anticancer activity of fungal metabolites from Meliaceae endophytes. The drug targets of 276 Meliaceae endophytes were predicted by SwissTargetPrediction. Cancer-related genes were retrieved from the GSE35972 ($\text{LogFC} \leq \pm 2$, $p \leq 0.05$). The protein-protein interaction (PPI) network of the differentially expressed genes (DEGs) was constructed using STRING and Cytoscape to identify hub genes. Functional enrichment (GO and KEGG) was performed using ShinyGO. A total of 326 DEGs were identified from 4,123 genes of GSE and 24,007 predicted genes. The PPI network comprised 324 nodes and 2,993 edges. The identified top hub genes included EGFR, MAPK3, JUN, MTOR, MDM2, STAT3, GSK3B, HDAC1, HSP90AA1, and GAPDH. The KEGG and GO enrichment analyses showed pathways involved in cell growth and survival, transcriptional and epigenetic control, protein quality regulation, metabolic rewiring, apoptosis, and cell migration, with interactions of rohitukine and its analogue flavopiridol to EGFR, mTOR, and MAPK3, and emodin to EGFR, STAT3, and MDM2. This study showed that Meliaceae endophytic fungi are a rich source of multi-target compounds that map onto central oncogenic modules. The identified hub genes and pathways provide rational priorities for experimental validation (biochemical assays, cell-based phenotyping, and *in vivo* models) and offer the potential for lead optimization and combination therapy.



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sciforum-178369: In Silico Pharmacokinetic Profiling and Molecular Docking of Margolonone Against the Oncogenic IDH1-R132H Mutant

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Mutations in the isocitrate dehydrogenase 1 (IDH1) enzyme, particularly the R132H substitution, are key drivers of several malignancies, owing to the neomorphic production of the oncometabolite D-2-hydroxyglutarate. Targeting the different catalytic pocket of IDH1-R132H remains a critical therapeutic blueprint. This research mainly examines the biophysical viability and binding effectiveness of Margolonone, a novel bioactive compound, as a potential selective inhibitor of the IDH1 mutant. Computational pharmacokinetic profiling was executed using SwissADME to assess lead-likeness and physicochemical stability. To determine binding effectiveness, molecular docking simulations were performed using AutoDock Vina via the Webina framework. The structural model of the IDH1-R132H mutant (PDB ID: 6ADG) was utilised as the receptor. A highly specific (20 X 20 X 20) Å search space was centred around the mutated His132 residue to evaluate allosteric and competitive binding modes. Pharmacokinetic evaluation revealed that Margolonone exhibits excellent biophysical parameters, strictly bound to Lipinski's Rule of Five with zero violations. The compound demonstrated an ideal molecular weight of 314.4 g/mol and a favourable lipophilicity profile (XLogP3 = 2.9), suggesting high cell membrane permeability and gastrointestinal absorption. Molecular docking simulations corroborated these favourable properties, yielding a strong, spontaneous binding affinity of -6.607 kcal/mol within the IDH1-R132H active site, driven by specific non-covalent interactions within the target pocket, notably strong hydrogen bonding with the ASN96 residue. The combination of optimal lipophilicity, no structural violations, and a highly favourable binding thermodynamic energy indicates that Margolonone acts as a potent, stable ligand for the IDH1-R132H mutant. These in silico findings present Margolonone as a highly executable pharmacokinetic scaffold, warranting immediate in vitro validation for targeted oncological interventions.



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sciforum-171678: Intracellular and Erythrocyte Partitioning of Venetoclax and its Metabolites: A Multi-Compartmental Pharmacokinetic Model Derived from Paired Patient Samples using High-Resolution Mass Spectrometry

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Venetoclax is a pivotal BCL-2 inhibitor, yet its plasma pharmacokinetics (PK) often fail to predict clinical outcomes accurately. Since the pharmacological target is intracellular, plasma concentrations may not reflect actual exposure in Peripheral Blood Mononuclear Cells (PBMCs) or sequestration in erythrocytes (RBCs). We aimed to develop a multi-compartment PK model to quantify the distribution of Venetoclax and its two major metabolites across plasma, RBCs, and PBMCs. Peripheral blood from 15 patients undergoing Venetoclax therapy was collected and processed to separate Plasma, RBCs, and PBMCs. We developed a high-resolution analytical method using a Shimadzu Nexera X3 coupled to a Sciex ZenoTOF 7600 system for simultaneous quantification in all matrices. MATLAB was used to construct a compartmental PK model defining rate constants (k_{in} , k_{out}) for drug transfer between plasma and cellular compartments. The UPLC-QTOF method demonstrated high sensitivity, successfully detecting Venetoclax and metabolites even at low intracellular concentrations. Preliminary data indicate significant partitioning of the parent drug into cellular compartments, suggesting RBCs may act as a drug reservoir. The MATLAB model describes the dynamic equilibrium between plasma fraction and intracellular accumulation. Detailed kinetic parameters, including PBMC-to-plasma accumulation ratios and metabolite impact, will be presented. This study models Venetoclax kinetics simultaneously in plasma, RBCs, and target PBMCs within the same patient cohort. By shifting the focus from plasma TDM to intracellular pharmacokinetics, this approach offers a more precise tool for understanding drug resistance mechanisms and optimizing dosage in precision oncology.



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sciforum-171745: Lamotrigine Inhibits Breast Cancer Progression Through FoxO3a/TXNIP axis

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Background

Endocrine resistance remains a major challenge in the treatment of estrogen receptor a-positive (ER+) breast cancer (BC), highlighting the need for novel strategies to overcome hormonal therapy resistance. The antiepileptic drug Lamotrigine (LTG), previously shown to induce the tumor suppressor FoxO3a in Tamoxifen-sensitive and resistant ER+ BC, may serve as a potential adjuvant. This study investigated LTG's effects on another key tumor suppressor, Thioredoxin-Interacting Protein (TXNIP), thought to be transcriptionally regulated by FoxO3a.

Methods

ER+ MCF-7 cells, their tamoxifen-resistant counterpart (TamR), and patient-derived metastatic BC cells were used as experimental models. Gene and protein expression and functional effects were evaluated by RT-qPCR, Western blotting, ChIP assays, Trypan Blue exclusion assay, Boyden chamber migration and invasion assays, and siRNA-mediated gene silencing.

Results

LTG induced ROS production and increased mRNA and protein expression of FoxO3a and TXNIP in MCF-7 and TamR cells. Consistently, ChIP assays demonstrated that LTG promotes FoxO3a recruitment to a FoxO-responsive element within the TXNIP promoter in both cell lines. Silencing of TXNIP partially reversed LTG's inhibitory effect on cell proliferation in MCF-7 and TamR cells. Similarly, FoxO3a or TXNIP silencing significantly attenuated the effects of LTG on cell proliferation and migration, with enhanced impact observed upon combined silencing of both genes, particularly in TamR cells. Finally, LTG reduced tumor spheroid size in MCF-7 and TamR cells. Moreover, LTG inhibited proliferation and migration and induced FoxO3a and TXNIP expression in patient-derived metastatic BC cells.

Conclusions

These data suggest that Lamotrigine, for its ability to activate the promising therapeutic targets FoxO3a and TXNIP, could represent a potential candidate for drug repurposing in BC treatment, particularly for patients resistant to conventional hormonal therapies.

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sciforum-171464: Molecular Docking and Molecular Dynamics Approaches to Evaluate the Specificity of the AS1411–Lapatinib Aptamer Complex in HER2-Positive Breast Cancer

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HER2-positive breast cancer is an aggressive subtype characterized by the overexpression of the HER2 tyrosine kinase receptor, which promotes uncontrolled cell proliferation and tumor progression. Lapatinib is a dual EGFR/HER2 inhibitor widely used in targeted therapies; however, its limited bioavailability and adverse effects associated with systemic distribution highlight the need for more selective molecular targeting strategies. In this context, DNA aptamers have emerged as promising platforms for specific molecular recognition and the development of targeted drug delivery systems.

The AS1411 aptamer, which is rich in guanine regions and capable of adopting stable conformational structures, represents a potential candidate for the selective transport of therapeutic agents. As an initial step in the structural design of the aptamer–drug complex, multiple conformations of the ligand Lapatinib were generated in order to represent its molecular flexibility and obtain energetically favorable geometries for subsequent interaction studies.

Additionally, potential binding cavities were identified using structural site detection algorithms. The analysis revealed seven possible interaction sites, with Site 1 identified as the main cavity, showing a size of 78, a PLB value of 1.54, and 10 hydrophobic features, associated with 62 nucleotide residues, including DG9, DT10, DT11, DG12, DT13, DG15, DT16, DG17, DG18, DG26, DG27, and DT28. These characteristics suggest a structurally favorable region for interactions with aromatic ligands.

The results obtained establish a structural basis for subsequent molecular docking studies and molecular dynamics simulations aimed at evaluating the stability of the AS1411–Lapatinib complex and its potential application in targeted delivery strategies for HER2-positive breast cancer.



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sciforum-171757: Network pharmacology-based elucidation of the multi-target mechanisms of piperlongumine targeting oncogenic survival and immune-evasive pathways in pancreatic cancer

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Pancreatic cancer (PC) remains one of the most aggressive malignancies, largely due to late diagnosis, rapid metastatic progression, and the limited efficacy of current therapeutics. Piperlongumine, a bioactive alkaloid isolated from *Piper longum*, has attracted attention for its selective cytotoxicity toward cancer cells and its ability to modulate multiple oncogenic pathways. However, its molecular mechanisms in PC remain insufficiently understood. In this computational systems pharmacology study, a network pharmacology strategy combined with molecular docking was used to investigate the molecular targets and pathways associated with piperlongumine's anticancer activity. Targets of piperlongumine and PC-related genes were retrieved from public databases and intersected to identify shared targets. Overlapping targets were used to construct a protein-protein interaction network using STRING platform. Hub genes were identified using the CytoHubba plugin using six topological algorithms. Functional enrichment analyses (Gene Ontology and KEGG pathways) were performed using ShinyGO 0.85 platform. Prognostic relevance of the hub targets was evaluated using Kaplan-Meier Plotter, while immune cell infiltration patterns were explored using TIMER. Molecular docking was conducted using AutoDock Vina to validate ligand-target interactions. A total of 237 intersecting genes were identified. Network analysis revealed several central hub genes, including TP53, Akt-1, STAT-3, CTNNB-1, IL-6, TNF- α , and Bcl-2. KEGG pathway analysis highlighted PC as the most enriched pathway, together with the PD-1/PD-L1 pathway, TNF signaling, and other cancer-related pathways. Survival analysis revealed significant prognostic associations for several hub genes, while TIMER analysis suggested correlations with tumor-associated immune cell infiltration. Molecular docking confirmed favorable binding affinities of piperlongumine toward key oncogenic targets, particularly Bcl-2 (-7.2 kcal/mol), TP53 (-6.2 kcal/mol), CTNNB-1 (-6.2 kcal/mol), and Akt-1 (-5.8 kcal/mol). Collectively, this study uncovers piperlongumine's anticancer potential in PC, mediated through coordinated regulation of apoptosis, inflammatory, and immune pathways, highlighting its promise for future experimental and translational investigations.



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sciforum-178068: Rational Design of SIRT2 Inhibitors Using Combined 3D-QSAR, Docking, and Machine Learning Methods

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Sirtuin 2 (SIRT2) is a key regulator of apoptosis, DNA repair, and the cell cycle, making it a promising target for anticancer therapy. Achieving high selectivity remains challenging due to the conserved NAD⁺ binding site among sirtuin family members. Derivatives of 5-((3-amidobenzyl)oxy)nicotinamide are among the most potent and selective SIRT2 inhibitors, providing a foundation for further exploration. [1] In this study, a 3D-QSAR model was constructed using 86 nicotinamide-based SIRT2 inhibitors, complemented by GRIND-derived pharmacophore modelling. [2] The model, developed using partial least squares regression, achieved $R^2 = 0.89$ and $Q^2 = 0.69$, with no outliers in the applicability domain. Model interpretation highlighted the positive influence of steric features, secondary amide groups, and nitrogen atoms in the pyridine ring on SIRT2 activity. Fine-tuning the propynyl and central phenyl groups produced derivatives with predicted enhanced potency. [3] Molecular docking on SIRT1–3 isoforms enabled the development of two machine learning classification models (Naive Bayes and k-nearest neighbours) to predict SIRT1/2 and SIRT2/3 selectivity profiles. Several selective SIRT2 inhibitors were identified in silico, and these will be synthesised and tested in vitro, supporting the development of novel SIRT2-targeted anticancer therapies. [3]

By integrating 3D-QSAR, selectivity modelling, and ADMET predictions, several promising selective SIRT2 inhibitors were identified. [3] These candidates will be synthesised and tested in vitro to validate their efficacy and selectivity, advancing the development of novel SIRT2-targeted anticancer therapies.

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sciforum-177763: Restoring therapeutic vulnerability in Multidrug-Resistant Ovarian Cancer with a first-in-class disruptor of the BRCA1–BARD1 interaction

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Ovarian cancer (OC) remains largely incurable due to the emergence of multidrug resistance (MDR) following platinum–taxane therapy through rewiring of DNA repair, metabolism, and drug efflux pathways. Strategies capable of collapsing this stress-adaptation network remain limited [1]. We developed BBIT20, a first-in-class small-molecule disruptor of the BRCA1–BARD1 interaction, essential to homologous recombination (HR) repair and genome stability.

BBIT20 was evaluated in BRCA-proficient and -mutated OC cell lines, MDR cells, patient-derived organoids (PDOs), and xenograft and patient-derived xenograft (PDX) mouse models. Activity was assessed alone and in combination with paclitaxel, carboplatin, and PARPi. Mechanistic studies included DNA repair profiling, apoptosis, and immune-evasion markers.

BBIT20 displayed BRCA status-independent cytotoxicity (IC₅₀ 4–6 µM), favorable selectivity over non-tumoral cells, and retained activity in MDR models without cross-resistance. In wtBRCA1 PDOs, BBIT20 reduced BRCA1 and RAD51 levels, inducing DNA damage and apoptosis consistent with HR collapse. BBIT20 also modulated the E2F1–c-MYC–HDAC3 axis, triggered mitochondrial stress, and reduced ABCB1 drug-efflux expression.

Combination therapy showed strong synergy with paclitaxel, carboplatin, and PARPi (CI 0.08–1), reducing effective doses by up to 20-fold in both sensitive and resistant OC models. In vivo, BBIT20 (2 mg/kg) reduced ascites formation and tumor burden in PDX models and achieved greater tumor growth inhibition than olaparib in xenografts. Combination therapy further suppressed proliferation, HR and NHEJ repair, EMT, and angiogenesis markers while remaining well tolerated.

BBIT20 induces DNA repair–metabolic stress collapse and resensitizes MDR tumors to platinum, taxanes, and PARP inhibitors, supporting its development for refractory OC.

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sciforum-168149: Selective PERK inhibition as a strategy to overcome hypoxia-induced survival in colorectal cancer cells

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Hypoxia-driven signaling contributes substantially to therapy resistance in colorectal cancer, in part through activation of the PERK-mediated stress response. The present study examined whether pharmacological inhibition of PERK produces selective anti-tumor effects in colon cancer cells and influences apoptosis-related pathways.

Human HT-29 colorectal carcinoma cells and non-malignant CCD 841 CoN colon epithelial cells were exposed to increasing concentrations of a PERK inhibitor for 16, 24, and 48 hours. Cellular viability was evaluated using standard cytotoxicity assays. Changes in PERK-associated stress response genes were quantified by qPCR and verified at the protein level by Western blotting. Cell-cycle alterations were assessed through cyclin D1 expression analysis.

Treatment with the PERK inhibitor resulted in a dose-dependent reduction in HT-29 cell viability across all incubation periods, with the strongest effect observed at concentrations up to 50 μ M. In contrast, normal CCD 841 CoN cells showed no detectable loss of viability under identical conditions, indicating cancer-selective activity and lack of toxicity toward healthy colon epithelium. Molecular analyses revealed that the PERK blockade in hypoxic HT-29 cells elevated expression of ATF4, DDIT3/CHOP, and BCL2L1/BIM, while suppressing anti-apoptotic BCL2. Additionally, cyclin D1 levels were markedly reduced following PERK inhibition under hypoxia, consistent with cell-cycle arrest at the G2/M transition and impaired progression into G1.

Collectively, these findings demonstrate that PERK inhibition selectively compromises survival of hypoxic colon cancer cells while sparing normal tissue, supporting PERK as a promising therapeutic target in colorectal cancer.

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sciforum-171632: Synthesis and Pharmacological Evaluation of N-(2-Bromo ethyl) Phthalimide-Based Hybrid Compounds

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The heterocyclic ring has always been essential to the development of anticancer drugs in synthetic organic chemistry, and when combined with other ring systems, it may improve the biological activities of those drugs. Different kinds of biological activities are possessed by a distinct group of heterocyclic compounds.

Objective: This work describes the effective and practical synthesis of a unique, hybrid series of N-(2-Bromoethyl) Phthalimide compounds and their pharmacological activity against the human colon cancer cell line (HCT-116).

Methodology: A number of N-2 (Bromo ethyl) Phthalimide-based hybrids, 1-8, were synthesized by reacting N-2 (Bromo ethyl) Phthalimide with various carboxylic acid-based analogues, which served as reacting agents, in the presence of N,N-dimethylformamide (DMF) as a solvent and potassium carbonate (K_2CO_3) as a catalyst. The reaction mixture was agitated at ambient temperature for approximately 15–24 hours, resulting in the formation of new phthalimide acid derivatives. The synthesized analogs were then characterized, and their structures were elucidated using several spectroscopic analyses, such as NMR, UV, IR, and EI-MS. The cytotoxic effects of newly synthesized compounds were compared to Doxorubicin in an in vitro MTT cytotoxicity assay. With micromolar (μM) half maximum inhibitory concentration (IC_{50}) values against tumor cells, the first screening revealed good to moderate anticancer efficacy for these recently synthesized compounds, with a high degree of cell line selectivity. The involvement of molecular fragments such as phthalimide, linker, and terminal tails in relation to activity was validated by the SAR analysis of these derivatives. Analyses of the extensive structure–activity relationship (SAR) were also performed.

Result: A study of the pharmacokinetic profile of hybrid 2-(1,3-dioxoisindolin-2-yl) Ethyl 6-chloronicotinate (7) revealed long-term behavior and strong cytotoxic activity against the human colon cancer cell line (HCT-116). This design provided strong, specific anticancer Phthalimide leads for additional cancer drug discovery optimization.



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sciforum-172859: Targeting EPS8 by CRISPR/Cas9 Genome Editing Reduces Gemcitabine Resistance in Pancreatic Cancer Cells

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Background: PDAC is characterized by high aggressiveness and poor therapeutic response, largely due to the rapid development of gemcitabine resistance. EPS8 regulates cytoskeletal dynamics, cell motility, and pro-survival signaling. Its elevated expression in multiple cancers correlates with enhanced invasiveness and reduced chemotherapy sensitivity. Therefore, EPS8 represents a potential therapeutic target. In this study, CRISPR/Cas9 technology was used to knockout EPS8 in pancreatic cancer cells and assess its impact on gemcitabine resistance and tumor-related cellular behaviors.

Materials and Methods: Two sgRNAs targeting the EPS8 genomic sequence were designed and cloned into a CRISPR/Cas9 expression vector. The construct was introduced into the pancreatic cancer cell line with the highest EPS8 expression. After transfection, puromycin selection was applied to enrich edited cells and isolate single clones. Gene disruption was confirmed by genomic PCR and Sanger sequencing. EPS8 expression levels in edited clones were analyzed using RT-qPCR and western blot. To evaluate the impact of EPS8 loss on chemoresistance, wild-type cells and edited clones were treated with gemcitabine, and cell viability was assessed using an MTS assay.

Results: EPS8 knockout in PDAC cells was confirmed by sequencing, showing loss of target site integrity. Loss of EPS8 expression was further verified in edited clones, which exhibited reduced viability after gemcitabine treatment compared to wild-type controls. Changes in drug-response curves indicated increased sensitivity following EPS8 knockout. No significant morphological abnormalities were observed during routine culture.

Conclusion: Disruption of the EPS8 gene significantly increased the susceptibility of PDAC cells to gemcitabine, indicating that EPS8 contributes to gemcitabine resistance in pancreatic cancer. Targeting EPS8 may help overcome drug resistance and improve the effectiveness of gemcitabine in PDAC chemotherapy. Further studies using additional pancreatic cancer cell lines and in vivo models with clinical samples are needed to clarify the role of EPS8 in gemcitabine resistance.



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sciforum-169030: The effect of the degree of oxidation and the molecular structure of cobalt complexes with imidazole on the metabolic profiles of CCD 841 CoN and HT-29 cells

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Colorectal cancer is among the most prevalent causes of cancer-related morbidity and mortality on a global scale, underscoring the necessity of novel chemotherapeutic strategies that exhibit enhanced selectivity and diminished systemic toxicity. The present study investigates the biological impact of three structurally diverse cobalt complexes bearing imidazole: the polymeric $[\text{Co(II)(imid)}_2]_n$, the dimeric $[\text{Co(III)(Himid)(L-(}\alpha\text{)-histidine)}_2]_2\text{O}_2^{2-}$, and the mononuclear $\text{Co(II)(Himid)}_2(\text{H}_2\text{O)}_2\text{CO}_3$. The first complex, $[\text{Co(II)(imid)}_2]_n$, is regarded as a paradigm of a coordination compound that crystallizes in an infinitely polymeric network, wherein each cobalt atom is linked via imidazole bridges to four adjacent cobalt atoms. The second complex, $[\text{Co(III)(Himid)(L-(}\alpha\text{)-histidine)}_2]_2\text{O}_2^{2-}$, is a dimeric, diamagnetic complex with an O_2 molecule coordinated in the peroxide form with an O_2^{2-} (μ -peroxo) bridge between two cobalt ions oxidized to Co(III). The third complex, $\text{Co(II)(Himid)}_2(\text{H}_2\text{O)}_2\text{CO}_3$, represents the first documented instance of a carbonate group functioning as a bidentate ligand in a solid cobalt complex. The biological effects of the aforementioned compounds were evaluated against normal human colon epithelial cells (CCD 841 CoN) and colonic adenocarcinoma cells (HT-29). MTT assays revealed that the dimeric Co(III) complex exhibited no cytotoxic effect on either cell line. In contrast, both the polymeric and mononuclear Co(II) compounds elicited a substantial, concentration-dependent enhancement in cell viability in HT-29 cells, reaching up to 400 % relative to the control, and a non-significant cytotoxic effect in CCD 841 CoN cells. The results suggest that both Co(II) complexes might trigger a pseudohypoxic metabolic shift in colorectal cancer cells, whereas the Co(III) complex remains biologically inert.



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sciforum-168514: Vimentin facilitates ubiquitination and degradation of NCOA4 to promote resistance to olaparib-induced ferroptosis in glioblastoma

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Glioblastoma (GBM) represents one of the most prevalent types of tumors in the central nervous system. PARP inhibitors are novel targeted therapies for cancer patients, primarily functioning through synthetic lethality mechanisms that selectively exploit defects in DNA repair pathways in tumor cells. However, patients with GBM have a minimal benefit from PARP inhibitor monotherapy. Hence, understanding the underlying mechanisms and developing innovative strategies for enhancing their efficacy against GBM is imperative. Here, we demonstrate that blocking ferroptosis attenuates olaparib-induced cell death and impairs its anti-GBM efficacy both in vitro and in vivo. Furthermore, depleting nuclear receptor coactivator 4 (NCOA4) mitigates olaparib-induced ferroptosis. Notably, we identified vimentin (VIM) as a novel NCOA4-interacting protein through multimodal screening. VIM inhibition markedly increased NCOA4 abundance through suppression of HERC2-mediated NCOA4 ubiquitination and degradation, subsequently potentiating the ferroptosis response. More importantly, withaferin A (WFA, a specific VIM inhibitor) combined with olaparib exhibited synergistic antitumor efficacy in orthotopic GBM xenografts via the induction of ferroptosis. Collectively, our data establishes that VIM modulates NCOA4 ubiquitination and degradation to govern the olaparib-induced ferroptotic response and enhances the sensitivity of GBM to olaparib treatment. These findings not only uncover a novel mechanism of VIM-mediated PARP inhibitor resistance in GBM but also provide a potential combined therapeutic strategy for clinical GBM treatment.



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Session 4. Cancer Survivorship and Quality of Life

sciforum-161312: The Impact of Mobile Health on the Quality of Life of Cancer Patients: An interventional study

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Background: Traditional oncology rehabilitation services are primarily delivered within healthcare institutions. Mobile health may offer a cost-effective method of oncology rehabilitation.

Objective: This study aims to assess the impact of mobile health on the quality of life of cancer patients in China.

Methods: Participants were recruited through insurance companies and cancer rehabilitation institutions. This mobile health intervention utilized an online platform for 16 weeks, and comprised five components: (1) pre-intervention assessment; (2) online health education; (3) online peer education; (4) question answering by experts; and (5) post-intervention assessment. Internationally recognized scales were used to measure outcome indicators, including quality of life, nutritional status, sleep, appetite, and fear of cancer recurrence.

Results: Participants aged over 18 years with a cancer diagnosis or in the cancer recovery phase were included, while those who had been cured were excluded. In total, 208 participants were recruited, but 23 participants were excluded as they were unable to adhere to the intervention or complete outcome measure assessments. A total of 185 participants, aged 45.5 ± 9.08 years, completed the final intervention. Significant improvements were observed in multiple aspects: QLQ-C30 scores showed significant improvements in overall health status, physical function, and other functional domains, and reductions in symptoms such as nausea and vomiting, fatigue, and others ($P < 0.05$). Participants' nutritional risk, malnutrition, sleep quality, fear of cancer recurrence, and appetite were also improved ($P < 0.05$). Finally, regression analysis revealed that appetite and social functioning positively influenced quality of life among cancer patients, while financial hardship, nausea and vomiting, pain, and fatigue exerted negative effects.

Conclusions: Mobile health intervention can enhance the quality of life of patients by improving nutritional status, reducing fear of cancer recurrence, improving sleep quality, and enhancing appetite.



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sciforum-178005: Breast Cancer in South India: Clinical Patterns and Lifestyle Associations in the Tiruchirappalli district

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Background:

Breast cancer (BC) is the most frequently diagnosed malignancy among women globally and represents a significant and rising public health burden in India. Despite the role of genetic susceptibility, the epidemiological and hereditary patterns of breast cancer in South Indian populations, particularly in southern Tamil Nadu, remain poorly understood. SRM Medical College Hospital and Research Centre (SRMMCHRC), Tiruchirappalli, has reported increasing breast cancer cases, especially among women from rural backgrounds where consanguinity is prevalent.

Methods:

A retrospective study was conducted using anonymized clinical records of breast cancer patients diagnosed at SRMMCHRC between 2021 and 2024. Data on age, demographic characteristics, family history, consanguinity, tumor features, and geographic origin were systematically collected. Descriptive statistical analyses were performed to evaluate temporal trends, regional distribution, and age-specific incidence patterns.

Results:

Breast cancer cases increased steadily from 2021 to 2023, peaking in 2023, followed by minor fluctuations in 2024. Geographical analysis showed higher case concentrations in Trichy and “Other districts,” indicating regional disparities. Age-wise distribution revealed that the majority of cases occurred in women aged 45–65 years, with the highest incidence in the 55–60 age group, while younger and older populations contributed fewer cases.

Conclusion:

The findings highlight a rising burden of breast cancer with notable regional and age-related patterns. Hereditary factors, including consanguinity, along with lifestyle-related conditions, may contribute to disease risk. These results underscore the need for targeted screening, early detection, and improved risk stratification to enhance breast cancer management in this population.



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sciforum-178419: Clinical outcomes of Sacituzumab Govitecan in metastatic breast cancer: evidence of survival and quality of life from a systematic review and meta analysis

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Introduction: Sacituzumab Govitecan is an antibody–drug conjugate (ADC) consisting of a humanized anti-Trop-2 protein monoclonal antibody linked with the active metabolite of irinotecan. It is indicated for the treatment of metastatic triple-negative breast cancer and hormone receptor-positive, HER2-negative breast cancer. The aim of this study was to identify and evaluate the most reliable survival and quality-of-life parameters associated with treatment using Sacituzumab Govitecan in patients with triple-negative breast cancer.

Materials and methods: A consistent and well-defined search and selection protocol was developed to identify eligible articles. The search criteria included publications from the last five years that were freely accessible in full text. The selected publication types comprised meta-analyses, systematic reviews, clinical studies, comparative studies, observational studies, and randomized controlled trials. The entire procedure followed the guidelines of PRISMA 2020. The search strategy employed the most relevant keywords combined with appropriate Boolean operators to ensure a comprehensive and systematic literature retrieval.

Results: Treatment with Sacituzumab Govitecan improved median progression-free survival, and the presence of an objective response to therapy was higher in patients receiving Sacituzumab Govitecan. However, the rates of adverse events and treatment-discontinuation-related adverse events were also higher. A comparison was performed against chemotherapy. Sacituzumab Govitecan led to significantly longer progression-free survival than chemotherapy among patients with advanced triple-negative breast cancer who were not candidates for treatment with PD-1 inhibitors or PD-L1 inhibitors.

Conclusion: Continued efforts to develop therapies for all stages of breast cancer should be implemented, on the one hand, from the perspective of the substantial scientific progress achieved and the increasingly detailed understanding of the molecular mechanisms underlying cancer cells. On the other hand, screening programs should not be overlooked, together with the development of public health policies aimed at expanding access to these simple detection methods wherever they are needed.



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sciforum-178219: Decision-making patterns of adjuvant endocrine therapy among women with breast cancer: A qualitative study

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Introduction: While 5-10 years of adjuvant endocrine therapy (AET) substantially reduces recurrence risk and improves survival in breast cancer patients, adherence remains suboptimal. Research has documented various factors influencing adherence, including psychological distress and AET-related side effects. However, breast cancer patients may adopt different decision-making patterns when confronted with factors, which may influence adherence outcomes. A clearer understanding of these patterns during AET is needed to inform targeted adherence interventions to improve AET adherence.

Methods: From February 2025 to February 2026, semi-structured online interviews were conducted with 21 breast cancer patients recruited through purposive sampling. Interview data were analyzed using thematic analysis to identify participants' decision-making characteristics, from which distinct decision-making patterns were derived. Data interpretation was guided by Janis and Mann's conflict decision-making model.

Results: Four distinct decision-making patterns corresponding to the model were identified: 1) Vigilance pattern. Patients with this pattern proactively used multiple information sources before decision-making, demonstrated careful deliberation and active participation during the process, maintained stable post-decision attitudes. This pattern showed high medication adherence; 2) Hypervigilance pattern. This pattern was marked by information overload, leading to high decisional pressure and excessive deliberation. These factors prompted stress-driven responses to treatment challenges, post-decision regret, and ultimately resulted in unstable medication adherence; 3) Unconflicted change pattern. Patients with this pattern demonstrated limited information-seeking, relied on intuitive decision-making, and participated passively. Consequently, they engaged in minimal post-decision reflection, and their medication adherence was readily influenced by external circumstances; 4) Defensive avoidance pattern: This pattern was characterized by deliberate avoidance of negative information, limited engagement in decision-making, and reliance on others while resisting personal responsibility for decisions, ultimately resulting in physician-led medication adherence.

Conclusion: Decision-making patterns during AET are associated with medication adherence and exhibit distinct characteristics. Tailoring interventions to these patterns may improve AET adherence and health outcomes.



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sciforum-163628: Influence of Health Literacy on Quality of Life in oncology patients

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Background

Lower levels of patient health literacy (HL) have been associated with poorer self-perceived quality of life (QoL).

Aim

We aimed to evaluate the influence of HL on QoL in oncology patients.

Methodology

A systematic review and meta-analysis were performed. Both observational and interventional studies evaluating both health literacy (HL) and quality of life (QoL) among cancer patients were included. HL was evaluated using various instruments that categorized participants into high, medium, or low levels; QoL was assessed using the Functional Assessment of Cancer Therapy-General (FACT-G), which classified QoL into four subdimensions: physical well-being, social/family well-being, emotional well-being, and functional well-being.

Results

We gathered data from four records and conducted additional analyses for each screened study based on the FACT-G sub-dimensions. Overall, our findings suggested substantial heterogeneity in the fields of physical, emotional, and functional well-being. Nevertheless, the Forest Plot revealed a clear trend toward poorer outcomes in low HL groups, and also revealed that patients with lower HL also reported lower QoL. This pattern was further supported in the social/family well-being subdimension.

Conclusions

HL may represent an essential instrument to achieve higher levels of QoL. However, several key factors should be considered that could limit the generalizability of the included studies, since most patients suffering from cancer diseases reported low QoL levels and low HL levels, too. This trend has been explained by several difficulties in enrolling patients with very low HL due to numerous barriers in self-administration of questionnaires. Thus, most patients with low HL are usually excluded from enrollment.



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sciforum-173856: Mind–Body Intervention for Symptom Management in Breast Cancer Survivorship: A Feasibility Qigong Pilot Study

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Introduction: Breast cancer (BC) survivors often experience various medically unexplained symptoms after surgery, including fatigue, pain, and psychological distress, which can negatively affect patients' quality of life (QoL). These have led to a growing interest in integrative therapies to manage psychosomatic symptoms with mind-body interventions. The aim of this pilot study is to evaluate the effects of Qigong mind-body intervention on symptoms and QoL in post-surgical BC survivors.

Methods: This single-arm pilot study was conducted at the AMICO Clinic (IRCCS-CROB, Southern Italy), where fourteen women (aged 42–73 years; stage I–III BC) were enrolled. Participants attended weekly 60-minute supervised Qigong sessions for 8 weeks and were instructed to engage in home practice with a minimum target of 2–3 hours/week. Outcomes were assessed at baseline and post-intervention using the Edmonton Symptom Assessment System and the 12-Item Short Form Health Survey. Post-intervention qualitative exit interviews were conducted to explore participants' experiences and perceived benefits.

Results: The Qigong intervention was well tolerated, with improvements observed across both physical and psychological domains. Participants demonstrated reductions in pain (–28%), fatigue (–28%), anxiety (–43%), mood disturbances (–28%), sleep disturbances (–22%), and melancholy (–22%). Hot flashes decreased by 7%, with greater reductions noted among younger participants, especially when combined with light aerobic activity. Qualitative findings were like quantitative outcomes, with participants reporting improvements in overall well-being, enhanced emotional regulation, increased body awareness, strengthened social connectedness, and greater engagement in self-care.

Conclusions: This pilot study suggests Qigong is a feasible and acceptable intervention for the management of symptoms in BC survivors. Delivered in a public integrative oncology setting, the proposed mind-body practices demonstrate the applicability of Qigong in a real-world clinical context of BC care.



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sciforum-168971: Pingyangmycin-lipiodol Emulsifier Embolisation Via Transarterial Versus Resection For Hepatic Hemangioma: A Retrospective Controlled Study

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Background: Hepatic hemangiomas are predominantly benign, however symptomatic, macroscopic, or progressive lesions require active intervention. Transcatheter arterial chemoembolization (TACE) using pingyangmycin-lipiodol (PYM-Lipiodol) and liver surgery (LS) are widely adopted, yet comparative evidence on their efficacy and safety remains limited.

Methods: This retrospective study examined Chinese patients who received treatment for hepatic hemangioma at the Second Affiliated Hospital of Soochow University between January 2018 and February 2025. Eighty-one patients were divided into two groups (TACE, $n = 42$ or LS, $n = 39$). Postoperative target lesion shrinkage rate, complication rates, costs and quality of life were compared between the two groups. Further subgroup analysis was performed to investigate differences in effectiveness and complications.

Results: Six months after surgery, the hemangioma shrinkage rate was lower in the TACE group than in the LS group ($79.41 \pm 16.03\%$ vs. $99.19 \pm 4.01\%$, $\beta = 19.31$, 95% CI: 14.07 - 24.55, $P = 0.001$). However, remission rates were comparable (97.62% vs. 100.00% , $RR = 0.997$, $P = 0.494$). The TACE group experienced a lower overall complication rate, shorter hospital stays and lower total costs. Notably, the quality of life in the TACE group was significantly improved at 3 days postoperatively (97.74 ± 4.71 vs. 66.54 ± 11.31), with all relevant P -values < 0.001 . However, the reintervention rate in the TACE group was 21.43% .

Conclusion: LS is superior in achieving immediate shrinkage in hepatic hemangiomas. TACE effectively reduces lesion size while minimizing the risk of complications and resource consumption, which is particularly beneficial for patients with multiple hepatic hemangiomas measuring 5–10 cm who are seeking less invasive procedures and faster recovery.



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sciforum-158108: Survival impact of surgery and radiotherapy in malignant phyllodes tumors: Meta-Analysis of cohort studies

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Background: Phyllodes tumors of the breast (PTs) are uncommon fibroepithelial lesions exhibiting tremendous biologic diversity, ranging from benign to highly aggressive malignant neoplasms. Surgical excision is the mainstay of treatment; however, the comparative survival benefit of mastectomy versus breast-conserving surgery (BCS) and the role of adjuvant postoperative radiotherapy (RT) in malignant PTs remain controversial. Existing evidence is fragmented, and clinical decision-making is largely extrapolated from retrospective series.

Methods: We conducted a PRISMA-compliant systematic review and meta-analysis of cohort studies evaluating survival outcomes in patients with primary malignant PTs treated with mastectomy or BCS, with or without postoperative RT. PubMed, Scopus, Cochrane Library, and PROSPERO databases were searched for eligible studies published between 2005 and 2025. Pooled hazard ratios (HRs) for overall survival and odds ratios (ORs) for cancer-related mortality were estimated using random-effects models in R software v4.5.2. Meta-regression and propensity score-adjusted analyses were applied to account for tumor grade, surgical margins, and clinicopathologic confounders. In total, 8,779 patients with malignant PTs and available postoperative follow-up were included.

Results: Mastectomy, compared with breast-conserving surgery, was associated with significantly improved overall survival among patients with grade II–III malignant PTs (pooled HR=0.29, 95% CI=0.20–0.42; $I^2=72\%$, $p=0.001$). Postoperative radiotherapy did not confer a survival benefit and was associated with a higher risk of cancer-related mortality (pooled OR=3.27, 95% CI=2.55–4.17; $I^2=38\%$). These findings remained consistent across sensitivity and subgroup analyses adjusted for tumor grade and margin status.

Conclusions: Complete surgical resection remains the most critical determinant of survival in malignant phyllodes tumors. Our findings do not support the routine use of postoperative radiotherapy and suggest that RT should be reserved for carefully selected cases on an individualized basis. Overtreatment minimization, surgical treatment decisions, and future prospective trial designs, in a clinically significant manner, impact survivorship-focused cancer treatment and health care policy.



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sciforum-178240: The role of the European Cancer Information System on the pancreatic cancer surveillance

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Introduction

Pancreatic cancer is the fourth most common causes of cancer death in Europe and remains one of the malignancies with the poorest survival. The European Cancer Information System (ECIS) provides cancer incidence and mortality data from Population-Based Cancer Registries (PBCRs). The study aimed to explore geographical and time trend differences in the incidence and mortality of pancreatic cancer in Europe.

Methods

Age-standardised incidence and mortality rates were extracted from ECIS for cases ≥ 20 years, stratified by PBCR, sex and age group (20-49; ≥ 50 years). Geographic analysis included PBCRs with data from 2019 onwards. Ninety-five percent confidence intervals (95%CI) and mortality-to-incidence ratios were computed. Annual percent changes in incidence and mortality were estimated using Joinpoint regression in PBCRs with ≥ 10 years of data.

Results

Thirty-six PBCRs from 18 countries were analysed. Incidence ranged from 14.5 (95%CI:14.0-15.0) to 32.4 (95%CI:29.7-35.1) per 100,000 person-year in males and from 11.1 (95%CI:10.7-11.5) to 25.2 (95%CI:23.6-26.8) in females, with German PBCRs representing the extremes. The highest mortality rates were observed in Castellón, 48 (95%CI:41.4-54.6) in males and 29.8 (95%CI:25.1-34.5) in females, and the lowest in Brandenburg-Berlin for males at 15.3 (95%CI:14.9-15.7) and in the lowest in Agrigento for females at 8.8 (95%CI:4.7-12.9). Approximately 80% PBCRs reported significantly higher incidence and mortality rates in males. Mortality-to-incidence ratios were close to 1 in 90% PBCRs. In the 20-49 age group, incidence in both sexes and mortality in females were stable in over 80% of PBCRs, while mortality decreased significantly to 30.3% in males. Among cases in the ≥ 50 age group, incidence increased significantly in 40% of PBCRs and mortality in 30%.

Conclusions

Pancreatic cancer shows geographical differences in incidence and mortality across Europe, with higher rates in males and increasing trends in the ≥ 50 age group. A mortality-to-incidence ratio close to 1 highlights persistently poor survival. ECIS provides incidence and mortality indicators, although survival data were not available.



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Session 5. Causes, Diagnosis and Treatment of Cancer

sciforum-178018: A Conceptual Nanotheranostic Platform Using Functionalized Metal Quantum Dots for Targeted Cancer Imaging and Therapy

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The development of selective and minimally invasive strategies for cancer diagnosis and treatment remains a major challenge in modern oncology. Conventional imaging and therapeutic approaches often suffer from limited specificity, resulting in unintended damage to healthy tissues. In this study, we propose a multifunctional nanotheranostic platform based on functionalized metal-based quantum dots and nanoparticles for targeted cancer imaging and therapy.

The proposed system involves the synthesis of gold and silver quantum dots/nanoparticles followed by surface modification with biocompatible polymers and tumor-targeting ligands such as peptides or folic acid. These ligands are intended to enable selective recognition of overexpressed receptors commonly found in solid tumor cells, including breast and lung cancers. Owing to their unique optical and plasmonic properties, the engineered nanostructures are expected to provide high-contrast fluorescence and surface-enhanced imaging for real-time visualization of malignant cells.

Upon selective cellular uptake, the nanoplatform is designed to generate localized photothermal and reactive oxygen species-mediated cytotoxic effects under controlled light irradiation, leading to targeted destruction of cancer cells while minimizing adverse effects on surrounding healthy tissues. The incorporation of biocompatible surface coatings is expected to enhance stability, circulation time, and biosafety.

This conceptual study outlines an integrated approach combining diagnosis and therapy within a single nanosystem, offering a promising framework for precision oncology. Future in vitro and in vivo investigations are planned to validate the feasibility, safety, and therapeutic efficacy of the proposed strategy.



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sciforum-171288: Heparan Sulfates Regulate Angiogenic Signaling and Drug Response in Aggressive Ovarian Cancer

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Introduction

Heparan sulfate proteoglycans (HSPGs) are critical regulators of growth factor availability and angiogenic signalling within the tumour microenvironment. Dysregulation of heparan sulfate (HS) biosynthesis has been implicated in tumour progression; however, the mechanisms by which altered HS architecture spatially controls angiogenic signalling and therapy response in ovarian cancer remain incompletely understood. This study investigates the role of exostosin glycosyltransferase 1 (EXT1), a central enzyme in HS biosynthesis, in regulating angiogenesis and platinum resistance.

Methods

EXT1 was overexpressed in ovarian cancer cells to modulate HS biosynthesis and deposition. HS accumulation was assessed, and levels of angiogenic mediators in conditioned media were quantified. Endothelial tube formation was evaluated using conditioned medium and direct co-culture assays with human umbilical vein endothelial cells (HUVECs). Platinum sensitivity was assessed in EXT1-high cells, with or without enzymatic degradation of HS using heparinase, to determine the functional impact of HS-mediated sequestration.

Results

EXT1 overexpression significantly increased pericellular HS deposition, creating a localized reservoir for chemokines and pro-angiogenic growth factors. Conditioned medium from EXT1-overexpressing cells contained reduced levels of VEGFR, EDN1, IL6, and IL8 and exhibited diminished capacity to induce endothelial tube formation. In contrast, direct co-culture of EXT1-overexpressing ovarian cancer cells with HUVECs markedly enhanced tube formation, indicating that HS promotes angiogenesis through localized, contact-dependent paracrine signalling rather than freely diffusible factors. Additionally, elevated HS levels contributed to platinum resistance by sequestering therapeutic agents, impairing drug penetration, and altering receptor–ligand interactions. Enzymatic degradation of HS restored platinum sensitivity in EXT1-high cells.

Conclusions

These findings demonstrate that EXT1-driven HS remodelling regulates angiogenesis by spatially controlling growth factor bioavailability and contributes to therapy resistance, positioning HS structures as promising therapeutic targets and potential scaffolds for ligand-mediated drug delivery strategies in ovarian cancer.



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sciforum-168260: The Role of DGKH in Cervical Carcinogenesis: Mechanisms and Implications

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Introduction: Persistent high-risk human papillomavirus (hr-HPV) infection is the primary cause of cervical cancer. Integration of the HPV genome into the host chromosome is a key carcinogenic event. However, previous research has focused on alterations in genes adjacent to integration sites, leaving long-range effects on distal genes poorly understood. This study aimed to investigate how HPV integration at 13q22.1 distally regulates expression of diacylglycerol kinase θ (DGKH) and elucidate DGKH's biological functions and molecular mechanisms in cervical carcinogenesis.

Methods: We performed bioinformatics analysis using multi-omics data from public databases and our cohort to identify distally upregulated genes by comparing transcriptomes of patients with or without HPV integration at 13q22.1. Functional validation was conducted using a 13q22.1-specific HPV knock-in HaCaT cell model and cervical cancer cell lines through Western blot, siRNA interference, plasmid transfection, CCK-8, and Transwell assays. Mechanistic insights were explored using RNA interference, ChIP-PCR, and RNA sequencing.

Results: DGKH was upregulated in cervical cancer samples with HPV integration at 13q22.1. Its high expression correlated with poor patient prognosis and low CD8⁺ T cell infiltration. Knockdown of DGKH inhibited, while overexpression promoted, proliferation, migration, and invasion of cervical cancer cells. The transcription factor ELF1, upregulated post-integration, directly binds to the DGKH promoter to activate transcription. Furthermore, DGKH enhanced macroautophagy, which may facilitate tumor cell survival under stress.

Conclusions: This study demonstrates that HPV integration can exert long-range transcriptional regulation on distal genes. We reveal a critical oncogenic role of DGKH in cervical cancer, where its expression is upregulated via ELF1 following HPV integration. DGKH promotes tumor proliferation and invasion, likely by enhancing macroautophagy, leading to poor prognosis. These findings deepen understanding of HPV-driven carcinogenesis and identify DGKH as a potential prognostic biomarker and therapeutic target.



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sciforum-171015: A comprehensive study of HMG-CoA reductase in Uterine cancer with an *in silico* perspective

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Introduction: Uterine cancer (UC) remains one of the most predominant gynaecological malignancies in Asia and is often associated with high mortality owing to the unavailability of reliable precision markers and targeted therapy. Also, the option of hysterectomy renders a woman infertile as part of its current treatment course. Therefore, it is the need of the hour to develop new drug targets to efficiently formulate a new treatment regimen.

Methods: With recent advances in the field of multi-omics studies, it is now possible to mine data from several publicly available data repositories, thereby accelerating the search for a suitable biomarker and drug target. Thus, bioinformatic analyses were performed using various web applications like UALCAN, Gepia2, OncoDB, and cBioPortal to understand the impact of HMG-CoA reductase (HMGCR) and its effects on both subtypes of uterine cancer by extracting data from TCGA and GTEx.

Results: TCGA data accessed through cBioPortal revealed a higher percentage of mutational anomalies in the UCEC (6%) patients compared to UCS (1.75%). By accessing the transcriptomics data, it was found that the UCEC type, the most abundant form of UC, showed significantly higher expression of HMGCR (TPM) compared to the normal tissues ($p < 0.05$). However, the changes in mRNA level expression in the case of UCS and its normal counterparts were found to be non-significant ($p > 0.05$). Subsequent studies also reconfirm the claim in pre-menopausal women, where preserving fertility is a major concern.

Conclusion: HMGCR catalyses an important step in the cholesterol biosynthetic pathway. Often, statins are prescribed for managing LDL levels, which are inhibitors of this enzyme. HMGCR is significantly increased at transcript levels in the UCEC samples but not in the UCS samples. Therefore, statins might serve as an alternative medication to harness UC in pre- and perimenopausal women and are yet to be confirmed through *in vitro* studies.



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sciforum-170842: A Cross-Sectional Evaluation of Guideline-Adherent Screening Eligibility Among Zimbabwean Patients Diagnosed with Lung Cancer

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Introduction

Lung cancer screening enables earlier detection at more treatable stages, reducing mortality and healthcare costs. For high-risk individuals—identified by age and smoking history—it offers timely, effective treatment options. However, current screening criteria, mainly from the US and Europe, may not suit African populations due to differing demographics, risk factors, and life expectancy. This study assessed Zimbabwean cancer patients' eligibility for lung cancer screening using four established criteria.

Methodology

This cross-sectional study reviewed all lung cancer cases treated at Parirenyatwa Hospital in Harare, Zimbabwe over five years. We assessed each patient's eligibility for lung cancer screening one year prior to diagnosis using American Cancer Society (ACS), American Association for Thoracic Surgery (AATS), U.S. Preventive Services Task Force (USPSTF) and European Society of Radiology (ESR) criteria.

Results

A total of 30 female and 43 male lung patients were reviewed and had median age of 65 years (IQR52–71) and 61 years (IQR54–69), respectively. A history of smoking was present in 81% of males and only 3% of females with a median pack-year history of 28 (IQR15–40). Histologically non-small cell carcinoma comprised 97% in females and 94% males and 77% had distant metastases. Based on the ACS, AATS, USPSTF and ESR criteria 30%, 27%, 30% and 16% of the lung cancer patients were eligible for screening. The varied significantly between males and females- ACS 49% vs 3% (OR 0.04, 95% CI 0.005–0.3, $P=0.0018$); AATS 44% vs 3% (OR 0.04, 95% CI 0.005–0.3, $P=0.0032$); USPSTF 49% vs 3% (OR 0.04, 95% CI 0.005–0.3 $P=0.0018$ and ESR 26% vs 3% (OR 0.1, 95% CI 0.01–0.8, $P=0.03$).

Conclusion

The majority of lung cancer patients in Zimbabwe would not have qualified for screening under the current guidelines. This is partly a result of very low smoking rates among women and potentially other risk factors such as environmental exposures or genetic predispositions that require further investigation



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sciforum-161973: A Novel Butylated Neuropeptide Antagonist Targeting Hypoxia-Induced GRPR Overexpression in Small Cell Lung Cancer

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Small cell lung cancer (SCLC) is a highly aggressive neuroendocrine malignancy with few effective targeted therapies. As hypoxia is a central feature of solid tumours and contributes to resistance mechanisms, identifying therapeutic vulnerabilities linked to hypoxia-responsive pathways is crucial. The gastrin-releasing peptide receptor (GRPR) is commonly elevated in SCLC, yet its regulation under hypoxia has not been extensively characterised. In this study, we examined the effect of hypoxia on GRPR expression and evaluated the therapeutic potential of a butylated neuropeptide antagonist (Bu peptide) specifically designed to inhibit GRPR-mediated signalling. Exposure of DMS79 and COR-L24 SCLC cells to hypoxia led to a pronounced increase in GRPR expression. This was validated using Western blot analysis and BBN-FITC binding assays, confirming hypoxia-driven enhancement of receptor availability at the cell surface. The Bu peptide, synthesised through an optimised Boc-based solid-phase peptide synthesis strategy, demonstrated strong cytotoxic activity in both cell lines. Its potency was more pronounced under hypoxic conditions, aligning with elevated GRPR expression. Mechanistic studies showed that Bu peptide treatment effectively suppressed phosphorylation of AKT and ERK, two key downstream mediators of GRPR signalling involved in survival and proliferation. In addition, Bu peptide triggered significant apoptotic activation, as evidenced by increased caspase-3/7 activity, with stronger effects observed under hypoxia. Overall, our findings highlight GRPR as a hypoxia-inducible therapeutic target in SCLC and demonstrate that the Bu peptide selectively inhibits GRPR-driven pathways while inducing apoptosis in hypoxic tumour cells. These results underscore the translational relevance of GRPR antagonists and support further development of tailored peptide-based therapies for hypoxia-adaptive cancers.



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sciforum-171178: Analysis of Screening Results for Upper Gastrointestinal Cancer and Precancerous Lesions among High-Risk Individuals Aged 40–69 in the Chaoshan Region, Guangdong Province, China

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Background: China bears nearly half of the global burden of upper gastrointestinal cancers, but screening coverage in South China is low and data are limited. As the only national prospective cohort site for esophageal cancer in South China, the epidemiological characteristics of the disease in the Chaoshan region remain unclear.

Objective: The objective was to investigate the detection and distribution characteristics of cancer and precancerous lesions in a high-risk population of patients with upper gastrointestinal cancer in the Chaoshan area.

Methods: A cross-sectional survey design was used to include a total of 3,233 high-risk groups of upper gastrointestinal cancer patients aged 40–69 years in Chaoshan from 2019 to 2025. Participants underwent gastroscopy, and suspected lesions were biopsied for pathological examination.

Results: The detection rate of upper gastrointestinal cancers and precancerous lesions was 12.62% (408/3,233), including 44 cases of Barrett's esophagus (1.36%), 287 cases of low-grade intraepithelial neoplasia (8.88%), 33 cases of high-grade intraepithelial neoplasia (1.02%), 6 cases of early cancer (0.19%), and 38 cases of advanced cancer (1.18%). The positive detection rate was 2.38% (77/3,233), the cancer detection rate was 1.36% (44/3,233), and the early diagnosis rate was 50.65% (39/77). Gender distribution showed that the detection rate of cancers and precancerous lesions was significantly higher in males than in females (15.90% vs. 9.98%, $P=0.001$). Age distribution showed that the detection rate of low-grade intraepithelial neoplasia followed an inverted 'U'-shaped curve, peaking in the 50–54 age group.

Conclusion: The detection rate of upper gastrointestinal tract cancer and precancerous lesions in high-risk groups in the Chaoshan area is high, and men should be the primary focus of prevention and control efforts. Low-grade intraepithelial neoplasia showed specific age distribution characteristics, which provided a reference for optimizing the key age of screening and formulating precise public health prevention and control strategies.



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sciforum-171552: Associations of Functional Polymorphisms in Long Non-Coding RNAs MEG3 and GAS5 with Breast Cancer Risk and Gene Expression

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Background

Long non-coding RNAs (lncRNAs) regulate gene expression and have been implicated in breast cancer (BC) development. Functional polymorphic variants in lncRNA genes may alter their regulatory activity and influence cancer susceptibility. This study aimed to assess the association between selected lncRNA polymorphisms, breast cancer risk, and gene expression levels.

Methods

The study included 100 patients with breast cancer (paired tumor and adjacent normal tissue samples) and 59 women without a history of oncological diseases (control group). The following polymorphic markers were analyzed: *SNHG16* rs8038 (G>A), *GAS5* rs145204276 (ins/del CAAGG), *GAS5* rs55829688 (T>C), *MEG3* rs10132552 (T>C), and *MEG3* rs7158663 (A>G). Genotyping was performed using real-time PCR. Expression levels of three lncRNAs were evaluated in 20 paired breast cancer samples and 12 control samples.

Results

A significant association was observed between *GAS5* rs145204276 and breast cancer risk (OR = 3.88; 95% CI 2.39–6.30; p 0.0001). The del allele and del/del genotype were identified as risk factors. *GAS5* expression was higher in histologically normal breast tissue from patients compared to donors (p 0.05) and significantly reduced in tumor tissue relative to adjacent normal tissue (p 0.01). Lower *GAS5* expression was observed in ins/ins genotype carriers compared to ins/del + del/del.

MEG3 expression did not differ between controls and normal tissue but was significantly decreased in tumor tissue (p 0.05). The AA genotype (rs7158663) was associated with reduced *MEG3* expression in both normal and tumor tissues.

Conclusions

The del allele of *GAS5* rs145204276 and the AA genotype of *MEG3* rs7158663 are associated with increased breast cancer risk, likely through reduced lncRNA expression.

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sciforum-178191: Brain Cancer Gene Expression Analysis for Subtype Classification and Biomarker Discovery Using Machine Learning

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Brain cancer remains one of the most aggressive malignancies worldwide. Subtypes such as glioblastoma and ependymoma exhibit markedly different clinical behaviors and treatment responses, making accurate classification essential for diagnosis and therapy. This study analyzed the Brain_GSE50161 transcriptomic dataset, comprising 54,676 gene expression features across 130 samples representing four brain cancer subtypes and normal tissue. After preprocessing and standardization using StandardScaler, a multi-stage feature selection pipeline was applied, combining variance threshold filtering and Recursive Feature Elimination (RFE) to identify the most informative features. Machine learning models, including Logistic Regression and Random Forest classifiers, were developed and optimized using GridSearchCV. Model performance was evaluated using an 80/20 train-test split with 5-fold cross-validation and assessed via accuracy, precision, recall, and F1-score. Feature selection reduced the dataset to a refined 30-gene biomarker signature. The optimized Random Forest model achieved 92.31% classification accuracy, outperforming the Logistic Regression baseline (84.62%). Cross-validation confirmed model stability (89.23% average score). Volcano plot analysis revealed significantly up- and downregulated genes among tumor subtypes, while Principal Component Analysis (PCA) demonstrated distinct clustering, with the first two components explaining approximately 45% of variance. Several probes, including 200502_s_at, contributed strongly to diagnostic discrimination. This study demonstrates that integrating transcriptomic analysis with machine learning-driven feature selection provides a robust framework for brain cancer subtype classification and biomarker discovery. High-precision diagnostics can be achieved using targeted gene signatures rather than full-genome analysis. The identified biomarkers represent promising candidates for future clinical validation and the development of improved molecular diagnostics in precision oncology.



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sciforum-171608: Clinical Pharmacokinetics of Imatinib: Evidence of Sex-Related Differences in Drug Exposure

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Imatinib is a tyrosine kinase inhibitor (TKI) derived from 2-phenylaminopyrimidine, initially developed to target the platelet-derived growth factor receptor. It was subsequently shown to inhibit the BCR-ABL fusion protein and c-KIT. These kinases phosphorylate specific amino acids on substrate proteins, triggering signal transduction pathways involved in cell proliferation, differentiation, and survival. Constitutive activation of these pathways due to mutations or other mechanisms may lead to malignant transformation. By competitively inhibiting the ATP-binding site of ABL, imatinib prevents persistent tyrosine kinase activation and induces apoptosis in leukemic cells.

Imatinib plasma concentrations are known to correlate with clinical response, highlighting a strong pharmacokinetic–pharmacodynamic relationship. The aim of this study was to provide a comprehensive pharmacokinetic evaluation of imatinib exposure and to assess interindividual variability, with particular focus on differences related to sex and age, which are recognized as important determinants of drug pharmacokinetics.

Using a validated chromatographic method, plasma concentration data were collected from 329 treated patients. A statistically significant difference in imatinib concentrations was observed between sexes, with higher concentrations in females compared to males ($p = 0.001$). After exclusion of paediatric patients, sex remained significantly associated with concentration levels, with adult females exhibiting significantly higher concentrations than adult males ($p = 0.001$). Among adult patients, 156 out of 325 (48.0%) had concentrations within the range of 1–3 mg/mL. This proportion was 45.0% in males (85/189) and 52.2% in females (71/136); however, this difference was not statistically significant.

These findings confirm substantial interindividual variability in imatinib exposure and identify sex as a significant determinant of plasma concentration in adult patients. Consideration of sex- and age-related differences may support more individualized therapeutic drug monitoring strategies to optimize treatment efficacy and safety in oncology practice.



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sciforum-178243: Decoding Therapy-induced Senescence EVs: Proteomic and miRNomic Clues to NSCLC Chemoresistance

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Non-small cell lung cancer (NSCLC) remains one of the leading causes of cancer mortality, driven by molecular heterogeneity and therapy resistance. Standard treatments like chemotherapy and radiotherapy often fail to eradicate all tumour cells and instead trigger therapy-induced senescence (TIS), a state of permanent growth arrest with persistent metabolic activity. TIS cells undergo profound changes and secrete a complex senescence-associated secretory phenotype (SASP). SASP exerts dual effects: initially recruiting immune surveillance, later promoting tumour progression through matrix remodelling and growth factor release. Among SASP components, extracellular vesicles (EVs) are emerging as key intercellular messengers, capable of transferring functional cargo that affects the behaviour of recipient cells. However, the dynamic of senescence-derived EV cargo and its role in NSCLC chemoresistance remain poorly understood.

This study aimed to characterise the proteomic and miRNomic content of EVs from TIS lung cancer A549 at different time points, elucidate their contribution to chemoresistance and identify potential prognostic and therapeutic targets.

A549 cells were treated with doxorubicin to induce senescence, and EVs were isolated by sequential centrifugation. miRNA sequencing and mass spectrometry were performed on both intracellular and EV samples.

MiRNomic profiling identified the analysis of differential miRNA expression between control and senescent states—identifying 239 DEmiRNAs intracellularly and 39 in EVs—as well as differential sorting into vesicles. Enrichment analyses revealed that EV-associated DEmiRNAs were implicated in DNA damage, cancer-related, and senescence pathways. In parallel, proteomic analysis revealed a time-dependent remodelling of EV cargo, with pathway analyses highlighting upregulation of tight junctions, cell communication, p53, and interleukin signalling.

Collectively, these findings suggest that EV cargo remodelling may contribute to NSCLC chemoresistance, and ongoing multi-omics integration—including RNA-Seq and Proximity Extension Assay—aims to identify novel prognostic and therapeutic candidates.



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sciforum-178446: Deuterated α -Aminoisobutyric Acid (AIBA-d6) as a Novel Contrast Agent for Deuterium Magnetic Resonance Spectroscopy (DMRS)

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Introduction: Deuterium magnetic resonance spectroscopy (DMRS) is a promising approach for the non-invasive investigation of pathological conditions. Organic compounds with hydrogen atoms replaced by deuterium can serve as contrast agents for DMRS. Choosing the right contrast agent allows for obtaining spectra on 3T scanners and evaluating malignant tumors. In the study, we investigated α -aminoisobutyric acid with all six carbon-bound hydrogen atoms replaced with deuterium (AIBA-d6).

Methods: The biodistribution of AIBA-d6 was studied after a single intravenous administration in Wistar rats at a dose of 125 mg/kg. Concentrations were measured in plasma, 17 organs and tissues, urine, and feces from 5 minutes to 48 hours. Acute tolerability was assessed after a single high dose (2000 mg/kg). Tumor visualization was confirmed using 2-h DMRS in rodents with 4T1 breast carcinoma or C6 glioma. AIBA-d6's ability to detect human glioblastomas was tested using phantom models and a 3T scanner.

Results: Acute toxicity study showed no pathological changes within 7 days after a single intravenous administration at the maximum tested dose of 2000 mg/kg. AIBA-d6 reached its maximum plasma concentration ($C_{\max}$ 297.3 $\pm$ 131.7 μ g/mL) immediately after intravenous administration and then declined biphasically to 12.3 $\pm$ 4.2 μ g/mL at 48 h. AIBA-d6 was not metabolized; the highest concentration was observed in the kidneys ($C_{\max}$ 1028 $\pm$ 139 μ g/g; $T_{\max}$ $\approx$ 1 h), indicating renal clearance. Urinary concentrations were high during the 0–6 h interval (2203 $\pm$ 1131 μ g/mL), whereas fecal excretion was minimal. Accumulation in tumors was confirmed by DMRS on a Bruker 7T scanner. This accumulation was associated with overexpression of A/SNAT1-2 transporters. Phantom studies showed that tumor levels were high enough for detection in human brain tumors using a clinical 3T scanner within 17–30 minutes.

Conclusions: AIBA-d6 is a promising contrast agent for the visualization and detection of malignant brain tumors by DMRS.



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sciforum-178317: Diagnostic Performance of High-Resolution Anoscopy in Detecting High-Grade Anal Lesions in an Anal Cancer Screening Programme

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Introduction:

Anal cancer screening programmes targeting high-risk populations rely on high-resolution anoscopy (HRA) as the primary diagnostic tool for detecting high-grade squamous intraepithelial lesions (HSIL) and invasive carcinoma. While HRA is widely endorsed as the reference technique, real-world data on its diagnostic performance within structured screening programmes remain limited. Evaluating detection rates and biopsy yield in routine clinical practice is essential to optimise screening protocols.

Methods:

A retrospective analysis of 33 consecutive HRA examinations performed within a structured anal cancer screening programme at a specialised colorectal unit was conducted. All examinations included targeted biopsies guided by intraoperative assessment. Histopathological analysis served as the reference standard. Diagnostic performance metrics including detection rate, biopsy positivity rate, and overall programme yield were calculated. High-grade disease was defined as HSIL or invasive squamous carcinoma.

Results:

Among 33 examinations, histopathological analysis identified 3 high-grade lesions (2 HSIL, 1 invasive carcinoma), yielding an overall high-grade detection rate of 9.1%. All 33 examinations resulted in biopsy sampling, with a high-grade biopsy positivity rate of 9.1%. Notably, all high-grade lesions were detected in examinations classified as low visual suspicion, suggesting that programme yield depends on systematic rather than selective biopsy strategies.

Conclusions:

HRA demonstrated a clinically relevant detection rate within this screening programme. These findings support the implementation of systematic biopsy protocols independent of intraoperative visual impression, with implications for standardising HRA-based screening in high-risk populations.



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sciforum-169390: Distinct YAP-TEAD signaling states revealed by integrated mRNA and protein analysis in thymic epithelial neoplasms

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Background: Thymic epithelial tumors (TETs) are rare and biologically heterogeneous. As Hippo pathway dysregulation can manifest through altered YAP/TEAD-dependent transcription and compartment-specific protein distribution, we integrated RT-qPCR and immunohistochemistry (IHC) to identify coordinated expression and localization patterns within the YAP-TEAD axis. **Methods:** In formalin-fixed, paraffin-embedded (FFPE) TET samples, *MST1*, *SAV1*, *LATS1*, *MOB1A*, *YAP1*, and *TEAD4* were quantified by RT-qPCR using the $2^{-\Delta\Delta C_q}$ method relative to pooled normal. IHC was scored separately for nuclear and cytoplasmic positivity and staining intensity. Associations between mRNA and IHC were assessed using Spearman correlation. Principal component analysis (PCA) was conducted, and sampling adequacy was evaluated using the Kaiser-Meyer-Olkin (KMO) measure. The PCA model (overall KMO = 0.71) included mRNA expression and nuclear/cytoplasmic IHC of YAP1, phosphorylated YAP (AYAP), and TEAD4. **Results:** No significant mRNA-protein associations were observed for upstream markers (*MST1*, *SAV1*, *LATS1*, *MOB1A*; all $p > 0.05$). In contrast, *YAP1* mRNA positively correlated with cytoplasmic (R = 0.49, $p = 0.016$) and nuclear YAP1 positivity (R = 0.47, $p = 0.024$). AYAP showed the strongest coupling between mRNA and protein readouts (cytoplasmic R = 0.60, $p = 0.002$; nuclear R = 0.49, $p = 0.017$). *TEAD4* mRNA correlated with cytoplasmic TEAD4 positivity (R = 0.45, $p = 0.032$) but not with nuclear TEAD4 (R = 0.29, $p = 0.182$). PCA PC1 captured coordinated overall variation across mRNA and protein compartments, whereas PC2 reflected a contrast between *TEAD4* transcript/cytoplasmic TEAD4 and nuclear YAP/AYAP patterns. Type A thymomas tended toward higher PC1, B1/B2 toward lower PC1, B3 displayed heterogeneity, and thymic carcinomas shifted predominantly along PC2. **Conclusion:** Downstream effectors (*YAP1/TEAD4*) show stronger mRNA-protein concordance than upstream Hippo components. Integrative PCA reveals subtype-associated YAP-TEAD signaling states and supports compartment-resolved profiling as a complementary biomarker strategy in TETs.



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sciforum-168193: Evaluation of Interobserver Agreement in the Classification of Peritoneal Implants in Ovarian Serous Borderline Tumors and Low-Grade Serous Carcinomas: A Multi-Reviewer Study

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Background/Objectives: The precise distinction between invasive and non-invasive peritoneal implants in ovarian serous borderline tumors (SBTs) and low-grade serous carcinomas (LGSCs) is crucial for clinical management, as it determines surgical approach and prognosis. However, diagnostic reproducibility among pathologists remains variable. The aim of this study was to evaluate interobserver agreement in the classification of these implants. **Methods:** Twenty-four cases of ovarian SBT and LGSC with 33 samples of extraovarian implants were independently reviewed by three gynecologic pathologists and three general pathologists. Diagnostic criteria included destructive invasion, micropapillary architecture, and retraction clefts. The Fleiss' Kappa statistic was used to measure interobserver agreement, with consensus diagnoses determined by the majority of gynecologic pathologists. **Results:** Patients in the SBT group were younger than patients in the carcinoma group but these differences were not statistically significant. FIGO staging showed that most cases in both groups were advanced (stage III-IV) with 75.0% in SBTs and 91.0% in LGSC. Stage II was rare, accounting for 15% and 9% for each group, respectively. According to the consensus diagnosis, 42.4% biopsies were classified as metastases of SCLGs and 57.6% as non-invasive implants of SBTs. The most commonly detected single patterns of omentum and peritoneum metastases were destructive invasion and clefts in fibrotic stroma (both 28.5%). The mixed architecture was identified in five cases. When interobserver reproducibility was measured, gynecologic pathologists showed substantial to near-perfect agreement ($\kappa=0.876-0.937$), while general pathologists showed moderate agreement ($\kappa = 0.467-0.698$). Overall reproducibility was substantial ($\kappa=0.61$). **Conclusions:** The results showed that current diagnostic reproducibility remains suboptimal, particularly among general pathologists, underscoring the need for improved training and standardized criteria. Ultimately, a multidisciplinary approach combining morphological expertise, immunohistochemical validation and molecular stratification will be essential for optimizing the diagnosis and treatment of peritoneal implants to ensure tailored therapies that balance oncological safety and quality of life, especially for young patients who wish to preserve their fertility.



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sciforum-170762: Evaluation of the epigenetic signatures of BRCA1 and TP53 as tools for metastatic prognosis: Translational study on a cohort of Moroccan women

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Epigenetic inactivation of tumor suppressor genes plays a key role in cancer aggressiveness. This study evaluates the impact of methylation of BRCA1 and TP53 promoters on the risk of metastatic dissemination in women with breast cancer.

We analyzed the status of BRCA1 and TP53 gene promoter hypermethylation in patients with sporadic breast cancer. Associations were evaluated by the exact Fisher test and logistic regression (Odds Ratio). In addition, the co-occurrence was analyzed via the Spearman correlation coefficient.

The result reveals that 52% of samples are methylated and that these positives show that this epigenetic factor is remarkable in women over 47 years old. Overall, the Odd Ratio (OR) is 4.2, which means that the probability of presenting a methylation of BRCA1/TP53 genes is 4.2 times higher in patients with Metastasis than in those with Malignant Tumor stage. This demonstrates that a strong co-occurrence of methylation between BRCA1 and TP53 has been observed ($p=0.62$). The analysis shows that BRCA1 methylation is significantly associated with the metastatic stage ($p=0.004$) and associated with tumor aggressiveness.

The methylation of BRCA1, particularly when associated with that of TP53, constitutes a robust biomarker of tumor aggressiveness. These results suggest that the evaluation of the epigenetic profile could improve the prognostic stratification of patients.



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sciforum-171760: Genetic Susceptibility to Chemotherapy-Induced Heart Failure: A Systematic Review

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Background: Chemotherapy-induced heart failure (CHF) is a serious adverse effect that can limit treatment efficacy and compromise patient survival. Individual susceptibility varies significantly, and genetic factors are thought to play a crucial role. This systematic review synthesizes the current evidence on genetic variants associated with an increased risk of CHF, focusing on their biological pathways, clinical relevance, and potential for risk stratification.

Methods: We conducted a systematic review of studies published from database inception to December 2025. Our search was performed exclusively in the PubMed electronic database for English-language studies. The review encompassed various study designs, including cohort studies, case-control studies, genome-wide association studies (GWAS), and systematic reviews, to comprehensively capture the genetic evidence on this condition. A total of 20 studies were selected for final inclusion from an initial 1,405 identified records after a rigorous, multi-stage screening process.

Results: A total of 20 studies were included. The research landscape was dominated by North America and Europe, with a significant focus on anthracyclines. Key genetic variants were identified in pathways governing drug transport (e.g., SLC28A3 rs7853758, protective), drug metabolism (e.g., CBR3 rs1056892, risk; UGT1A6 rs17863783, risk), and transcriptional regulation (e.g., RARG rs2229774, risk). The most robust evidence supports the consideration of genetic testing for RARG, SLC28A3, and UGT1A6 in pediatric patients before anthracycline therapy. Common limitations across studies included small sample sizes, heterogeneous definitions of cardiotoxicity, and a lack of ethnic diversity.

Conclusion: Specific genetic variants significantly modulate the risk of CHF. The implementation of pharmacogenomic testing, particularly in high-risk populations, holds promise for personalizing cancer therapy and preventing cardiotoxicity. Future research must focus on large, multi-ethnic prospective studies, standardized endpoints, and functional validation of genetic associations to translate these findings into routine clinical practice.



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sciforum-177853: Geographical and temporal incidence patterns of childhood central nervous system tumours in Europe: Insights from the European Cancer Information System

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Introduction:

Central nervous system tumours (CNSTs) are the most common solid childhood malignancies and comprise heterogeneous histological subtypes. The European Cancer Information System (ECIS) collects incidence data from Population-Based Cancer Registries (PBCR) across Europe. Identifying spatial and temporal variations is essential for cancer control and hypothesis generation on potential risk factors. This study analysed geographical and temporal incidence patterns of childhood CNST in Europe.

Methods:

Incidence data for children under 15 years were obtained from the ECIS. PBCRs updated to ≥ 2019 were selected. Geographical analyses covered the 2017–2021 period (29 PBCRs, 17 countries). Temporal trends were assessed in 16 PBCRs with ≥ 10 consecutive three-year periods (1982–2023). Age-standardised incidence rates (ASIR) with 95% confidence intervals (95%CI) were computed. The Joinpoint regression estimated Average Annual Percent Change (AAPC).

Results:

Astrocytoma was the most frequent subtype (26%–47%). Geographical variations were observed for overall CNST, ASIRs ranging from 15 per million children-year (95%CI: 6.1–24.1) in Cyprus to 64 (95%CI: 54.0–74.6) in Emilia-Romagna, which are the lowest and highest values. Astrocytoma ASIRs varied from 5.8 (95%CI 3.4–8.2) in Austria to 25.2 (95%CI 19.4–31.0) in Croatia. Significant increases in overall CNST were observed in 11 PBCRs with AAPCs between 2.4% (95%CI 1.0–3.9) and 8.3% (95%CI 6.1–9.8), and mainly for other specified intracranial and intraspinal neoplasms in 9 PBCRs, with AAPCs between 7.6% (95%CI 1.9–13.3) and 73.6% (95%CI 20.5–148.6). The incidence remained stable in the Basque and Veneto PBCRs.

Conclusion:

Childhood CNST incidence shows marked geographical variations and increasing time trends in most European PBCRs. ECIS is a valuable tool for monitoring these tumours, though with some limitations such as lack of sex-specific data and incomplete updates in some registries.



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sciforum-171751: Global Longitudinal Strain Compared to Left Ventricular Ejection Fraction for Early Identification of Subclinical Cardiotoxicity in Cancer Patients: A Systematic Review

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Background: Cancer therapies, while life-saving, can cause cancer therapy-related cardiac dysfunction (CTRCD). Left ventricular ejection fraction (LVEF) has limitations in detecting subclinical myocardial injury. This systematic review synthesizes the current evidence on the diagnostic and prognostic utility of global longitudinal strain (GLS), derived from speckle-tracking echocardiography, compared to LVEF for the early identification of subclinical cardiotoxicity.

Methods: We systematically searched PubMed and Science Direct from inception to September, 2025 for studies comparing GLS to LVEF for detecting CTRCD in cancer patients. Data on study characteristics, patient demographics, cancer and therapy types, diagnostic accuracy, and prognostic value were extracted. The risk of bias was assessed using the Cochrane Risk of Bias 2 (RoB 2) tool.

Results: A total of 47 studies were included. The evidence consistently demonstrates the superior sensitivity of GLS over LVEF for the early detection of subclinical CTRCD. GLS changes often preceded a significant LVEF decline by weeks to months. A preserved GLS had a high negative predictive value (often >90-95%) for ruling out future LVEF-defined cardiotoxicity. Furthermore, abnormal GLS was associated with a higher risk of subsequent clinical heart failure events. One randomized controlled trial (the SUCCOUR trial) showed that a GLS-guided management strategy reduced the incidence of CTRCD compared to an LVEF-guided strategy.

Conclusion: GLS is a more sensitive and prognostically valuable tool than LVEF for the early identification of subclinical cardiotoxicity. Its integration into routine surveillance protocols for patients receiving cardiotoxic cancer therapy is strongly supported by the evidence. A GLS-guided approach for initiating cardioprotective therapy should be considered to improve cardiac outcomes in oncology patients.



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sciforum-170356: Guilty by association: calcium-mediated apoptosis regulated at the ER by a newly discovered mTOR-STAT3 pathway

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STAT3 is a pleiotropic transcription factor often constitutively activated in Triple-Negative Breast Cancer (TNBC). STAT3 canonical transcriptional activity is mediated by Y705 phosphorylation (pY); in contrast, phosphorylation of S727 (pS) orchestrates transcription-independent activities in distinct cellular compartments. The mechanisms that orchestrate the sub-cellular distribution of pS-STAT3 are however unknown. We have recently described pS-STAT3's ability to control Ca²⁺ release and Ca²⁺-mediated apoptosis at the Endoplasmic Reticulum (ER) in TNBC cells, by promoting proteasomal degradation of the Ca²⁺ channel IP3R3. Consistently, STAT3 and IP3R3 protein levels are inversely correlated in highly aggressive human basal-like breast tumors, where STAT3 is often constitutively activated.

To elucidate the mechanisms regulating pS-STAT3 at the ER, a network of ER-STAT3 interactors was generated, identifying mTOR as a potential STAT3 S-kinase. Accordingly, mTOR and STAT3 interact at the ER, as shown by both co-IP and PLA and pan mTOR inhibition by Torin-1, but not by mTORC1 inhibition via Rapamycin, which could hinder pS-STAT3 within the ER, IP3R3 degradation, and Ca²⁺-mediated apoptosis, mirroring STAT3's silencing effects. Our data suggest that STAT3-mTOR interaction does not require either mTORC1 nor mTORC2, since co-IP is still observed upon RAPTOR and RICTOR ablation, respectively. Accordingly, AlphaFold 3 modelling indicates that STAT3 interacts with the Armadillo region of mTOR via its coiled-coil domain, and with the mTOR catalytic pocket via its carboxyterminal region, which contains S727. The assessment of mTOR and pS-STAT3 protein levels in patient-derived tumor samples is in progress.

This data demonstrates for the first time localized control of pS-STAT3, in this case occurring at the ER downstream of mTOR, leading to enhanced apoptosis resistance via IP3R3 degradation. Dissecting these molecular details may provide clues as to how to disrupt apoptotic resistance in STAT3-dependent TNBC cells as well as in other tumors carrying constitutively active pS-STAT3.



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sciforum-171241: Heparan Sulfate-Mediated Mechanotransduction Promotes EMT and Aggressiveness in Ovarian Cancer

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Introduction: Cancer cells integrate biochemical and mechanical cues from the tumour microenvironment to regulate cellular phenotype, invasiveness, and therapy response. Heparan sulfate proteoglycans (HSPGs) are central mediators of extracellular signalling; however, their role in mechanotransduction in ovarian cancer remains poorly understood. We investigated how dysregulated heparan sulfate (HS) biosynthesis driven by exostosin glycosyltransferase 1 (EXT1) influences mechanical signal transduction and therapeutic vulnerability in ovarian cancer.

Methods: EXT1 expression was assessed in ovarian cancer tissues and cell lines and correlated with clinical outcome. Mechanosensitive responses were evaluated using polydimethylsiloxane (PDMS) substrates with tunable Young's modulus. Cell migration, invasion, and epithelial-mesenchymal transition (EMT) markers were analysed following EXT1 overexpression or silencing. Activation of mechanotransduction pathways, including Rho-dependent cytoskeletal remodelling, focal adhesion kinase (FAK), and TGF β signalling, was assessed biochemically. Therapeutic responses were evaluated using enzymatic HS degradation (heparinase), pharmacological inhibition of FAK and TGF β receptor I, and platinum-based chemotherapy.

Results: EXT1 was selectively upregulated in aggressive ovarian tumours and cell lines, correlating with reduced progression-free survival and enhanced EMT. EXT1 overexpression increased cellular sensitivity to matrix stiffness, promoting migration, invasion, and activation of Rho, FAK, and TGF β signalling pathways. In contrast, EXT1 silencing attenuated mechanotransduction signalling and partially reversed mesenchymal traits. Combined inhibition of HS and blockade of FAK and TGF β receptor I synergistically suppressed aggressive phenotypes and enhanced sensitivity to platinum-based chemotherapy.

Conclusions: These findings identify EXT1-dependent HS remodelling as a critical regulator of mechanotransduction in ovarian cancer and suggest that targeting HS-mediated mechanical signalling may improve therapeutic efficacy.



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sciforum-170879: Hyaluronic acid-functionalized CaCO_3 crystals as novel polyelectrolyte multilayer reservoirs for CPT-RB (Chemotherapy and Photodynamic therapy) targeting multiple myeloma

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The properties of calcium carbonate (CaCO_3) make it a suitable option for drug delivery, particularly for medicinal substances with short half-lives, poor stability, limited solubility, and poor bioavailability, as well as restricted distribution or penetration. A significant step in CaCO_3 fabrication is the production of polyelectrolyte multilayered capsules. Isolated soyasaponin-integrated CaCO_3 crystals were functionalized with (chitosan/polyacrylic acid) and (polydopamine/hyaluronic acid) as multilayers. Rose Bengal as photodynamic therapy and camptothecin as chemotherapy were integrated during fabrication separately and simultaneously. The characterization of CaCO_3 crystals was investigated by using SEM, TEM, FTIR, XRD, and zeta potential measurements. Results showed an assembled structure of CaCO_3 crystals with strong integration of Rose Bengal and Camptothecin. Polyelectrolyte multilayered capsules obtained by CaCO_3 removal were observed to have cellular uptake in multiple myeloma cell lines. Hyaluronic acid-functionalized capsules were investigated in fibroblast normal cell lines under confocal microscopy to detect their application as targeted therapy for multiple myeloma. The flow cytometry and confocal microscopy confirmed ROS generation in both irradiated and non-irradiated multiple myeloma cell lines. It concluded that polyelectrolyte multilayered capsules are a good reservoir for encapsulating both chemotherapy and photodynamic therapy molecules simultaneously, and this could increase the potential therapeutic application.

Acknowledgments

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sciforum-167979: In Silico Gene Expression Profiling Maps the Drivers of Pan-Cancer Progression

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Background:

Clear cell renal cell carcinoma (ccRCC), hepatocellular carcinoma (HCC), lung adenocarcinoma (LUAD), and pancreatic ductal adenocarcinoma (PDAC) are highly lethal malignancies originating from distinct tissues yet sharing convergent molecular mechanisms that drive tumour progression. Although cancer-specific biomarkers have been reported, systematic pan-cancer analyses aimed at identifying shared molecular biomarkers across these malignancies remain limited.

Objective:

This study aimed to identify common dysregulated genes and potential pan-cancer biomarkers across ccRCC, HCC, LUAD, and PDAC using integrative bioinformatics and survival analyses.

Methods:

Microarray expression datasets for the four cancer types were retrieved from the Gene Expression Omnibus (GEO) database and analyzed to identify differentially expressed genes (DEGs). Disease-associated gene targets were collected from the Comparative Toxicogenomics Database (CTD), DISEASES, and GeneCards. Shared genes across all cancers were identified using Venn diagram-based intersection analysis. Functional enrichment analysis was performed using ShinyGO to elucidate biological processes and pathways. Protein-protein interaction (PPI) networks were constructed using STRING and further analyzed in Cytoscape with the CytoHubba plugin to identify hub genes. Prognostic relevance was assessed using Kaplan-Meier survival analysis via KM-Plotter.

Results:

Ten candidate biomarker genes, *HGF*, *CDK1*, *CCNB1*, *RRM2*, *KIF14*, *DCN*, *SERPINE1*, *CCNA2*, *DLGAP5*, and *MAD2L1*, were consistently dysregulated across ccRCC, HCC, LUAD, and PDAC. Functional enrichment revealed significant involvement of these genes in key oncogenic pathways, particularly cell cycle regulation and tumour proliferation. Survival analyses demonstrated that aberrant expression of these hub genes was significantly associated with poor prognosis across multiple cancer types.

Conclusion:

This pan-cancer integrative analysis identifies shared molecular drivers underlying diverse malignancies and highlights robust candidate biomarkers with prognostic and therapeutic relevance. These findings provide a foundation for cross-cancer biomarker development; future experimental studies are required to confirm their translational utility.



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sciforum-176520: In Silico Transcriptomic Identification of Recurrent Transmembrane Receptors Across 12 Major Cancers for Targeted Non-Viral Gene Therapy

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Introduction: Cancer remains a leading cause of mortality worldwide, and therapeutic selectivity continues to be a major clinical challenge. Transmembrane receptors overexpressed in tumor tissues represent strategic molecular entry points for targeted gene delivery. Identifying receptors recurrently overexpressed across multiple cancer types may enable the development of broadly applicable, receptor-mediated non-viral gene therapies.

Methods: An in silico transcriptomic analysis was conducted using 86 GEO datasets comprising human solid tumor tissues and corresponding non-cancerous controls across 12 high-incidence cancers. After applying strict homologation criteria (≥ 5 samples per group, standardized gene identifiers, exclusion of cell lines and blood-derived samples), 45 datasets were retained. Differential expression analysis was performed using GEO2R with thresholds of $p \leq 0.05$ and $\log_2FC > 0$ to identify significantly overexpressed genes in tumor tissues. Overexpressed gene lists were functionally classified using Gene Ontology (PANTHER), filtering for proteins annotated as “transmembrane signal receptors.” Curated receptor datasets were subsequently integrated and comparatively analyzed in R to determine recurrence frequency across datasets and cancer types.

Results: From 245,070 significantly overexpressed genes, 3,394 encoded transmembrane receptors. Comparative analysis identified six highly recurrent receptors: TEK, ACKR1, TGFBR3, SFRP1, DDR2, and IL6ST. These receptors were shared across 8-10 cancer types and are functionally linked to angiogenesis, extracellular matrix remodeling, immune modulation, and TGF- β /IL-6 signaling pathways, processes central to tumor progression and metastasis.

Conclusions: This multi-level transcriptomic screening strategy identified shared transmembrane receptors with strong translational potential as molecular gateways for receptor-mediated delivery of non-viral gene therapy vectors.



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sciforum-171934: Integrated Clinical and Functional Analysis Identifies miR-16-1-3p as an Active Passenger Strand Associated with Osteosarcoma Progression and Chemoresistance

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Background

Osteosarcoma progression is a major determinant of poor clinical outcome, yet molecular regulators that reliably reflect disease advancement remain insufficiently defined. Guide miRNA strands are important for regulating gene expression after transcription, while the accompanying passenger strands are generally considered non-functional and less researched. The aim was to systematically analyze miR-16-1-3p, a passenger strand derived from the miR-16-1 gene, to identify target genes that are prognostically significant in OS progression.

Methods

Transcriptomic and clinical data from the TARGET-OS cohort were analyzed to investigate the association between miR-16-1-3p regulatory activity and osteosarcoma progression. miR-16-1-3p activity was inferred indirectly through expression patterns of its predicted target gene set using gene set enrichment analysis and cumulative Z-score-based scoring. Associations with progression status and clinical outcomes were assessed. To validate intrinsic miR-16-1-3p target binding activity in living cells, a fluorescent miRNA sensor system was developed. Functional impact of miR-16-1-3p targeting was further examined using proliferation, migration and cisplatin sensitivity.

Results

The miR-16-1-3p target gene set was significantly enriched in patients with progressive disease, and higher cumulative target gene expression scores were associated with unfavorable clinical outcomes. The fluorescent sensor system directly confirmed that miR-16-1-3p recognizes and suppresses complementary target sequences, demonstrating bona fide regulatory activity. Functional assays showed that miR-16-1-3p overexpression suppressed multiple progression-associated malignant phenotypes and reduced tumor growth and metastasis in the CAM model.

Conclusion

These findings identify miR-16-1-3p as a functionally active passenger strand whose regulatory activity is associated with OS progression. The study effectively merges clinical transcriptomic analysis with sensor validation and functional models, underscoring the vital role played by miRNA passenger strands in disease progression and presenting innovative insights into miRNA regulation in OS.



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sciforum-171688: Interconnections of p53 Status and TGF- β Signaling orchestrate tumor-suppressive and tumor-promoting Effects Irrespective of Tumor Cell Origin.

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Background: TGF- β plays a crucial role in cancer by suppressing early-stage tumors, inhibiting cell growth, and promoting apoptosis in epithelial cells. At advanced stages, TGF- β plays a major role in metastasis, immune evasion, and blood vessel formation through tumor microenvironment alterations. The determinants that govern this functional switch remain incompletely understood. The tumor suppressor p53 is a key regulator of cellular stress responses and may critically modulate TGF- β -driven phenotypic effects in cancer cells.

Methods: Human cancer cell lines U2OS, A549 (p53wt), H1299 (p53-deleted), and MDA-MB-231 (p53 GOF mutated) were used to systematically evaluate the effects of TGF- β stimulation on tumor cell behavior. Self-renewal capacity was assessed by colony formation assays, while cell collective (2D) and confined (3D) migrations were analyzed using wound-healing and Transwell assays, respectively. The influence of p53 status on TGF- β -induced cellular phenotypes was explored in p53-knock-out U2OS and A549 cell sublines.

Results: TGF- β treatment induced the highest increase in migratory effect in MDA-MB-231 cells, whereas in H1299 and U2OS cells was observed the intermediate and lowest one, respectively, indicating independence of cellular origin and p53 status. Notably, loss of p53 in U2OS and A549 cells further potentiated TGF- β -induced migration and invasion. The impact of TGF- β on self-renewal ability varied among different cell types: cell lines with wild-type p53 (U2OS, A549) and p53GOF (MDA-MB-231) demonstrated lower clonogenic survival compare to p53-KO or p53-deficient (H1299) cell lines.

Conclusion: This study demonstrates that TGF- β consistently promotes cancer cell migration across multiple tumor models, where p53 functions as an important modulator of this effect. Wild-type p53, being a co-factor for SMADs, likely activates cell cycle arrest, while absent p53 allows TGF- β to promote survival of cancer cells. The results may provide mechanistic insight into the context-dependent roles of TGF- β -p53 axis during cancer progression.



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sciforum-171295: Iron Oxide Nanoparticles as Potential Agents for Combined Radiotherapy

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Iron oxide nanoparticles (NP) represent a promising theranostic platform for combined radiotherapy: the sensitized activity of iron oxide associated with ionizing irradiation enhances oxidative stress while magnetic properties may provide additional features as controlled therapeutics delivery.

In this study the sensitizing efficacy of nanosized metal-organic frameworks (nMOF) composed of Fe₃O₄ magnetic core double-coated with carboxymethyl - dextran sodium salt (CMD) and polyethyleneimine (PEI) was tested on *C. elegans* animal model, which were exposed subsequently to X-ray irradiation. nMOF used in the range from 0.016 µg/mL to 10 mg/mL alone, or in combination with 1, 3, 5, 7, 10 and 15 Gy irradiation. The nMOF delivery to *E. coli* OP50 and its further allocation within *C. elegans* body were confirmed by Prussian blue staining.

nMOF alone in the range 10 µg/mL - 10 mg/mL exhibited geroprotective effect for *C. elegans* over 30 days of the experiment, in contrast to the toxic effect at low 0.016-10 µg/mL, compared to the control intact nematodes. *C. elegans* irradiation with 10 Gy showed the most toxic effect (decreased survival rate from 39 to 56%) after treatment of nematodes with 0.016-2 µg/mL nMOF, while at 15 Gy the *C. elegans* survival was in average on 13% higher, compared to control intact nematodes. Testing the low irradiation doses showed the dose-dependent effect of nMOF on nematodes survival. Spectrophotometric method showed that 66% of *E. coli* OP50 bacteria at 10 µg/mL nMOF after 24 hours of incubation irreversibly bind to bacteria. The penetration of nanoparticles into the digestive tract of nematodes was confirmed by microscope analysis of fixed nematodes after Prussian blue staining.

Our study has shown that the greatest lytic effect of *C. elegans* is the combination of 0.4 µg/mL nMOF with 1 Gy irradiation, which lead to 44% reduction of nematodes population compared to intact animals.

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sciforum-157598: KRAS activity improves overall survival and fosters an anti-tumor microenvironment in colorectal cancer

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Introduction: Although *KRAS* mutations are key drivers of colorectal cancer (CRC) progression and resistance to treatment, the prognostic and immunomodulatory impact of *KRAS* gene expression remains unclear. This study investigated *KRAS* activity to reveal links with tumor stage, survival, immune landscape and pathways in CRC.

Methods: RNA-seq and clinical data from 549 TCGA-COAD/READ patients were downloaded via TCGA Bioinformatics. Samples were stratified by median *KRAS*TPM into high- and low-activity groups. Immune infiltration was estimated using CIBERSORTx and xCell, compared with Wilcoxon tests and Spearman correlations. Differentially expressed genes were identified using DESeq2 (FDR 0.05, $|\log_2\text{FC}| > 1$), with GO/KEGG enrichment analysis via clusterProfiler. Overall survival was evaluated by Kaplan–Meier curves and log-rank tests.

Results: High *KRAS* activity was significantly associated with earlier tumor stages (stage I–II: 53% vs. 46% in low *KRAS* activity; $P = 0.05$). Kaplan–Meier analysis demonstrated significantly improved overall survival in the high *KRAS* activity group ($P = 0.05$; HR 1). Immune profiling revealed elevated Th1 CD4⁺ T cells ($P = 2 \times 10^{-16}$) and dendritic cells ($P = 0.018$), but reduced Tregs ($P = 5.9 \times 10^{-8}$) and CD8⁺ T cells ($P = 0.017$) in high-*KRAS*-activity tumors. Correlations confirmed positive links with Th1 ($r = 0.6$) and DCs ($r = 0.08$), negative with Tregs ($r = -0.33$), CD8⁺ ($r = -0.15$) and Th2 ($r = -0.2$) cells ($P = 0.05$). Enrichment analysis showed upregulated hormone/antioxidant functions ($P = 2.3 \times 10^{-7}$) and downregulated taste receptor pathways ($P = 4.2 \times 10^{-9}$) in the low-*KRAS*-activity group.

Conclusions: Elevated *KRAS* activity is associated with improved prognosis and Th1-skewed anti-tumor immunity in CRC, where Th1/DC surveillance compensates for reduced CD8⁺ T-cell infiltration. Thus, *KRAS* expression serves as a critical biomarker and immunotherapy target.



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sciforum-170793: Lung Cancer Detection Based on Machine Learning with Data Augmentation Approaches

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Class imbalance is a common challenge in medical data analysis and can significantly affect the performance of machine learning models by favoring majority classes while neglecting minority cases. This issue is particularly critical in lung cancer datasets, where uneven class distributions may lead to biased predictions and reduced diagnostic reliability.

In this study, we investigate the effectiveness of data augmentation techniques for improving lung cancer classification using machine learning approaches. The dataset used in this work consists of 283 positive lung cancer cases and 38 negative cases, resulting in a highly imbalanced class distribution. To address this problem, the Synthetic Minority Oversampling Technique (SMOTE) is employed as a data preprocessing method to enhance the representation of the minority class and improve model learning.

Several machine learning classifiers are trained and evaluated before and after applying SMOTE in order to assess the impact of data balancing on classification performance. The experimental results demonstrate that data augmentation significantly enhances the predictive capability of the models. Among the evaluated classifiers, Logistic Regression achieves the best performance, reaching an accuracy of 96.03% and a precision of 96.36% before optimization. After fine-tuning, the model's performance further improves, achieving an accuracy of 98.15%, an area under the ROC curve (AUC) of 99.92%, and a precision of 100%.

These results highlight the importance of addressing class imbalance in lung cancer datasets and confirm the effectiveness of data augmentation strategies in improving machine learning-based diagnostic systems. The proposed approach contributes to the development of more reliable and robust tools for lung cancer detection, with potential applications in computer-aided diagnosis and clinical decision support.



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sciforum-170531: MARCH5-Driven MFN2 Degradation Sustains Mitochondrial Fission and Drug Resistance in Multiple Myeloma

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Mitochondrial dynamics, governed by the balance between fusion and fission, are critical for malignant plasma cell survival and therapeutic resistance in multiple myeloma (MM); however, the underlying molecular mechanisms remain poorly defined. Here, we investigated the role of the mitochondrial E3 ubiquitin ligase MARCH5 in MM proliferation, metabolic adaptation, and drug resistance, with a particular focus on its regulation of the mitochondrial fusion pathway. MARCH5 was significantly overexpressed in primary MM cells and established cell lines compared with healthy controls. Functional analyses revealed that MARCH5 interacts with the mitochondrial fusion protein mitofusin-2 (MFN2), promoting its ubiquitination and proteasomal degradation, thereby shifting mitochondrial dynamics toward fission. Silencing of MARCH5 stabilized MFN2, induced mitochondrial hyperfusion, impaired oxidative phosphorylation (OXPHOS), and triggered mitochondrial dysfunction and apoptosis. Similar phenotypic effects were observed following genetic overexpression or pharmacological activation of MFN2 using leflunomide, a repurposed FDA-approved drug, both in vitro and in MM xenograft models. Transcriptomic profiling of MARCH5-depleted cells revealed downregulation of OXPHOS-related pathways associated with venetoclax resistance. Consistently, MARCH5 knockdown or MFN2 induction enhanced venetoclax sensitivity and reduced mitochondrial respiration, whereas MARCH5 overexpression restored OXPHOS activity and attenuated drug responsiveness. Collectively, these findings identify the MARCH5–MFN2 axis as a key regulator of mitochondrial dynamics and metabolic fitness in MM and suggest that targeting this pathway may overcome venetoclax resistance and improve therapeutic outcomes in multiple myeloma.



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sciforum-171446: Merkel cell carcinoma: prevalence and impact of delayed presentation in an international aggregated 949-patient database

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Introduction:

Merkel cell carcinomas (MCCs) are skin cancer predominantly affecting the elderly, who often delay seeking medical opinions for asymptomatic lesions which initially resemble less aggressive skin lesions. This study aims to investigate the direct impact of patient-related delays for seeking medical opinions on clinical outcomes in MCC.

Methods:

A detailed international database was compiled, merging anonymous data from 303 MCC patients across Canada, France, and Australia with published individual patient data from an additional 646 cases. The combined databases comprised 949 patients. Descriptive and comparative analyses were performed, focusing on the time interval before patients sought medical opinion and subsequent disease stages at presentation, recurrence rates, and survival.

Results:

Among the 949 patients, a quantifiable time interval before seeking medical evaluation was recorded in 322 (33.9%), with the median being 4 months (range 0-60). Those presenting earlier (shorter than the median delay) and later (longer than the median delay) were compared for initial stages (localized, nodal, or metastatic), recurrence rates, and 5 years overall and cause-specific survival. Statistical analyses including chi-square and log-rank tests were applied. Results indicate that delayed presentation is associated with a trend for advanced-stages disease at diagnosis: 73.6% localized, 21.5% nodal and 3.5% distant disease, versus 82.5% localized, 14.7% nodal and 2.3% distant disease for those with 4 mos ($P=0.09$, chi-square test). The rate of disease recurrence in any sites after treatment was 63.9% vs. 62.1% ($P=0.74$, chi-square test). The 5-year overall survival rates were 30.2% versus 36.1% ($P=0.37$, log-rank test). The 5-year cause-specific survival rates were 51.6% versus 59.0% ($P=0.47$, log-rank test).

Conclusion:

Patient delay in seeking medical opinion in MCC may compromise outcomes by predisposing to advanced disease. Urgent strategies to reduce diagnostic delays—such as targeted patient education, improved clinical diagnostic protocols, and early use of biomarkers (e.g., MCC polyomavirus titre)—are crucial.



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sciforum-171973: miR-200c and PRR11: A Diagnostic Duo in HPV-Driven Cervical Cancer—Unraveling Their Inverse Regulation for Early Detection

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Introduction: The persistent infection of Human Papillomavirus (HPV) is one of the most significant risk factors for the development of cervical cancer (CC). The complexity of the disease process involves multiple factors that are not completely understood. Recent studies show that in cervical cancers associated with HPV infections, the tumor suppressor miR-200c is downregulated, whereas proline-rich protein 11 (PRR11), which stimulates oncogenesis, is upregulated. Nonetheless, the potential of miR-200c and PRR11 to be in an inverse regulatory relationship in Moroccan patients suffering from CC and the possibility of using them in combination as cancer diagnostic tools remains unexplored.

Objectives: The objective of this study is to examine the expression profiles of miR-200c, PRR11 and HPV in CC biopsies and review the potential of these genes and virus as diagnostic markers for HPV-positive cervical cancer.

Materials and Methods: The expression levels of miR-200c, PRR11, and the HPV virus were quantified using RT-PCR in 200 cervical biopsies (100 malignant biopsies and 100 healthy tissues). The statistical significant correlations, as well as the estimation of diagnostic potential, were performed using Jamovi statistical software.

Outcome: There was notable identification of reverse correlation of miR-200c and PRR11 in relation to SCC with HPV. Cancer tissue samples showed significant upregulation of PRR11 and downregulation of miR-200c when compared to samples from healthy individuals. HPV related miR-200 dysregulation and PRR11 was found to be significant in relation to the disease process (p 0.05). For the purpose of diagnosis, the evaluation of miR-200c and PRR11 was the strongest with 97.85 % sensitivity, 89.67 % specificity and AUC of 0.910 which supports the potential for diagnosing cervical cancer.

Summary: The upregulation of PRR11 and the downregulation of miR-200c provides the basis of the etiology for CC HPV-induced. The evaluation of PRR11 and miR200c jointly provides an opportunity for early diagnosis.



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sciforum-170882: Neoadjuvant DOS Versus SOX for HER2-Negative Locally Advanced Gastric Adenocarcinoma: Pathological Response and Perioperative Safety in a Multicenter Real-World Cohort

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Background

Phase II evidence suggests that adding docetaxel to S-1/oxaliplatin may deepen pathological response in HER2-negative locally advanced gastric cancer (LAGC), but large head-to-head real-world evidence versus the standard SOX regimen is limited.

Methods

We retrospectively reviewed consecutive HER2-negative gastric adenocarcinoma patients (cT2N+ or cT3–4NanyM0) treated with ≥ 2 cycles of neoadjuvant DOS (docetaxel/oxaliplatin/S-1) or SOX (oxaliplatin/S-1) at four high-volume Chinese centers (2010–2024). Major pathological response (MPR; Mandard TRG 1–2) was the primary endpoint; perioperative outcomes included R0 resection and severe postoperative complications (Clavien–Dindo $\geq$ III). Confounding was addressed using propensity-score matching (PSM, 1:1) and inverse probability-of-treatment weighting (IPTW). Robustness was assessed by effect-size metrics (OR/RR) and E-values.

Results

Among 1,283 eligible patients (DOS 461; SOX 822), PSM yielded 446 well-balanced pairs (all SMD0.10), and IPTW achieved good balance with stabilized/truncated weights. DOS consistently improved MPR versus SOX across analytic cohorts: unadjusted, 25.7% vs 17.8% ($P=0.002$); PSM, 25.7% vs 17.8% ($P=0.009$); and IPTW, 24.8% vs 17.4% ($P=0.005$). In the matched cohort, DOS increased MPR (OR 1.59, 95% CI 1.14–2.23; RR 1.44, 95% CI 1.10–1.88), with E-values >1.8 across cohorts. Surgical quality and safety were comparable: R0 rates $>95\%$ among radical gastrectomy patients, severe complications were rare and identical in the PSM cohort (2.2% vs 2.2%), and perioperative mortality was 1% in both groups.

Conclusions

In a large multicenter real-world cohort, neoadjuvant DOS achieved higher MPR than SOX without compromising perioperative safety, supporting taxane-based triplets as an effective perioperative option for fit HER2-negative LAGC patients.



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sciforum-170770: Plasma Micrnas in Assessing the Risk of Recurrence in Triple-Negative Breast Cancer

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Triple-negative breast cancer (TNBC) accounts for 15-20% of all breast cancer cases and is common in patients under 50. Our retrospective study analyzed the association between pre-treatment circulating microRNA levels in TNBC patients and disease outcome.

The study included plasma samples from the Blokhin National Medical Research Center of Oncology collected before treatment. MicroRNAs were isolated using miRNeasy Serum/Plasma Advanced Kit (Qiagen); reverse transcription and ddPCR were performed using TaqMan® MicroRNA Reverse Transcription Kit, TaqMan® MicroRNA Assay probes (ThermoFisher Scientific), and TaqMan probe mix (RainSure). The results were processed using GeneCount Analysis software (RainSure) and the Hiplot (ORG) cloud service (<https://hiplot.cn/>).

Four patient groups were identified. Group 1 was characterized by a decreased concentration of miR-124a, miR-137, and miR-148a to 0.0-0.5 copies/μL and included patients aged 40-42 years, T3-T4, N1-N3; regional progression was observed in 67%, and brain metastases were observed in 5% of cases. Groups 2 and 3 were characterized by a gradual increase in miR-124a, miR-137, and miR-148a levels to 5-7 and 7-10 copies/μL and included patients aged 48-67 years; metastasis was absent in both groups, and patients in group 3 did not show disease progression during the 18 months of observation. Patients in group 4 had miR-124a levels of 15-32 copies/μL, miR-137 and miR-148a levels of 7-10 copies/μL, and elevated miR-34c-3p levels (12-17 copies/μL) compared to other groups. There was no disease progression in patients in group 4 over an 18-month follow-up period, and all patients achieved a pathologic complete response following the administration of neoadjuvant chemotherapy.

Analysis of circulating microRNA levels, particularly miR-124a, miR-137, miR-148a, and miR-34c-3p, before treatment can be used to assess the risk of TNBC progression. However, further studies of these microRNA levels in the plasma of healthy volunteers are needed.



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sciforum-177089: Pralsetinib for RET Fusion-Positive Advanced Ascending Colon Cancer with Liver Metastasis: A Case Report and Literature Review

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Background & Objective: Colorectal cancer is a common malignant tumor, and advanced patients with liver metastasis have a poor prognosis, especially elderly patients with limited treatment options. RET fusion is a rare driver mutation in colorectal cancer (0.2%–1.2%), and clinical data on pralsetinib (a highly selective RET-TKI) in such patients are scarce. We observed and explored the efficacy and safety of pralsetinib in an elderly patient with RET fusion-positive advanced ascending colon cancer and liver metastasis. **Methods:** We admitted a 70-year-old male patient with advanced ascending colon cancer and liver metastasis. Next-generation sequencing (NGS) detected an NCOA4-RET fusion (mutation abundance 28.18%), with wild-type KRAS/NRAS/BRAF, negative PD-L1 expression, and microsatellite stability (MSS). After two cycles of first-line cetuximab combined with FOLFOX chemotherapy (evaluated as progressive disease, PD), he received oral pralsetinib targeted therapy, and the therapeutic effect and adverse reactions were closely followed up. **Results:** The patient had good tolerance to pralsetinib without severe adverse reactions. After pralsetinib treatment, the primary tumor was effectively controlled, the liver metastases were significantly reduced, and the progression-free survival (PFS) reached 11 months. Disease progression occurred again after 11 months of pralsetinib treatment, and the patient gave up further treatment due to personal reasons and was lost to follow-up thereafter. **Conclusions:** Pralsetinib may be a safe and effective treatment option for patients with RET fusion-positive advanced colorectal cancer, providing a clinical basis for the individualized treatment of such rare target tumors and expanding new directions for the treatment of elderly patients with advanced colorectal cancer. Limitations include a single case and limited follow-up time, which need to be verified by multi-center and large-sample studies.



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sciforum-178332: Predictive Value of Visual Assessment During High-Resolution Anoscopy in Anal Cancer Screening

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Introduction:

Anal cancer screening programmes aim to detect high-grade squamous intraepithelial lesions (HSIL) before progression to invasive carcinoma. High-resolution anoscopy (HRA) is widely considered the reference technique for evaluating suspected anal dysplasia in high-risk populations. During the procedure, targeted biopsy decisions are often guided by the surgeon's intraoperative visual impression of the mucosa. However, the reliability and predictive accuracy of visual assessment alone remains uncertain.

Methods:

A retrospective episode-based analysis was performed including 33 HRA examinations carried out in a specialised colorectal unit. Visual suspicion documented in operative reports was categorised as high or low suspicion according to the surgeon's intraoperative assessment of the anal mucosa. Histopathological analysis of all biopsy specimens served as the reference standard. High-grade disease was defined as HSIL or invasive carcinoma.

Results:

Among the 33 analysed episodes, visual suspicion was classified as high in 4 examinations and low in 29. Histopathological evaluation identified three high-grade lesions (2 HSIL, 1 invasive carcinoma), all occurring in examinations initially categorised as low suspicion. Visual assessment demonstrated a sensitivity of 0%, specificity of 86.7%, positive predictive value of 0%, and negative predictive value of 89.7%.

Conclusions:

Visual assessment alone during HRA demonstrated no predictive value for high-grade anal lesions in this cohort. The failure to identify any high-grade lesion within the high-suspicion group highlights a significant diagnostic limitation. These findings support the routine implementation of systematic biopsy protocols within anal cancer screening programmes.



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sciforum-171771: Primary Cardiac Angiosarcoma: A Systematic Review of Clinical Presentation, Management, and Outcomes

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Background: Primary cardiac angiosarcoma (PCA) is an exceptionally rare and aggressive malignancy with a poor prognosis. This systematic review synthesizes the current evidence on the epidemiology, clinical presentation, diagnostic approaches, management strategies, and outcomes of PCA to guide clinical practice.

Methods: We conducted a systematic review of studies published from inception to December 2025. Our search was performed exclusively in the PubMed electronic database for English-language studies. This review encompassed various study designs, including case reports, case series, cohort studies, and systematic reviews, to comprehensively capture the available evidence on this rare condition. A total of 49 studies were selected for final inclusion from an initial 710 identified records after a rigorous, multi-stage screening process.

Results: A total of 49 studies were included. PCA predominantly affected middle-aged adults (median age 40s-50s) with a significant male predominance ($\approx 69\%$). The vast majority of tumors (92%) originated in the right atrium. Clinical presentation was often non-specific, including pericardial effusion, heart failure symptoms, and hemoptysis. Diagnosis relied on multimodality imaging (Echocardiography, Cardiac MRI, CT) and was confirmed by biopsy and immunohistochemistry (positive for CD31, CD34). Management was multimodal, with complete surgical resection (R0) being the cornerstone of potentially curative treatment. Adjuvant or neoadjuvant chemotherapy (often paclitaxel-based) and radiotherapy were frequently employed. Despite treatment, overall prognosis remained poor, with a median survival of approximately 6-26 months. Poor prognostic factors included metastatic disease at diagnosis, incomplete surgical resection, and large tumor size.

Conclusion: PCA is a devastating disease often diagnosed at an advanced stage. A high index of suspicion in patients with right-sided cardiac masses or unexplained pericardial effusion is crucial. Early diagnosis via multimodality imaging, prompt biopsy, and an aggressive, multimodal treatment strategy offer the best chance for improved survival. International collaboration is urgently needed to establish standardized guidelines.



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sciforum-170884: Progression Control With Neoadjuvant DOS Versus SOX in HER2-Negative Locally Advanced Gastric Cancer: Multicenter Real-World Survival and Subgroup Evidence

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Background

Whether neoadjuvant DOS (docetaxel/oxaliplatin/S-1) improves long-term outcomes compared with SOX (oxaliplatin/S-1) in HER2-negative LAGC remains uncertain, particularly in routine practice.

Methods

This multicenter retrospective cohort included consecutive HER2-negative cT2N⁺ or cT3–4NanyM0 gastric adenocarcinoma patients receiving ≥2 cycles of neoadjuvant DOS or SOX (four Chinese tertiary centers, 2010–2024). Disease-free survival (DFS; surgery to relapse/death) and overall survival (OS; surgery to death) were secondary endpoints. Survival analyses used Kaplan–Meier and Cox proportional hazards models after PSM (1:1) and IPTW. A perioperative-consistency sensitivity cohort (same regimen pre- and post-operatively) and MPR-survival association analyses were performed. Prespecified subgroup analyses assessed effect heterogeneity.

Results

A total of 1,283 patients were analyzed (DOS 461; SOX 822). DFS analyses were performed in R0-resected radical surgery patients (median follow-up 35.1 months; 430 DFS events), and OS analyses in the entire cohort (median follow-up 34.9 months; 519 deaths). In unadjusted DFS comparisons, DOS did not significantly outperform SOX; however, adjusted analyses showed favorable trends (PSM HR 0.82, 95% CI 0.66–1.02; IPTW HR 0.82, 95% CI 0.66–1.02). In multivariable Cox models, DOS significantly reduced progression risk in IPTW (HR 0.74, 95% CI 0.59–0.93; P=0.010) and was borderline in PSM (HR 0.82, 95% CI 0.65–1.00; P=0.052). OS was similar across regimens in all cohorts. Findings were consistent in the perioperative-consistency sensitivity cohort. Achieving MPR was associated with longer DFS (HR 0.64, 95% CI 0.50–0.82) and OS (HR 0.72, 95% CI 0.56–0.92). DFS benefit of DOS was most evident in patients aged ≥65 years, those with lower tumor burden (cT2–3 or cN0–1), and proximal tumors.

Conclusions

Neoadjuvant DOS improved progression control versus SOX after rigorous adjustment without an OS difference at current follow-up; MPR strongly correlated with survival, and selected subgroups may derive greater DFS benefit.



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sciforum-177141: Ratiometric TGF- β -MMP Biomarkers Capture Pathway Imbalance and Stratify Colorectal Cancer Progression

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Introduction: Colorectal cancer (CRC) remains a leading cause of cancer-related mortality worldwide, highlighting the need for biomarkers that improve disease stratification. The transforming growth factor beta (TGF- β) signaling pathway shows stage-dependent effects in CRC, acting as a tumor suppressor in early disease but promoting invasion and metastasis in advanced stages. Matrix metalloproteinases (MMPs) further contribute to extracellular matrix degradation and tumor progression. We hypothesized that ratiometric assessment of TGF- β signaling components relative to MMPs may better capture pathway-level imbalance between regulatory and pro-invasive signaling associated with tumor progression.

Methods: Tissue homogenates from 103 patients undergoing colorectal surgery were analyzed, including benign tissue samples (BTG, n = 29) and colorectal carcinoma samples (MTG, n = 74) stratified by TNM stage. Protein levels of TGF- β 1, TGF- β receptor II (TGF- β RII), SMAD4, MMP-7, and MMP-9 were quantified by ELISA. Ratios between TGF- β pathway components and MMPs were calculated and evaluated using receiver operating characteristic (ROC) analysis to assess their discriminatory performance across disease stages.

Results: Several ratiometric markers demonstrated strong discriminatory capacity between benign tissue and CRC stages. The TGF- β 1/MMP-7 ratio decreased with advancing tumor stage and demonstrated excellent performance, reaching area under the curve (AUC) values up to 1.00 in specific stage comparisons. A similar stage-related decrease was observed for the TGF- β RII/MMP-9 ratio (AUC, 0.77–0.84). The TGF- β RII/MMP-7 ratio consistently showed high diagnostic performance (AUC, 0.94–0.97), while the TGF- β RII/SMAD4 ratio achieved AUC values of 0.98–1.00 across several stage comparisons.

Conclusions: Ratiometric combinations of TGF- β signaling components and MMPs improve discrimination between benign tissue and CRC stages compared with individual biomarkers. In particular, the TGF- β RII/MMP-7 and TGF- β RII/SMAD4 ratios show strong potential as indicators of CRC progression. These findings support further validation of ratiometric biomarkers and their potential use in multi-marker diagnostic panels and minimally invasive liquid biopsy approaches.



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sciforum-178329: Retrorectal Hamartoma Presenting as a Presacral Mass: Surgical Management and Diagnostic Challenges

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Introduction

Retrorectal tumors are rare lesions that arise in the presacral space and include a heterogeneous group of congenital, inflammatory, and neoplastic entities. Among them, retrorectal hamartomas, also known as tailgut cysts, are uncommon congenital lesions originating from remnants of the embryonic hindgut. Their clinical presentation is often nonspecific, which frequently delays diagnosis and complicates management.

Methods

We report the case of a patient diagnosed with a retrorectal mass detected during imaging evaluation for nonspecific pelvic symptoms. Radiological assessment with pelvic magnetic resonance imaging demonstrated a well-defined presacral lesion located posterior to the rectum. The patient underwent elective surgical resection through a posterior approach. Intraoperative findings, surgical technique, and postoperative outcomes were analysed.

Results

Complete excision of the presacral mass was achieved without intraoperative complications. The lesion was carefully dissected from surrounding structures within the confined retrorectal space. Histopathological examination confirmed the diagnosis of a retrorectal hamartoma. The postoperative course was uneventful, and the patient remained asymptomatic during follow-up.

Conclusions

Retrorectal hamartomas are rare congenital lesions that may present as presacral masses with nonspecific clinical manifestations. Accurate radiological evaluation and complete surgical excision are essential for definitive diagnosis and management. Awareness of these uncommon entities is important for surgeons managing presacral lesions in order to ensure appropriate treatment and avoid potential complications.



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sciforum-171251: Retrospective Registry for Uveal Melanoma in Lebanon: 10-year Single-Center Experience of a Major Referral Center in the Middle East and North Africa

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Introduction: Uveal melanoma (UM) is the most common primary intraocular malignancy in adults, comprising 80% of ocular melanomas. Despite advances in tumor control, metastatic potential remains high, with the liver, lungs, and bone being the most common sites. Once metastasis occurs, survival drops to 6–12 months. The aim of this study is to summarize the data available on patients with uveal melanoma treated in the past 10 years at the American University of Beirut Medical Center, focusing on factors affecting disease severity, clinical progression, and treatment modalities.

Methods: This study reviews the clinical, molecular, and histopathologic data of these patients. Data was retrieved from electronic health records, including baseline demographics, tumor characteristics, treatment modalities, and disease progression. Patients above 18 years with confirmed uveal melanoma were included, while those treated outside AUBMC or lost to follow-up were excluded. Descriptive statistics and regression analysis was conducted to identify factors influencing disease severity and outcomes.

Results: The mean age at diagnosis of our sample was 49.7 $\pm$ 20.13 years, predominantly comprised of male (66.67%), middle eastern (100%) patients aged > 60 (60%). Tumors lacked heterochromia (100%), portrayed melanocytotic (75%), and mostly occurred in the choroid macula or choroid macula to the epicenter. The mean thickness at presentation was 7.32 $\pm$ 6.33 mm. Tumors were most commonly brown (50%), then yellow (30%), and mixed (20%), and 55% of lesions contained subretinal fluid. Tumors were mostly in stage 1 (45%), did not involve nearby lymph nodes (60%), and did not have evidence of metastasis at diagnosis (88.89%). In total, 63.63% of our sample underwent surgery initially, with enucleation being the most common (55.56%).

Conclusion: UM remains a challenging malignancy with high metastatic potential if not detected early. This study provides valuable insights into the demographic, clinical, and treatment-related factors affecting UM outcomes in Lebanon. Further studies are needed, however, to better understand the molecular and clinical factors that influence disease progression.



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sciforum-171108: Serum from Subjects with High Body Mass Index Modulates Multiple Myeloma Cell Phenotype

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Introduction: Global prevalence of obesity has risen sharply in the last decade, raising the incidence and clinical progression of multiple myeloma (MM), a B-cell neoplasia resulting from the clonal proliferation of malignant plasma cells in the bone marrow, which accounts for 10-15% of all haematological malignancies. Obese patients exhibited a distinct serum profile characterized by low-grade inflammation, altered metabolic markers and elevated-derived hormones, which might influence MM progression. However, the molecular connection between obesity and MM is still not completely unraveled. The aim of this study was to evaluate the impact of the serum from healthy donors, stratified by body mass index (BMI), on modulating the MM cell phenotype.

Methods: RPMI-8226 and U-266 human MM cell lines were used as experimental models. Serum samples from healthy donors were pooled according to BMI into normal weight (n=20, NW; 25.0 kg/m²) and overweight/obese (n=20, OW/Ob; ≥ 25.0 kg/m²) groups. In vitro assays were performed to assess cell viability, proliferation, migration, and invasiveness. Serum secretion profiles were analyzed using multiplex bead-based immunoassays. Protein-protein interaction was explored through STRING bioinformatic analysis.

Results: OW/Ob serum increased MM cell colony formation, migration and invasion compared to NW serum. In addition, OW/Ob serum exhibited elevated concentration of pro-inflammatory and pro-tumorigenic mediators and reduced amounts of immune-modulator factors. The differentially expressed molecules formed a protein network associated with cancer signalling and inflammatory pathways, with IL-8/CXCL8 acting as the central hub.

Conclusions: Our data demonstrated that serum from OW/Ob donors, characterized by an altered cytokine profile, promotes MM cell aggressiveness compared to NW serum. These findings suggest that the pro-inflammatory milieu fostered by high IL-8/CXCL8 provides a supportive environment for MM progression.



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sciforum-178291: Serum levels of adipokines in women with cervical cancer

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Cervical cancer remains one of the most common malignancies among women worldwide and represents a major public health problem. Adipose tissue functions as an active endocrine organ that secretes biologically active molecules known as adipokines, including leptin and adiponectin. These mediators regulate important physiological processes such as inflammation, immune response, angiogenesis, and cell proliferation. Dysregulation of adipokine secretion has been associated with tumor development and progression in several malignancies. Therefore, evaluation of adipokine levels in women with cervical cancer may provide insight into the metabolic mechanisms involved in tumor progression.

Aim: The aim of this study was to evaluate serum levels of leptin and adiponectin in women with cervical cancer and to determine their association with disease stage.

Materials and Methods. The study included women diagnosed with cervical cancer and a control group of healthy individuals. Venous blood samples were collected from all participants, and serum adipokine levels were measured using enzyme-linked immunosorbent assay (ELISA).

Results. Significant differences in adipokine levels were observed between patients with cervical cancer and healthy controls. Serum leptin levels were significantly higher in patients than in the control group (32.8 ± 6.4 ng/mL vs 18.5 ± 4.2 ng/mL, $p = 0.001$). In contrast, adiponectin concentrations were significantly lower in patients (5.9 ± 1.3 μ g/mL vs 9.8 ± 2.1 μ g/mL, $p = 0.001$). Stage-based analysis showed that leptin levels increased with disease progression, reaching 38.6 ± 5.8 ng/mL in stage III compared with 27.4 ± 4.9 ng/mL in stage I ($p = 0.009$). Conversely, adiponectin levels decreased as the disease advanced (4.8 ± 1.1 μ g/mL in stage III vs 6.7 ± 1.4 μ g/mL in stage I, $p = 0.043$).

Conclusion. Cervical cancer is associated with significant alterations in adipokine balance. Increased leptin and decreased adiponectin levels may reflect metabolic and inflammatory mechanisms contributing to tumor progression.



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sciforum-169131: Significance of HER2-related factor in HER2-low breast cancer

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Human epidermal growth factor receptor 2 (HER2)-targeted therapies are widely used to treat of HER2-positive breast cancer. HER2 expression is evaluated by the HER2 protein using immunohistochemistry (IHC), and ERBB2 gene amplification by fluorescence in situ hybridization (FISH) is performed in routine clinical practice for breast cancer. Some studies have suggested that increased ERBB2 mRNA expression is involved in the HER2-dependent progression of breast cancer. In addition, various binding proteins for HER2 and HER2-dependent signaling are promoted by their interactions. In this study, we aimed to investigate the relationship between HER2 expression in IHC, ERBB2 expression, and HER2-binding proteins and to clarify the characteristics of cases with different levels of HER2 expression. The subjects were 58 cases from Tohoku University Hospital. ERBB2 expression was determined by RNA-scope, and HER2-binding proteins, NRG1 (neuregulin 1), ERBIN (erbb2 interacting protein), Grb2 (growth factor receptor-binding protein 2), CEACAM6 (carcinoembryonic antigen-related cell adhesion molecule 6), and HER3, were detected by IHC. ERBB2 expression showed a positive correlation with HER2 expression. HER3 expression was significantly higher in HER2-low breast cancers than in HER2-negative breast cancers. Cluster analysis showed that HER2-negative breast cancers classified into the same cluster as HER2-low breast cancers exhibited high HER2 binding protein expression. Furthermore, clusters containing breast cancers with positive, low, and negative HER2 expression were characterized by high ERBB2 scores and high expression of HER2 binding protein, suggesting the possibility that breast cancer may be promoted in a HER2-dependent manner through interaction with HER2 binding protein. These results suggest that HER2-low and HER2-negative breast cancers contain cases with similar characteristics to HER2-positive breast cancers, particularly when focusing on HER2 binding proteins and treatment targeting HER3 and other HER2 binding proteins.



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sciforum-169185: Stem Cell Exhaustion Defines an Immunogenic Niche and a Circulating Biomarker for Nasopharyngeal Carcinoma

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Background

The inadequacy of chronological age as an indicator of biological aging has spurred the development of biomarkers that quantify hallmarks of the aging process. Stem cell exhaustion (SCE) is a recognized hallmark of cellular senescence; however, its clinical significance in nasopharyngeal carcinoma (NPC) remains unclear, and scalable tools for its assessment are lacking.

Methods

We computed an SCE score from transcriptomic data of 181 non-metastatic NPC patients. Its relationship with the tumor immune microenvironment was characterized using bioinformatic and spatial transcriptomic analyses. To develop a clinically applicable tool, we derived a Circulating Stemness Exhaustion Signature (CSES) from routine blood parameters via an artificial neural network. The CSES was validated in three independent cohorts: an internal cohort (n = 492), an external cohort (n = 122), and an immunotherapy-treated cohort (n = 42).

Results

A high SCE score independently predicted improved overall survival (HR = 0.03, 95% CI: 0.00–0.65, P = 0.025) and delineated an immunologically active TIME characterized by enhanced T-cell cytotoxicity and elevated MHC-I expression. The CSES strongly correlated with the SCE score (r = 0.844, P = 0.001) and consistently stratified patient survival in validation cohorts. In the immunotherapy cohort, a high CSES predicted a significant survival benefit (difference in restricted mean survival time at 36 months: 7.47 months, P = 0.039) and was independently associated with superior treatment response.

Conclusion

Our study establishes SCE as a critical determinant of the immune niche and prognosis in NPC. Furthermore, we introduce the CSES as a practical, non-invasive biomarker capable of guiding prognostic stratification and informing immunotherapy decisions.



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sciforum-170890: Subependymal Giant Cell Astrocytoma: A Rare Central Nervous System Tumour with a Complex Histology

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Introduction

Subependymal giant cell astrocytomas (SEGAs) are rare, low-grade neuroglial tumours that are strongly associated with the tuberous sclerosis complex (TSC). They are preferentially located in the walls of the lateral ventricles, and are characterised by marked cellular heterogeneity within the same lesion, which may complicate diagnosis, particularly for less experienced pathologists. This work aims to highlight the main histological and immunohistochemical characteristics of this entity.

Methods and Results

A 13-year-old male patient with no relevant medical history presented with seizures, persistent vomiting, and severe headaches during the span of a week. Laboratory investigations were unremarkable, and an encephalic MRI revealed a 4 cm solid-cystic intraventricular mass associated with hydrocephalus. Complete surgical resection was performed for symptomatic relief.

Histological examination showed a well-demarcated tumour with moderate to high cellularity arranged in nodules and short fascicles, composed of spindle, gemistocyte-like, and neuronal-like cells. No necrosis or microvascular proliferation was observed, and mitotic activity was low.

Immunohistochemically, tumour cells showed dual positivity for glial and neuronal markers, with strong positivity for GFAP, S100, NSE and neurofilament protein, while OLIG2 remained negative, and synaptophysin staining was focal. The Ki-67 index was approximately 5%.

Based on morphological features, immunoprofile, and tumour location and size, a diagnosis of CNS WHO grade 1 SEGA was established, and evaluation for TSC was recommended. The patient showed rapid clinical improvement following surgery.

Conclusion

SEGA is a rare, slow-growing CNS WHO grade 1 tumour with symptoms that are mainly due to obstructive hydrocephalus. Diagnosis relies on recognition of its characteristic cellular morphological heterogeneity and dual glioneuronal differentiation. Complete surgical resection remains the cornerstone of treatment and is associated with favourable outcomes.



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sciforum-171744: The Link Between Malignancy and Arterial Thrombotic Events: A Systematic Review Across Cancer Types

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Background: A diagnosis of cancer is associated with an elevated risk of arterial thrombotic events (ATEs), including myocardial infarction (MI) and ischemic stroke. This systematic review synthesizes the current evidence on the epidemiology, risk factors, time-dependent risks, and outcomes of ATEs across a spectrum of malignancies to guide clinical practice and future research.

Methods: We systematically searched PubMed and Science Direct from inception to December 2025 for studies reporting on ATEs in cancer patients. Data on patient demographics, cancer types, treatment modalities, ATE outcomes, and risk estimates were extracted. The risk of bias was assessed using appropriate tools.

Results: We included 43 studies. The evidence demonstrates a clear association between cancer and an increased risk of ATEs (HR/OR range: 1.5-3.0). High-risk malignancies included lung, pancreatic, gastrointestinal, and brain cancers. The risk was most pronounced in the peri-diagnostic period and first 6–12 months after diagnosis. Key contributing factors included advanced cancer stage, specific chemotherapies (e.g., platinum-based agents), radiotherapy, and the perioperative period. Traditional cardiovascular risk factors compounded this risk. Despite the established link, evidence for optimal prophylactic strategies is lacking.

Conclusion: Cancer confers a significant and time-dependent increased risk of ATEs, necessitating increased clinical vigilance. A proactive, multidisciplinary approach involving cardio-oncology is essential for risk stratification, aggressive management of traditional risk factors, and patient education. Future research must focus on mechanistic studies, predictive biomarker development, and randomized controlled trials to establish effective prevention and treatment strategies.



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sciforum-171644: The Role of Oncology Nurses in Recognizing and Managing Neuropsychological Effects of Cancer Immunotherapies: An integrative review

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Background: Cancer immunotherapies can cause substantial neuropsychological toxicities that are often under-recognized in practice, despite oncology nurses' central role in early detection and management.

Aim: This integrative review synthesizes current evidence on how oncology nurses recognize, assess, and manage neuropsychological effects associated with cancer immunotherapies.

Methods: A PRISMA-guided integrative review was conducted following Whitemore and Knaf's framework. Five reviewers independently searched four major databases (PubMed/MEDLINE, CINAHL, Scopus, and ScienceDirect) for English-language studies published between 2013 and 2025 involving adult cancer patients receiving immunotherapy, with a focus on neurologic or psychiatric outcomes and nursing roles. Study selection, Joanna Briggs Institute quality appraisal, and data extraction were performed in duplicate with consensus resolution.

Results: Twenty-three studies of diverse designs (observational, randomized trial, qualitative, case series, and narrative/expert reports) consistently described neurocognitive and psychiatric toxicities across interleukin-2, immune checkpoint inhibitors, and CAR-T-cell therapies, including memory impairment, delirium, anxiety, depression, and mood changes. Oncology nurses were central in routine neurologic and mental status assessments, anticipatory patient and caregiver education, psychosocial support, and coordination of multidisciplinary care, yet many reported limited training and a lack of standardized screening tools.

Limitations: Restriction to English-language publications and the inclusion of heterogeneous study designs, with only one randomized controlled trial, limit the strength, consistency, and generalizability of the evidence and preclude meta-analysis.

Conclusion: Oncology nurses function as pivotal clinical sentinels and psychosocial advocates in managing immunotherapy-related neuropsychological toxicities, but systematic screening protocols, targeted education on immune-related adverse events, and robust evaluation of nurse-led interventions are urgently needed to optimize patient safety and quality of life.



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sciforum-171144: Transcription factor NR5A1 enhances wild-type p53 transactivation

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Despite advances in therapy, cancer continues to be a major health challenge in the 21st century, with mortality rates still hovering around approximately 20%. The tumor suppressor p53, a protein critical for cancer development and prevention, is regulated by various interacting partners. In our previous unpublished findings, we identified that NR5A1 (also called steroidogenic factor-1, SF-1, the master regulator for adrenal and gonadal steroidogenesis) is able to module p53 activity. Consequently, in this investigation, we broaden our exploration to examine how NR5A1 regulates p53 transactivation using the p53(14X)RE-LUC system. Generally, H1299 (p53 NULL) cells in a 24-well plate were transfected with the p53(14X)RE-LUC plasmid and with or without different expression plasmids by the Fugene HD transfection method. After 48 hours of transfection, luciferase activities were analyzed by the Dual-Luciferase Reporter System. Western blot analysis was analyzed for protein expression. We first found that NR5A1 enhances wild-type (WT) p53 transactivation in a dose-dependent manner in H1299 cells. This result is confirmed by testing JDP2 (we reported earlier that JDP2 activates WT p53 transactivation) and NR5A1 in the same experiments. Given that MDM2 is the major negative regulator of p53, we then tested whether NR5A1 could counteract MDM2-mediated p53 repression. We found that NR5A1 reverses MDM2-mediated p53 transactivation, suggesting that NR5A1 may have the ability to bind to both p53 and MDM2 in order to abolish MDM2-mediated p53 repression. Finally, we found that NR5A1 increases wild-type (WT) p53, but not G245S (hotspot mutation) p53, transactivation. Taken together, our preliminary results demonstrate that NR5A1 is a novel protein that regulates p53 activity likely involving MDM2 competition due to the possible p53-NR5A1 interaction. This data substantiates the concept that p53's activity is governed by a complex and still-expanding network of interactions.



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sciforum-171155: Urinary Dual OncomiR Signature of miR-21 and miR-155: A Non-Invasive Approach for Bladder Cancer Detection in a Moroccan Cohort

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Bladder cancer (BCa) remains a major global health burden, particularly in low-to-middle-income countries such as Morocco, where access to invasive diagnostic tools is limited. While several urinary biomarkers have been explored, most studies focus on single molecules and are rarely population-specific. The present study aimed to assess, for the first time in a Moroccan cohort, the diagnostic utility of a dual urinary microRNA signature combining microRNA-21 (miR-21) and microRNA-155 (miR-155). Expression levels of miR-21 and miR-155 were quantified by quantitative real-time polymerase chain reaction (RT-qPCR) in urine samples from 70 BCa patients and 30 healthy controls. ΔC_t values normalized to U6 small nuclear RNA (snRNA) were used for relative quantification. Diagnostic performance was evaluated using Receiver Operating Characteristic (ROC) curves, while multivariate logistic regression and clinicopathological correlations were performed to assess predictive value. Both miR-21 and miR-155 were significantly upregulated in BCa patients compared with controls ($p = 0.0001$). Individually, miR-21 and miR-155 achieved AUCs of 0.876 and 0.845, respectively. Their combined analysis provided superior accuracy (AUC = 0.907), outperforming single-marker approaches. Elevated expression correlated with advanced tumor stage, higher grade, and muscle invasion. Multivariate analysis identified miR-21 as an independent predictor of BCa (OR = 0.575, $p = 0.023$). This study highlights a novel dual urinary miRNA signature for BCa detection and risk stratification, with demonstrated relevance in a North African population. Unlike previous studies centered on single markers or non-representative cohorts, our findings emphasize the translational potential of combining miR-21 and miR-155 as a non-invasive, accessible, and effective diagnostic approach, which is particularly valuable for resource-limited settings.



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Session 7. Novel Methods and Technologies for Research and Treatment

sciforum-169576: Exploring the mechanism of ID1-dependent liver inflammation induced by dietary fat and a therapeutic approach to target IDs in cancer

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Introduction:

High dietary fat and fructose-induced metabolic dysfunction-associated steatohepatitis (MASH) is a major risk factor for hepatocellular carcinoma (HCC), yet mechanisms linking steatosis to chronic liver inflammation remain poorly defined. ID1, a dominant-negative helix-loop-helix transcriptional regulator, is selectively upregulated in liver-resident macrophages (Kupffer cells; KCs) in murine MASH models and patient biopsies, but not in metabolic dysfunction-associated steatotic liver disease (MAFLD). This study investigates the functional role of KC-specific ID1 in MASH pathogenesis and explores therapeutic KC-localized targeting of ID proteins using nanoparticle-encapsulated protein degraders.

Methods:

KC-specific Id1 knockout mice were generated by introducing iCre into the Clec4f locus and validated via td-Tomato lineage tracing. Mice were maintained on standard chow or high-fat, high-fructose Western diet with fructose-supplemented drinking water for up to 24 weeks to induce MASH. Disease progression was assessed by serum liver enzymes (ALT, AST, ALP) and histological NAS scoring. We employed lipid- or fucoidan-based nanoparticle formulations of the ID degraders AGX51 and AGXA to evaluate the potential for therapeutic intervention in MASH.

Results:

Global Id1 deletion protected mice from diet- and CCl₄-induced MASH, prompting evaluation of KC-specific effects. Clec4f-iCre-mediated Id1 depletion significantly reduced hepatic steatosis, NAS scores, and serum ALT, AST, and ALP following prolonged high-fat, high-fructose feeding. Transcriptomic profiling of KCs identified anti-inflammatory and lipid-regulatory genes, including Serpina1e, Serpin a3k, Abcg5, and Pcsk9, supporting an ID1-dependent inflammatory program and KC-hepatocyte crosstalk. Translationally, Cy5-labeled lipid nanoparticles efficiently localized to Kupffer cells in vivo, supporting the feasibility of nanoparticle-mediated ID1 targeting in inflammatory liver disease.

Conclusion:

These findings identify KC-specific ID1 as a critical regulator of inflammatory pathways driving MASH progression and highlight ID1 as a promising therapeutic target. Nanoparticle-based ID degradation demonstrates translational potential for inflammation-driven liver disease and aggressive cancers.



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sciforum-168079: Revisiting Cancer Cell Polarity Through Artificial Intelligence: A Perspective on Image-Based Biomarkers for Precision Oncology

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Cancer research has traditionally emphasized genetic and molecular alterations, while fundamental biophysical characteristics such as cell polarity have received comparatively limited attention in diagnostic and therapeutic contexts. Cell polarity plays a critical role in normal tissue architecture, function, and homeostasis, and its disruption is a well-recognized feature of malignant transformation, invasion, and metastasis [1–4]. Despite its biological significance across both healthy and diseased tissues, polarity is rarely quantified or systematically incorporated into clinical workflows. This perspective proposes that recent advances in biomedical imaging and artificial intelligence (AI) provide a timely opportunity to reposition cell polarity as a meaningful, image-derived biomarker in cancer.

We outline a conceptual framework in which AI-enabled image analysis is applied to high-resolution microscopy and digital pathology images to assess polarity-related spatial organization within cells. Machine learning and deep learning approaches, particularly convolutional neural networks, have demonstrated strong capability in extracting complex spatial features from biomedical images [5,6]. Within this framework, AI models could be leveraged to quantify asymmetries in cytoskeletal organization, nuclear positioning, and intracellular feature distribution, enabling objective and scalable polarity assessment beyond conventional morphology-based evaluation.

From a conceptual standpoint, AI-driven polarity analysis has the potential to reveal phenotypic information associated with tissue organization, tumour aggressiveness, metastatic behaviour and therapeutic responsiveness. Prior work in computational pathology demonstrates that deep learning can uncover clinically relevant patterns not readily discernible to human observers [7]. Polarity-associated spatial signatures may therefore complement molecular and histopathological data, contributing to more nuanced cancer classification and risk stratification strategies.

In conclusion, cell polarity represents an underexplored yet biologically grounded target for AI-driven image analysis. Integrating spatial biology with AI-based imaging analytics may enable more holistic, interpretable, and data-driven approaches to cancer diagnosis, prognosis, and treatment evaluation in precision oncology.



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sciforum-177486: Digital Pathology Approach to Mapping Collagen VI Tumor Spatial Arrangement in COVID-19 Tissue Slides Using ImageJ

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Background:

Collagen VI is a structural component of the extracellular matrix that regulates cellular processes, including adhesion, migration and signaling, that contribute to tumor growth and migration. In malignancies, such as Hodgkin lymphoma, changes in collagen deposition and its spatial arrangement are indicative of tumor-associated stromal remodeling. Traditional histopathology does not adequately capture the spatial organization of collagen networks. This study presents a reproducible digital pathology workflow using ImageJ to quantify collagen VI cellular spatial interactions in diseased tissue.

Aim: To develop and validate a digital pathology workflow using ImageJ for quantitative assessment of collagen VI-cellular spatial arrangements in cancer-related tissue remodeling.

Methods:

A Hodgkin lymphoma tissue image was used to establish workflow, which was subsequently applied to a COVID-19 lung tissue cohort. Structural elements were binarized and skeletonized; branching-related topological parameters were quantified. Architectural complexity was summarized using a composite Branching Complexity Index (BCI), alongside density-based metrics including branch and junction densities. Collagen fractional area was quantified using color thresholding. Distributional analyses and Spearman's rank correlation assessed metric robustness and associations with collagen deposition. Reproducibility was evaluated using Bland-Altman and Spearman correlation analyses.

Results:

Branching-derived metrics were extracted and showed broad distributions with stable variability. BCI showed no meaningful association with collagen fractional area in normal lung tissue, whereas COVID-19 lung tissue demonstrated a positive association between BCI and collagen deposition, supporting the biological plausibility of the framework. Density-based metrics showed cohort-specific relationships with collagen fractional area, suggesting that branching abundance and network connectivity capture aspects of architectural remodeling. Bland-Altman analysis confirmed reproducibility for distance measurements.

Conclusion:

Skeleton-based branching analysis provides an approach for quantifying lung architectural remodeling in cancer. Branching metrics show associations with collagen deposition while extending beyond conventional area-based measures. This framework supports future integration with clinical data and application in other diseases involving tissue remodeling.

Acknowledgement:

We acknowledge the work done on the study titled "Multi-omic spatial profiling reveals the unique SARS-CoV-2 lung microenvironment and collagen VI as a predictive biomarker in severe COVID-19" to be the background of this study.



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sciforum-171655: A Self-Amplifying Redox-Based Combination Therapy Using an ROS-Responsive Prodrug and Pharmacologic Ascorbate for Targeted Triple-Negative Breast Cancer Treatment

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Introduction: Oxidative stress-based therapies exploiting elevated tumor reactive oxygen species (ROS) offer promise but are limited by insufficient selectivity and adaptive resistance. To overcome these barriers, we developed a combinatorial strategy that synergistically integrates a ROS-responsive prodrug with pharmacologic ascorbate, a tumor-selective pro-oxidant, to initiate a self-amplifying oxidative cycle specifically within the tumor microenvironment.

Methods: We evaluated the combination of pharmacologic ascorbate (P-Asch⁻) with a novel ROS-responsive prodrug across multiple cancer cell lines, including triple-negative breast cancer (TNBC) models (MDA-MB-231, MDA-MB-468). Cytotoxicity was assessed via MTT and clonogenic assays, while mechanisms were probed using flow cytometry for apoptosis (Annexin V/PI) and DNA damage (γH2AX). In vivo efficacy was evaluated in orthotopic and patient-derived xenograft (PDX) models of TNBC. Biosafety was assessed via serum chemistry and histopathology.

Results: The combination demonstrated strong synergistic cytotoxicity (combination index 0.5) across all TNBC lines, with significantly attenuated effects in non-malignant fibroblasts. Mechanistically, ascorbate selectively amplified H₂O₂ flux in cancer cells, triggering prodrug activation and establishing a feed-forward oxidative loop, evidenced by a 4-fold increase in γH2AX foci and 70% apoptosis versus monotherapies. In vivo, the combination achieved complete and durable tumor regression in 80% of PDX-bearing mice, with no recurrence over 120 days and no significant off-target toxicity.

Conclusions: This redox-based combination strategy establishes a novel paradigm for precision cancer therapy by dynamically manipulating tumor redox biology. The self-amplifying oxidative mechanism enhances prodrug specificity and potency while repurposing ascorbate as a targeted synergistic agent. This approach is now being advanced toward translational studies.



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sciforum-178400: Bioinformatic Identification of ACTN4 as a Candidate Master Regulator of Local Invasion in Glioblastoma

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Introduction

Glioblastoma is the most aggressive brain tumor. The main reason for its lethality is the tumor's broad invasion into brain tissue, which is influenced by tumor cell mechanics. Successful invasion necessitates dynamic cytoskeletal remodeling, altered cell adhesion, and interaction with neural structures. We hypothesized that previously defined, focused panels of mechanobiological markers capturing these functions would elucidate key drivers of glioblastoma invasiveness.

Materials and Methods

mRNA expression data were obtained from cBioPortal (TCGA, PanCancer Atlas) for 592 primary glioblastoma and 514 low-grade gliomas samples. We assessed 11 genes related to actin dynamics, cell movement, adhesion, and mechanotransduction: *ACTN4*, *PFN1*, *CFL1*, *FSCN1*, *ANXA2*, *ANXA6*, *MYH9*, *GSN*, *TAGLN*, *ECM1*, and *EZR*. Differential expressions between glioblastoma and low-grade glioma were assessed using the non-parametric Mann–Whitney U-test. The diagnostic power of individual genes and the composite panel score was measured using the Area Under the ROC Curve (AUC).

Results

Glioblastoma demonstrated significant dysregulation of 4 out of 11 mechanobiological genes compared to low-grade gliomas ($p < 0.01$): *FCN1* (immune mediator, ECM), *TAGLN* (actin-binding protein, contractility), *ACTN4* (actin crosslinking, migration), and *MYH9* (non-muscle myosin II, tension generation). The composite score of the panel showed a connection to tumor grade (AUC=0.67), while the score from 4 dysregulated genes was notably better (AUC=0.73). *ACTN4* emerged as the top diagnostic biomarker (AUC=0.83) in the single-gene analysis, which points to the significance of actin cytoskeleton regulation in brain invasion.

Conclusions

The four-gene mechanobiological signature effectively embodies the vital traits associated with glioma aggressiveness. *ACTN4* has emerged as a promising master diagnostic biomarker and a potential key molecular driver behind local invasion in glioblastoma. To establish its significance, validating its function in vitro and in vivo glioblastoma invasion models is crucial.



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sciforum-178362: Enhancing Analytical Rigor: A pathologist-guided Framework for Multiplex Immunofluorescence Profiling of the NSCLC Tumor Microenvironment

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Background/Objectives:

Multiplex immunofluorescence (mIF) is an emerging spatial biology technology enabling high-resolution characterization of the tumor microenvironment and revealing spatial interactions that extend beyond cell-count metrics. Reproducibility is limited by tumor heterogeneity, device variability and challenges in interpreting AI-assisted cell profiling measurements. This study delineates a pathologist-guided, error-focused analytical framework intended to mitigate major sources of analytical variability across visualization, segmentation, and classification workflows.

Methods:

A framework was developed based on a literature review and pathologists' annotations for selecting regions of interest across intratumoral, peri-/extratumoral, and tumor–stroma interface compartments in primary and recurrent bioptic, surgical, and cytological NSCLC samples analyzed entirely by mIF. Quality-control procedures included morphological verification, adaptive thresholds, and exclusion or resampling of low-cellularity or artifact-rich tissue. Prespecified cellularity cutoffs ensured stability of spatial metrics, and several positional indices were evaluated. A validated mIF panel (CD3, CD4, CD8, CD20, MPO, CD21, CD23, CD206, CD45, CD56, CD11b, CD66b, CD68, CD31, SMA, PNA_d, CK, PD-1, PD-L1, CTLA-4, LAG-3, TIM-3, TCF1, GranzymeB, and FOXP3) enabled comprehensive profiling of lymphoid and myeloid lineages, including TAMs, as well as stromal, vascular, and immune-checkpoint components. Immunophenotyping used pretrained deep-learning and forest-plot-based models with pathologist supervision to reduce classification and segmentation errors. Spatial analysis incorporated surrogate metrics of T-cell activity across immune compartments, and internal positive controls were documented to monitor staining performance.

Results:

The workflow ensured consistent multicompartment acquisition of spatial and immunophenotypic data, reducing analytical vulnerabilities. Morphological validation improved the accuracy of AI-assisted cell classification, and whole-slide-based ROI selection addressed limitations typical of tissue microarrays.

Conclusions:

A structured, pathologist-guided mIF workflow integrating standardized sampling, rigorous quality control, and spatial analytics enhances analytical robustness and interpretability of errors in NSCLC TME profiling, offering a practical template for reproducible spatial immuno-oncology studies and supporting clinical translation of mIF-based TME analysis.



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sciforum-169744: Machine Learning-Based Association of Copy Number Alterations in a Mechanobiological Gene Panel with Metastatic Status Across Cancer Types

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Introduction

Metastasis is the leading cause of cancer-related mortality, highlighting the need for molecular markers that distinguish primary and metastatic tumors. Genes in actin cytoskeleton organization and cell mechanics regulate cell migration and invasion and may reflect metastatic potential. This study investigated copy number alterations (CNAs) in a mechanobiological gene panel and evaluated their ability to predict metastatic status across multiple cancer types using statistical analysis and machine learning.

Methods

CNA data for FSCN1, GSN, ACTN4, EZR, CFL1, MYH9, PFN1, TAGLN, ECM1, ANXA2, and ANXA6 were obtained from cBioPortal breast, pancreatic, and gastric tumors. Breast cancer datasets (TCGA Cell 2015; Provisional 2021; INSERM PLoS Med 2016) included 930 primary and 465 metastatic samples, as well as cBioPortal annotations. Pancreatic and gastric datasets (Broad 2019; TCGA Firehose Legacy; TCGA Nature 2014) were class-balanced using the Synthetic Minority Over-sampling Technique (SMOTE), generating synthetic minority samples via interpolation; balanced sets contained 212 and 306 samples per class and were used for training only. CNA differences were assessed using the Kruskal–Wallis test. Machine learning models—k-nearest neighbors, decision tree, logistic regression, random forest—were trained, splitting the data into 80% training and 20% test sets with hyperparameter optimization via random search. Two strategies were compared, breast cancer-only training and combined multi-cancer training, with evaluation on an independent breast cancer cohort not used in training.

Results

Most genes showed statistically significant CNA differences between primary and metastatic tumors, with cancer-specific patterns. All MLMs achieved stable classification performance, with random forest performing best. Breast cancer-only training yielded an accuracy of 0.78, precision of 0.77, recall of 0.78, and F1 score of 0.76, while multi-cancer training improved performance to an accuracy of 0.85, precision of 0.84, recall of 0.85, and F1 score of 0.84.

Conclusions

CNA in a mechanobiological gene panel, analyzed using MLMs, represents a promising approach for distinguishing between primary and metastatic tumors. The improved performance under multi-cancer training indicates the pan-cancer relevance of this gene set and supports its potential utility as a predictive tool for metastasis prediction.



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sciforum-172100: Reprogramming T Cells via Minicircle DNA Platforms: A Novel Nonviral Strategy for CD19-Directed CAR-T Therapy in Leukemia

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Background:

Chimeric antigen receptor (CAR) T-cell therapy has emerged as a transformative immunotherapeutic strategy for hematological malignancies by redirecting T-cell specificity toward tumor-associated antigens. Despite the clinical success of viral vector-based CAR delivery systems, concerns regarding insertional mutagenesis, immunogenicity, manufacturing complexity, and cost have highlighted the need for safer and more efficient nonviral alternatives. Minicircle DNA vectors, devoid of bacterial backbone sequences, represent a promising next-generation gene delivery platform capable of sustaining robust and prolonged transgene expression with an improved safety profile.

Materials and Methods:

In this study, a second-generation CD19-specific CAR construct was engineered and cloned into a replicative minicircle vector (CAR-MC). Human peripheral blood-derived T cells were isolated and genetically modified via electroporation with the CD19CAR-MC construct. The functional efficacy of the generated CAR T cells was evaluated through in vitro co-culture assays using CD19-positive leukemia cells and CD19-negative control cells. CAR T-cell activity was assessed by measuring antigen-specific cytotoxicity, cytokine secretion profiles, and proliferative capacity.

Results:

Minicircle-engineered CD19 CAR T cells demonstrated highly selective and potent cytotoxic activity against CD19-expressing leukemia cells, while sparing CD19-negative targets. These CAR T cells exhibited significantly enhanced secretion of key proinflammatory cytokines, including interferon- γ and tumor necrosis factor- α , compared with non-transduced T cells, confirming effective CAR signaling and immune activation. Furthermore, minicircle-mediated gene delivery resulted in efficient CAR expression and sustained functional performance without evidence of vector-related cytotoxicity.

Conclusion:

This study establishes minicircle DNA as a safe, efficient, and non-integrating nonviral platform for CAR T-cell engineering. The absence of bacterial backbone elements enables high-level and durable CAR expression while minimizing immunogenicity and genomic risk. Minicircle-mediated CD19 CAR T cells effectively recognize and eliminate leukemia cells, underscoring the translational potential of this approach as a next-generation alternative to viral vectors for cancer immunotherapy.



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sciforum-165219: A Minimally Invasive 3D-Printed Microneedle Patch System for Effective Breast Cancer Treatment: Fabrication, Characterization and Preclinical Pharmacokinetic Evaluation

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Breast cancer remains the most commonly diagnosed cancer and the leading cause of cancer-related deaths among women worldwide. Although conventional treatments such as chemotherapy, surgery, and radiotherapy are widely used, they often damage healthy tissues and cause serious systemic side effects. These limitations highlight the urgent need for safer and more effective treatment strategies that can deliver drugs precisely to the tumor site while minimizing harm to the rest of the body. Microneedle-based drug delivery systems have emerged as a highly promising and patient-friendly approach. Microneedles are tiny, painless needle-like structures that can penetrate the skin without discomfort, allowing drugs to be delivered directly and efficiently. By enabling localized delivery, microneedles can concentrate the therapeutic agent at the tumor site and significantly reduce unwanted systemic effects. In the present study, polyethylene glycol diacrylate (PEGDA)-based microneedle patches were developed using an advanced three-dimensional (3D) printing technique known as Projection Micro-Stereolithography (PμSL). This method allowed the fabrication of microneedles with precise and reproducible geometry. The fabricated patches were thoroughly characterized and then coated with resveratrol, a compound known for its anticancer potential. Drug-coated microneedle patches were evaluated for their physicochemical properties, and in vitro drug release studies were carried out using a Franz diffusion cell. Drug administration was performed using a simple and effective “coat-and-poke” approach. The results showed that the microneedles provided sustained drug release for up to 48 hours. Preclinical studies in rats further demonstrated that microneedle-mediated delivery significantly enhanced key pharmacokinetic parameters. Importantly, drug delivery through microneedles achieved greater localization in breast tissue compared to oral administration of the pure drug. Overall, this study underscores the strong potential of PEGDA-based, 3D-printed, drug-coated microneedle patches as an effective, localized, and minimally invasive drug delivery system for improving breast cancer treatment outcomes.



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sciforum-171679: A Novel CAM-Based Dual-Reporter Imaging Platform to Study Secretome-Driven Vascular Remodeling in Sarcoma

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Introduction: Understanding tumor-vascular interactions requires experimental platforms that allow rapid, physiologically relevant assessment of tumor microenvironmental remodeling. The chick chorioallantoic membrane (CAM) model offers a highly vascularized in vivo system, yet its application for studying tumor secretome-driven vascular reprogramming remains underexplored. Here, we developed a combined secretome pretreatment and dual-reporter imaging strategy to investigate how tumor-cell-secreted soluble factors influence the vascularization during sarcoma progression.

Methods: Dual-reporter sarcoma (WEHI164, U2OS) cell lines stably expressing Katushka2S fluorescent protein and NanoLuc luciferase were generated for real-time monitoring of tumor growth and dissemination in the CAM model. CAM tissues were pretreated with a tumor cell-conditioned medium (TCM) prior to tumor cell implantation to simulate secretome-driven microenvironment priming. Tumor progression and vascular remodeling were evaluated using in ovo fluorescence imaging, immunofluorescence staining of tumor nodule sections, and multiplex secretome profiling. VEGFA inhibition with bevacizumab was applied to assess the functional impact of VEGFA in TCM.

Results: TCM pretreatment significantly enhanced tumor engraftment, vascular remodeling, and metastatic dissemination in the CAM model. Multiplex analysis identified enrichment of pro-angiogenic factors, particularly VEGFA, in TCM. VEGFA blockade partially reversed secretome-induced neovascularization and reduced tumor progression.

Conclusions: This study establishes a rapid experimental platform that utilizes secretome pretreatment and tumor cell implantation for dual-reporter imaging in CAM to investigate tumor-vascular interactions in vivo. The platform enables real-time assessment of tumor microenvironment changes and treatment effects, aiding cancer research and development of anti-angiogenic therapy.



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sciforum-178239: A Statistically Rigorous Multi-Scale Texture Analysis Framework for 3D Spheroid Characterization: Temporal Autocorrelation Correction and Molecular Validation

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Introduction

Three-dimensional tumor spheroids exhibit dynamic collective behaviors, including spontaneous reorganization, migration dynamics, and epithelial-mesenchymal transition, observable through label-free time-lapse microscopy. However, standard statistical methods fail to account for temporal dependencies inherent in longitudinal imaging data, treating autocorrelated timepoints as independent observations. This methodological limitation inflates effective sample sizes approximately 4-fold, yields anticonservative hypothesis tests, and compromises the reliability of spheroid-based drug screening applications.

Methods

We developed a validated computational framework integrating multi-scale texture analysis (37 features: GLCM, wavelet, Gabor descriptors) with autocorrelation-informed statistical testing. The framework incorporates: (1) global standardization addressing 24 orders of magnitude variance across feature types, (2) empirical autocorrelation characterization revealing 4-hour median decorrelation lags, and (3) block bootstrap resampling with 5-hour blocks enabling valid statistical inference. Validation was performed using non-small cell lung cancer spheroids (A549 and H1299 cell lines, 48 hourly observations per condition) treated with capecitabine (50 μ M), with external validation using Cancer Dependency Map RNA-sequencing data.

Results

The framework successfully discriminated treatment conditions with texture features, achieving over 100-fold improvement compared to the mean intensity baseline for mesenchymal-phenotype cells. External validation demonstrated quantitative correspondence between texture-derived discrimination ratios and independent molecular markers (VIM/CDH1 expression ratios), with agreement within 20%. All significant features remained significant under conservative block bootstrap testing with Bonferroni correction.

Conclusions

We present a novel statistical framework for rigorous morphological analysis of 3D tumor spheroid time-series. By addressing temporal autocorrelation—a commonly overlooked source of statistical invalidity—the framework enables reliable hypothesis testing for longitudinal cancer imaging studies. This methodology has immediate applications in anti-cancer drug screening, where statistically valid phenotypic profiling is essential.



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sciforum-178423: A systematic LC-HRMS urinary metabolomics framework for identifying urothelial malignancy biomarkers within a comparative multi-cancer study

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Urinary metabolomics is a promising field in non-invasive oncology, however, pre-analytical variability and difficulty in achieving tumour specificity often hinder the transition from discovery to clinical application. This study presents a validated high-resolution liquid chromatography-mass spectrometry (LC-HRMS) workflow designed to overcome matrix-induced biases and distinguish bladder cancer (BCa) signatures.

To maximize metabolomic panels, including tryptophan-kynurenine metabolites and the carnitine shuttle system, our methodology employs a systematically optimized extraction protocol (methanol-based protein precipitation, 2:1 v/v). High analytical stability was shown in the first validation of a demographically matched cohort (n = 50), with tight quality control (QC) clustering in unsupervised multivariate analysis (PCA). Significant dysregulation in proteolytic activity and membrane lipid remodeling specific to the BCa microenvironment was found.

The study was extended to include a pilot pan-cancer sub-cohort that examined metabolic profiles in patients with gastrointestinal tumors, gynecological cancers, and prostate cancer in order to further evaluate the diagnostic specificity of these markers. According to preliminary comparative analysis, specific kynurenine-to-tryptophan ratios and acylated carnitine profiles offer a distinguishing fingerprint for urothelial-specific pathologies, while other metabolic changes reflect systemic oncogenic stress, with opportunities for metabolic overlap determining between synchronous tumors in patients with multiple primary malignancies.

The current analytical approach facilitates the shift to personalized diagnostic approaches in genitourinary oncology, offering a basis for the development of high-throughput, non-invasive screening.



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sciforum-176295: AI systems and their responses to patient inquiries regarding common cancer symptoms

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Abstract

Patients and physicians are increasingly using Artificial Intelligence (1-2). We assess AI responses to patient inquiries regarding possible cancer symptoms. We rank (1-4) and grade (P/F) responses to assess if AI systems differ in quality for four hypothetical questions. We examine whether specialty affects AI assessments. We found that AI response quality differed regardless of physician specialty (3-5). Our study indicates that AI refinement is needed, though some findings were deemed acceptable initial responses to patient inquiries.

Methods

We evaluate four AI models [A1/Gemini 2.0, A2/ChatGPT turbo, A3/Claude 3.7, A4/ChatGPT3.5] responding to possible cancer symptoms (6-9). We examined whether systems differed in guiding patients to seek care, and if specialties differed in assessments (2 oncologists and 2 internists). Physicians ranked (1-4) and graded responses (pass/fail) regarding hypothetical patient inquiries:

"What should I do?"

Q1: "There was blood on the toilet paper in the bathroom".

Q2: "I have a lump in my breast".

Q3: "A mole changed color and bleeds sometimes."

Q4: "I chew tobacco and a sore in my mouth wont heal."

Results

Friedman test: $\chi^2=11.77$ ($p=0.0008$). AI rankings differed, but pairwise results did not (Wilcoxon's signed-rank test).

Chi-square: $\chi^2=18.04$ ($p=0.00043$). AI grades differed, as did AI-1($p=.0049$) AI-2($p=0.036$) vs AI-4 (Fisher's exact test).

Specialties did not differ in grading (Mann-Whitney U-Test was used for ranks, and Fisher's test was used for grades). Comments indicated "safety" and referral to medical professionals was important for grading.

Discussion

Physicians may not advocate AI usage, but patient usage does occur. We found variable quality in AI responses, which may lack context sensitivity or produce "hallucinations", generating misinformation (1-2). Question 4 scored lowest and included a risk factor, which indicates that context and complexity affect AI. Future research may assess real-world patient interactions (3). Our results suggest that Gemini and Claude do not differ significantly from ChatGPT4, which prior studies suggest was superior (10-11). AI programs were all upgraded as of mid-2025.



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sciforum-171557: An analysis of RCTs using PARP inhibitors in the treatment of breast cancer

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Introduction

Breast cancer is one of the most prevalent malignancies worldwide, especially among women, as a leading cause of high mortality. Poly (ADP-ribose) polymerases (PARP) inhibitors work via synthetic lethality and PARP1 trapping by targeting DNA repair pathways within the tumor cells, primarily the PARP enzymes, which are involved in base excision repair of single-stranded breaks in the DNA. Clinical evidence suggests that they are particularly efficient among homologous recombination repair-deficient cells, which are seen in BRCA mutated tumors.

Methods

A comprehensive analysis conducted in the Pubmed database included studies published between 2021 and 2026, with the inclusion of the keywords 'PARP inhibitor' and 'Breast cancer', yielding 829 studies. Exclusion criteria were non-English language articles, reviews and animal studies. A total of 10 randomized control trials (RCTs) were evaluated in this study.

Results

The median progression-free survival was much higher for the fuzuloparib monotherapy arm than fuzuloparib-apatinib combination arm, indicating better efficacy in the treatment group over the standard chemotherapy group. The scheduled gap (48hrs) research arm receiving carboplatin combined with olaparib and chemotherapy showed better event-free survival and overall survival rates in gBRCA patients. Three-year distant disease-free survival rates and progression-free survival rates were also substantially higher for the olaparib group in comparison to the placebo group. However, this enhanced tumor lysing property is accompanied by the caveat of undesirable adverse effects including normal tissue cytotoxicity in HRR proficient cells. Thrombocytopenia has been noted following niraparib use, while marked photosensitivity was observed in the case of rucaparib.

Conclusion

The chief effectiveness of PARP inhibitors is acting against BRCA-mutated tumors. Their efficacy in managing ovarian cancers is well documented; however, translating it to the domain of breast cancers is challenged by drug resistance via homologous repair (HR) reactivation, GI disturbances, anemia, and neutropenia among others and is still a subject of ongoing research.



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sciforum-178268: Beyond the Cytosol: Extracellular Targeted Protein Degradation for Remodeling the Tumor Immune Microenvironment

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Purpose: We aim to address the limitations of traditional proteolysis-targeting chimeras (PROTACs)—which are spatially restricted to the cytosolic ubiquitin-proteasome system—in targeting extracellular and membrane-bound immunoregulatory proteins, and to evaluate the potential of next-generation extracellular targeted protein degradation (eTPD) platforms in overcoming the "undruggable" barriers of the tumor immune microenvironment (TIME).

Methods: We systematically reviewed the recent literature and developmental pipelines concerning emerging eTPD modalities, including lysosome-targeting chimeras (LYTACs), transferrin receptor-targeting chimeras (TransTACs), and degrader-antibody conjugates (DACs). We analyzed their molecular architectures, mechanisms of trans-membrane degradation, and their biological impact on tumor-stroma immune interactions.

Results: Next-generation eTPD platforms successfully transcend cellular boundaries to physically eradicate immune checkpoints and metabolic mediators, thereby driving a profound, multidimensional remodeling of the highly immunosuppressive TIME. Furthermore, our examination of the latest clinical pipelines reveals significant translational progress alongside emerging challenges, including distinct pharmacokinetic barriers and novel adaptive resistance mechanisms associated with endolysosomal pathway defects.

Conclusion: eTPD represents a transformative paradigm in precision oncology, shifting the landscape from intracellular target inhibition to extracellular protein eradication. The strategic integration of artificial intelligence (AI) foundation models into molecular design and pharmacokinetic optimization offers a forward-looking approach to overcome current clinical bottlenecks and accelerate the translation of precision TPD immunotherapies.



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sciforum-178288: Circulating Tumor DNA as a Biomarker of Genomic Instability and Clonal Evolution in Breast Cancer

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Introduction. Breast cancer progression is driven by genomic instability and clonal evolution, processes that contribute to tumor heterogeneity, therapeutic resistance, and disease recurrence. Conventional tissue biopsies provide limited information on tumor dynamics because they represent only a single spatial and temporal snapshot of the disease. Circulating tumor DNA (ctDNA), a tumor-derived fraction of cell-free DNA released into the bloodstream, has emerged as a promising non-invasive biomarker capable of capturing tumor genomic alterations in real time. ctDNA analysis may therefore provide insight into tumor evolution and molecular heterogeneity during treatment and disease progression. This investigation aimed to evaluate the role of ctDNA in detecting genomic instability and clonal evolution in breast cancer.

Methods. A systematic review was conducted according to PRISMA 2020 guidelines. Original research articles investigating ctDNA in breast cancer and reporting genomic alterations or clonal dynamics were included, while reviews, editorials, case reports, and studies not involving ctDNA analysis were excluded. A search was performed for studies using the following keywords: circulating tumor DNA, ctDNA, liquid biopsy, breast cancer, genomic instability, and clonal evolution.

Results. In total, 124 records were collected, of which 45 articles were selected for full-text evaluation. Following application of the eligibility criteria, 25 studies published between 2014–2026 were included in the final analysis. ctDNA analysis revealed somatic mutations, copy number alterations, and resistance-associated variants, reflecting tumor heterogeneity and genomic instability. Longitudinal ctDNA monitoring frequently detected emerging resistance mutations prior to clinical progression and was associated with tumor burden and treatment response. In early breast cancer, ctDNA detection predicted molecular relapse before clinical or radiological recurrence.

Conclusions. ctDNA is a promising non-invasive biomarker for detecting genomic instability and monitoring clonal evolution in breast cancer. These findings highlight ctDNA as a powerful tool for capturing tumor dynamics and supporting precision oncology strategies.



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sciforum-178117: Cold Atmospheric Plasma–Mediated Disruption of Cell Adhesion Protein Interactions in Inflammatory Breast Cancer

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Introduction

Inflammatory breast cancer (IBC) is an aggressive subtype of breast cancer characterized by rapid metastasis and tumor embolization within lymphatic vessels [1]. Unlike many cancers, IBC cells retain strong epithelial cadherin (E-cadherin) expression, promoting stable cell–cell adhesion and multicellular cluster formation that enhances metastatic dissemination [2]. Disrupting E-cadherin-mediated adhesion may represent a strategy to destabilize tumor emboli and reduce metastatic potential. Cold atmospheric plasma (CAP) generates reactive oxygen and nitrogen species (RONS), including atomic oxygen (O), hydroxyl radicals (OH), hydrogen peroxide (H₂O₂), and singlet oxygen (¹O₂), which can induce oxidative modifications in biomolecules and alter protein–protein interactions in cancer cell adhesion [3].

Methods

All-atom molecular dynamics simulations were performed on the extracellular EC1–EC2 domains of the E-cadherin homodimer, forming the primary adhesive interface between neighboring cells. Oxidative modifications associated with CAP-generated RONS were introduced at oxidation-susceptible residues, including methionine at the adhesive interface. Thermodynamic integration (TI) was employed to compute the change in binding free energy (Δ BFE) upon oxidation. Alchemical transformations were performed for multiple configurations, including native and oxidized states of chain A and combined oxidation scenarios of both chains, enabling systematic evaluation of adhesion energetics.

Results

Preliminary simulations indicate that oxidation of interfacial residues disrupts key stabilizing interactions within the E-cadherin homodimer, including inter-chain hydrophobic contacts and hydrogen bonding networks. In particular, oxidation reduces the number and persistence of inter-chain contacts at the adhesive interface, suggesting decreased binding stability. Ongoing TI calculations will quantify Δ BFE across oxidation states and identify residues that contribute most to adhesion loss.

Conclusions

CAP-induced oxidative stress may weaken E-cadherin-mediated adhesion in IBC by reducing the binding free energy of the E-cadherin interface. This effect could compromise tumor embolus integrity and increase susceptibility to detachment-induced cell death, supporting plasma-based modulation of cell adhesion as a potential adjuvant therapeutic strategy in IBC.



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sciforum-171810: Comprehensive Computational Profiling of MSH3 Missense Mutations and Stability Effects in Cancers and Neurodegenerative Disorders

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Background/Objectives: MSH3 encodes a key component of the DNA mismatch repair (MMR) system, which is essential for maintaining genomic stability. Mutations in MSH3 have been associated with colorectal cancer (CRC), particularly within microsatellite instability and adenomatous polyposis syndromes. Beyond its oncogenic associations, MSH3 dysfunction has been linked to neurodegenerative disorders, such as Huntington's disease, where impaired repair promotes trinucleotide repeat expansion. Despite its clinical relevance, the structural and pathogenic impact of MSH3 missense mutations remains insufficiently characterized. This study aims to systematically characterize the impact of all possible missense mutations in MSH3 on protein stability and predicted pathogenicity. **Methods:** Using the predicted AlphaFold structure, we conducted a saturated mutagenesis analysis of 21,603 MSH3 missense mutations. Folding energy changes ($\Delta\Delta G$) were computed with FoldX, and pathogenicity was evaluated using Meta-SNP and AlphaMissense predictors. Clinically significant variants were cross-referenced from ClinVar, COSMIC, HGMD, and gnomAD databases. **Results:** Approximately 57.2% of variants destabilized MSH3 ($\Delta\Delta G > 0.5$ kcal/mol), whereas 10.9% showed signs of stabilizing ($\Delta\Delta G < -0.5$ kcal/mol). Notably, mutations G389W, G572W, G978W, G978Y, and G572Y introduced steric clashes that disrupted β -sheet packing, indicating conformational instability. Conversely, variations such as P64F, P64W, P64D, P6D, and P64R increased protein stability. Correlation analyses revealed partial agreement between predicted stability changes and pathogenicity scores, suggesting both structural and non-structural mechanisms underpinning disease risk. **Conclusions:** This comprehensive analysis defines the structural landscape of MSH3 missense mutations and identifies protein destabilization as a major contributor to variant pathogenicity. However, the incomplete concordance with predictive models indicates that additional non-structural mechanisms also influence disease risk. These findings provide a framework for interpreting MSH3 variants in cancer and neurodegenerative disorders and underscore the importance of integrating structural and functional evidence in variant classification.



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sciforum-170875: Development and External Validation of an Interpretable Machine-Learning Model for DFS After First-Line Neoadjuvant Chemotherapy in Gastric Cancer: A Four-Center Study

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Background

Recurrence risk after first-line neoadjuvant chemotherapy (NACT) and curative gastrectomy remains highly heterogeneous in gastric cancer. However, postoperative risk assessment still relies mainly on ypT/ypN staging, which may not adequately capture residual disease burden or support individualized postoperative management.

Methods

In this four-center study, we developed and externally validated an interpretable machine-learning model to predict disease-free survival (DFS) after first-line NACT for gastric cancer using routinely available clinicopathologic variables. Model performance was assessed by discrimination, calibration, and decision-curve analysis, and compared with a conventional ypT/ypN-based Cox model. SHAP was applied to improve interpretability and to quantify the contribution of individual predictors to patient-level risk estimates.

Results

The model demonstrated robust performance across multicenter cohorts and maintained predictive ability in independent external validation sets. It effectively stratified patients according to postoperative recurrence risk, yielded greater clinical net benefit than treat-all/treat-none strategies, and outperformed a conventional ypT/ypN-based Cox model. Its interpretable framework also enabled transparent identification of key variables driving individual predictions, thereby improving clinical plausibility and facilitating bedside interpretation. These findings support its transportability across heterogeneous real-world multicenter settings.

Conclusions

An interpretable ML model provided robust, externally validated prediction of DFS after first-line NACT for gastric cancer across heterogeneous multicenter cohorts. Beyond conventional postoperative staging, it may support risk-adapted surveillance, MDT discussion, and identification of patients who may benefit from closer follow-up, refined postoperative counseling, or further management strategies.



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sciforum-170432: Development of novel drug delivery systems based on extracellular vesicles and cell membranes for cancer therapy

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Introduction: Nanoscale drug delivery systems represent a promising approach for improving efficiency and safety of chemotherapy. However, many synthetic nanocarriers may cause toxicity and immune reactions, which limit their biomedical application. In this study, we developed hybrid nanoparticles based on extracellular vesicles and cell membranes. Such nanoparticles may combine the high biocompatibility of vesicles with membrane-derived biological functions and the ability to cross biological barriers.

Methods: Human embryonic kidney HEK293 cells were used as a source of extracellular vesicles and cell membranes. Hybrid nanoparticles were prepared by extrusion through polycarbonate membranes. To optimize particle size distribution, we tested different numbers of extrusion cycles (5, 10, 15, 20, and 25). Doxorubicin (DOX) loading was performed using two methods: a pH gradient and an ammonium sulfate gradient. The pH gradient method provides DOX diffusion through the membrane, followed by protonation and retention inside the particles, while the ammonium sulfate method relies on ionic gradients and the formation of poorly soluble sulfate complexes.

Results: The results demonstrated that 15 extrusion cycles were optimal for obtaining hybrid particles with the monodisperse size distribution. DOX loading using the pH gradient method produced particles with an average diameter of 250 ± 190 nm and a DOX concentration of 12 ± 1 $\mu\text{g/mL}$. In contrast, the ammonium sulfate gradient method resulted in a significant increase in particle size to 780 ± 360 nm, while the DOX concentration was 10 ± 3 $\mu\text{g/mL}$.

Conclusions: Overall, the pH gradient method was more suitable for the preparation of DOX-loaded hybrid nanoparticles with improved tumor accumulation. The developed hybrid system represents a biocompatible platform for further in vitro studies as a drug delivery approach for cancer therapy.

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sciforum-170867: Development Omnipose Neural Network-Based Analytical Module for Morphometric Analysis of Metastatic Cancer Cells

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Introduction. Assessing metastatic potential (MP) based on morphological parameters of cancer cells is a promising direction in experimental oncology. The shape of a cell often correlates with an invasive phenotype, characterized by greater elongation and decreased roundness. A deep neural network image-segmentation algorithm implemented in Omnipose lacks tools for obtaining morphological data and their subsequent analysis for MP evaluation. Our aim was to develop a specialized software module for complete morphometric analysis of cells in microscopic images without need in specific pre-processing or staining.

Materials and Methods. Custom Python code (used packages: matplotlib.pyplot, skimage, scipy, google.colab, cellpose) was integrated into a pre-trained Omnipose model. The created module performs end-to-end analytics and calculation of key morphologic parameters: Area, Perimeter, Major_axis, Minor_axis, Circularity, Aspect_Ratio, Roundness, Solidity. The main innovation is an algorithm that analyzes these parameters, assigns characteristics to each cell, and outputs averaged values for further assessment of MP. Segmentation performance was evaluated by comparison with manual analysis using microscopic images of 65 breast cancer cells with high (MDA-MB-231) and low (MCF-7) MP.

Results. The Omnipose neural network's cell recognition accuracy exceeded 80%, confirming the high reliability of the approach. Measured morphologic parameters: Area, Perimeter, Major_axis, Minor_axis demonstrated strong agreement with manual analysis, with errors below 5%. The shape descriptors: Circularity, Solidity, Roundness and Aspect_Ratio demonstrated high concordance, with a maximum deviation of 11% from manually calculated values.

Conclusions. This work developed an analytical module that transforms Omnipose from a segmentation tool into a platform for direct morphometric analysis of microscopic images. The module serves as a foundation for a convenient tool to quantitatively evaluate cancer cell metastasis.



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sciforum-178387: Emerging Strategies in Cancer Detection and Treatment: A Systematic Review of Immunotherapy, Gene Editing, and Artificial Intelligence

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Introduction: Cancer remains a leading cause of global mortality, with conventional therapies such as chemotherapy and radiotherapy limited by toxicity, resistance, and suboptimal efficacy. Since 2020, advances in immunotherapy, gene editing, liquid biopsy technologies, artificial intelligence, and targeted drug delivery systems have reshaped cancer management. This systematic review evaluates recent clinical and translational innovations

Methods: This review follows PRISMA 2020 guidelines. A systematic search of PubMed, Scopus, Web of Science, and ClinicalTrials.gov was conducted for studies published between January 2020 and December 2025. Search terms included: “cancer,” “immunotherapy,” “CRISPR,” “CAR-T,” “personalized mRNA vaccines,” “liquid biopsy,” “circulating tumor DNA,” and “artificial intelligence,” combined using Boolean operators (AND/OR). Inclusion criteria comprised clinical trials, observational studies, and regulatory approvals reporting measurable clinical outcomes. Exclusion criteria included preclinical-only studies, reviews, editorials, and non-peer-reviewed articles. Two reviewers independently conducted screening, data extraction, and risk-of-bias assessment using the Cochrane Risk of Bias tool and Newcastle–Ottawa Scale.

Results: From 312 initially identified records, 62 studies met the inclusion criteria and were included in the final analysis, comprising 38 clinical trials and 24 observational studies. CAR-T therapies showed response rates of 52–83% in hematological malignancies and 15–35% in solid tumors. Personalized mRNA vaccines demonstrated immune response rates of 60–80% in early-phase trials. Liquid biopsy assays showed sensitivity of 70–90% for early detection and >85% accuracy in monitoring residual disease. Artificial intelligence improved diagnostic accuracy by 10–25%. Most studies had a low-to-moderate risk of bias. The included studies varied in design, population, and outcome measures, which limited direct comparison and prevented meta-analysis. Some studies also had limitations such as small sample sizes, moderate risk of bias, and short follow-up periods, which reduced the overall strength of the evidence.

Conclusion: All of these inventions are transforming the world of cancer treatment into a more progressive, personalised, and even curative process. There are still problems related to large-scale production, equitable global supply, and continuous safety.



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sciforum-171917: Establishment of a Precise Mouse Model of Radiation Proctitis Using Localized Rectal Irradiation

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Aim: To establish a reproducible and anatomically precise mouse model of radiation proctitis (RP) using localized rectal irradiation, and to determine the optimal radiation dose that balances pathological fidelity and animal survival, providing a robust platform for mechanistic studies and therapeutic evaluation.

Methods: Eight-week-old male C57BL/6 mice were anesthetized and subjected to single-fraction localized rectal irradiation using a 6 MV X-ray linear accelerator. A defined rectal field (1 × 2 cm) was precisely positioned to target the rectum while sparing surrounding tissues. Mice were assigned to different dose groups (0, 10, 20, 40, 50, and 60 Gy; n = 12 per group). Rectal tissues were harvested at 7, 14, 21, and 28 days post-irradiation for histopathological evaluation using hematoxylin and eosin staining. Tissue injury severity, inflammatory infiltration, structural integrity, and animal survival were systematically assessed.

Results: Localized rectal irradiation successfully induced dose-dependent radiation-induced rectal injury. Low-dose groups (10–20 Gy) exhibited minimal or mild mucosal damage, with no significant mortality. High-dose irradiation (50–60 Gy) caused extensive transmural injury with loss of normal rectal architecture, accompanied by marked inflammatory cell infiltration and high mortality rates (50 Gy: 50% mortality within 14 days; 60 Gy: >90% mortality within 14 days). In contrast, the 40 Gy group demonstrated consistent and reproducible rectal injury, characterized by moderate-to-severe mucosal and submucosal damage, uniform pathological features, and low mortality (8% within 28 days). Partial tissue recovery was observed at 28 days post-irradiation, enabling longitudinal observation and interventional studies.

Conclusion: A localized rectal irradiation dose of 40 Gy reliably establishes a stable and reproducible mouse model of radiation proctitis with acceptable survival. This model closely mimics clinical radiation-induced rectal injury and provides a practical, translationally relevant platform for studying RP pathogenesis and evaluating therapeutic strategies.



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sciforum-178401: Evaluating Agentic AI for Autonomous Hypothesis Generation in Clinical Datasets

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Background:

Generative agentic AI systems are increasingly used to accelerate clinical research workflows, but their reliability for hypothesis discovery in patient datasets remains insufficiently evaluated. In this study, we evaluated whether an autonomous AI research agent could independently examine a deidentified clinical dataset, identify a significant association, select an appropriate statistical test, and produce a scientifically sound hypothesis.

Methods:

We evaluated ChatGPT in agent mode using structured prompt engineering and guardrails designed to reduce hallucination and improve its ability to detect patterns across patient records, identify similarities between cases, and uncover potential links and associations. As a benchmark task, we used the publicly available Brain Mets Lung MRI Path Segs dataset from The Cancer Imaging Archive, which contains clinical notes and pathology related information. We assessed whether the agent could independently identify a clinically relevant association and generate a significant hypothesis.

Results:

After guardrail based prompt refinement, the agent produced more grounded and auditable analyses. As an example of successful autonomous hypothesis generation, the workflow identified an association between the dataset field labeled PD L1 status and dominant lesion size, yielding a statistically significant result in the initial exploratory analysis. We manually reviewed the agent generated finding and confirmed that the identified association was statistically significant. Rather than being prespecified by the investigators, this hypothesis emerged from the AI system's autonomous detection of patterns within the dataset. To the best of our knowledge, this has not been previously published in the literature. We therefore present it as an AI-derived, hypothesis-generating result that illustrates the potential of agentic AI to support pattern discovery and early stage clinical hypothesis formation.

Conclusion:

Prompt constrained agentic AI can support autonomous pattern detection, hypothesis generation, and statistical testing in de identified patient datasets.



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sciforum-170767: Exploration of genes identified in antitumor resistance in triple-negative breast

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(1) Background: Breast cancer is the most common cancer among women worldwide, with more than 2 million new cases each year, and is the leading cause of cancer death in women. Triple-negative breast cancer (TNBC) is characterized by high aggressiveness, absence of hormone receptors, and variable response to immunotherapy, posing a major therapeutic challenge, and is an aggressive subtype characterized by the lack of hormone receptors and HER2, limiting targeted therapy options. Despite advances in immunotherapy, such as PD-1/PD-L1 inhibitors, frequent resistance persists due to an immunosuppressive tumor microenvironment (TME). Key among these mechanisms is the increased infiltration of regulatory T cells (Tregs), which suppress antitumor immunity. This study investigates the molecular signatures associated with this Treg-dominant infiltration in TNBC and their prognostic impact, aiming to identify novel therapeutic targets. (2) Methods: Bioinformatics analyses on TCGA-TNBC transcriptomic data to assess immune infiltration, identify genes associated with Treg accumulation, reduced CD8+ effector T cells, and immune checkpoint expression, and correlate these signatures with prognosis. (3) Results: A panel of overexpressed genes is strongly correlated with increased infiltration of immunosuppressive cells, a reduction in CD8+ T cells, and elevated immune checkpoints, contributing to an unfavorable tumor microenvironment and a poor prognosis. (4) Conclusions: These candidate genes represent potential biomarkers of immune resistance and therapeutic targets to restore antitumor immunity in TNBC.



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sciforum-171077: Extracellular vesicles as a targeted drug delivery platform for cancer treatment

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Introduction. Photodynamic therapy (PDT) is a commonly used cancer treatment method that generates cytotoxic reactive oxygen species upon light irradiation. However, its therapeutic efficacy is often limited by poor tumor selectivity and low intracellular accumulation of photosensitizers. Extracellular vesicles (EVs) are nanoscale structures released by cells of various tissues to mediate intercellular communication. Due to their natural origin, biocompatibility, and ability to carry therapeutic agents, EVs was proposed as promising drug delivery systems for cancer therapy. Tumor-derived EVs may preserve homotypic targeting properties, thereby enhancing drug accumulation in tumor tissue.

Materials and methods. EVs were isolated from A549 human lung adenocarcinoma cell line. Several EVs isolation methods were compared, including polyethylene glycol precipitation, anion-exchange chromatography and ultrafiltration. The porphyrin-based photosensitizer 5,15-bis(3-methoxy(4-(6-pyridylhexyloxy)phenyl)-10,20-di(ethynylphenyl)porphyrinato zinc (ZnP) was loaded in EVs via sonication, followed by removal of non-encapsulated ZnP using size-exclusion chromatography. The cytotoxic activity of ZnP-loaded EVs was evaluated on A549 cells after red light irradiation (660 nm). The generation of reactive oxygen species was analyzed using 2',7'-dichlorofluorescein diacetate probe.

Results. Ultrafiltration provide the efficient isolation of EVs with appropriate size characteristics and high protein content, indicating the effective vesicle recovery. The ZnP loading efficiency was approximately 40%. Neither free ZnP nor ZnP-loaded EVs showed dark toxicity on A549 cells at the tested concentrations. Photoactivity assay confirmed that ZnP preserve its photodynamic functionality after EVs loading. Flow cytometry analysis showed that ZnP-loaded EVs generated more reactive oxygen species compared to free ZnP, suggesting an enhanced oxidative effect.

Conclusions. Ultrafiltration proved to be an effective EVs isolation method. ZnP encapsulation in EVs preserved its photodynamic activity. Thus, the developed EVs-based system represents a promising approach for drug delivery.

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sciforum-171914: Feasibility of a Photocurable 3D Bioprinted Primary Colorectal Cancer Model for In Vitro Drug Evaluation

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Objective: To establish and validate the feasibility of a photocurable 3D bioprinted in vitro model using primary colorectal cancer (CRC) cells, aiming to better recapitulate tumor architecture and biological heterogeneity compared with conventional two-dimensional cultures.

Methods: Primary tumor tissues were obtained from patients with colorectal cancer and enzymatically dissociated into single-cell suspensions. A photocurable bioink composed of gelatin methacrylate (GelMA), hyaluronic acid methacrylate (HAMA), and lithium phenyl-2,4,6-trimethylbenzoylphosphine (LAP) was prepared and mixed with primary CRC cells. Three-dimensional tumor constructs were generated using a high-throughput light-based 3D bioprinting system and cultured under standard conditions. Model stability, morphology, and cell viability were monitored microscopically. Reproducibility was evaluated by repeated bioprinting and parallel drug exposure experiments.

Results: Photocurable 3D bioprinting successfully generated structurally stable and reproducible primary CRC constructs across multiple patient-derived samples. Tumor spheroids maintained compact architecture and sustained viability during long-term culture. The model demonstrated high experimental consistency, with low inter-batch variability and good repeatability in drug response assays. Compared with 2D cultures, the 3D bioprinted model exhibited increased resistance to chemotherapy, suggesting improved simulation of the in vivo tumor microenvironment.

Conclusion: Photocurable 3D bioprinting is a feasible and reliable approach for constructing primary colorectal cancer models in vitro. This platform provides a biologically relevant and reproducible system that better reflects tumor heterogeneity and drug response characteristics, supporting its application in translational research and precision oncology.



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sciforum-141251: Genetic Factors Affecting Tobacco Cessation

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Research into multi-causative disorders, such as substance dependence, makes it important to understand their neurobiological, genetic, and environmental foundations. The primary objective is to study the dynamic relationship of these factors to combat global health concerns like cancer, emphysema, and asthma.

Our research focuses on developing and applying precision preclinical models to investigate these disorders. It employs the use of bioinformatics and computational biology tools, including machine learning and AI-based methodologies such as UMAP (Uniform Manifold Approximation and Projection) using PYTHON and its libraries. Specifically, a structure-based functional analysis of sixteen genes associated with nicotine dependence has been performed using PDB, ChimeraX, BLAST, and Clustal Omega for Structural Bioinformatics, visualization, and sequence alignment, respectively. We found that CHRNA5 exhibited a maximum number of polymorphisms while MAOA's methylation is implicated. Nicotine dependence involves genetic variants in the CHRNA5-CHRNA3-CHRNA4 gene cluster affecting dopaminergic systems, alongside DRD2, DAT1, COMT, and CYP2A6. GABA contains a highly conserved region and base sequence changes in genes such as MAOA, MAOB, DAT1, DRD1, and GABA; COMT enzyme activity, influenced by the Val158Met polymorphism, modulates dopamine neurotransmission and effects nicotine susceptibility, with sex-specific differences noticed.

The application of dimensionality reduction techniques like UMAPs enables the visualization and analysis of genetic and epigenetic datasets, helping us to study patterns and relationships related to diseases of focus. In addition to this, AI-based methodologies facilitate the identification of novel biomarkers and potential therapeutic targets in a better way. This integrated approach demonstrates the immense potential for precision medicine approaches in areas like tobacco cessation.



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sciforum-170196: High-nitrogen artificial gas mixture-induced hypoxia decreases nanoparticle uptake in breast tumor cells with varying malignancy

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Introduction. The rapid and disorganized growth of tumors along with poor blood supply generates a hypoxic environment, causing cancer cells to adapt through HIF-1 signaling, which drives glycolysis (Warburg effect), stemness, and increased invasion. Previously, we demonstrated that nanoparticle (NP) uptake correlates with metastatic potential (MP) of breast cancer (BC) cells. Here, we investigated the high-nitrogen artificial gas mixture-induced hypoxia effect on NP uptake in non-tumorigenic mammary epithelial and BC cell lines.

Materials and methods. Breast cancer MDA-MB-231 (high-MP), MCF-7 (low-MP) and non-tumorigenic mammary epithelial MCF-10A cell lines were cultured under normoxic conditions (21% O₂, 5% CO₂, 74% N₂) in a standard cell incubator and then subjected to 4 h of artificial gas mixture hypoxic conditions (5% CO₂, 5% O₂, 90% N₂) in specially designed camera. Cells were subsequently incubated with 200 nm carboxylated fluorescent NPs for 1h, then washed with PBS and trypsin and fixed with 4% paraformaldehyde. Nuclei were stained with Hoechst. NP uptake was assessed by high content fluorescence microscopy, and Pearson correlation coefficients of NP colocalization with nucleus signals were calculated. Statistical significance between groups was evaluated using ANOVA.

Results. As expected, under all tested conditions, uptake of NPs was significantly higher in BC cells with high MP compared with low MP (by 1.64 times) and non-tumorigenic mammary epithelial cells (by 7.6 times). Gas mixture-induced hypoxia led to a reduction in nanoparticle uptake by 1.27-fold in cancer cells and by 3-fold in non-tumorigenic cells (p0.03).

Conclusions. High-nitrogen artificial gas mixture-induced hypoxia decreases nanoparticle uptake, indicating a possible reduction in cells' metastatic potential. The magnitude of this effect depends on cell malignancy: non-tumorigenic cells demonstrate the highest uptake reduction, whereas both cancer cell lines exhibit lower reductions. This differential response can indicate that increased hypoxia tolerance may represent an adaptive advantage in BC cells.



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sciforum-171739: Immune Checkpoint Inhibitor-Associated Myocarditis in Cancer Patients: A Systematic Review of Clinical Presentation, Management, and Outcomes

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Background: Immune checkpoint inhibitor-associated myocarditis (ICI-M) is a rare but life-threatening toxicity. This systematic review synthesizes the current evidence on the epidemiology, clinical presentation, diagnostic approaches, management strategies, and outcomes of ICI-M to guide clinical practice.

Methods: We systematically searched PubMed from inception to December 2025 for studies reporting on ICI-M in cancer patients. Data on patient demographics, clinical features, diagnostic findings, treatment, and outcomes were extracted. The risk of bias was assessed using appropriate tools.

Results: In total, 43 studies were included. ICI-M predominantly affected older adults (median age 65-74 years) with metastatic melanoma, non-small cell lung cancer, or renal cell carcinoma. The highest risk was associated with combination ICI therapy (anti-PD-1/PD-L1 + anti-CTLA-4). Clinical presentation ranged from asymptomatic biomarker elevation to fulminant heart failure, with a high frequency of concurrent myositis. Key diagnostic findings included elevated troponin (>90% of cases), ECG abnormalities, and reduced global longitudinal strain on echocardiography. Management universally involved ICI discontinuation and high-dose corticosteroids. Second-line immunosuppression (e.g., IVIG, infliximab, abatacept) was used in refractory cases. Despite treatment, mortality remained high (25-50%). Poor prognostic factors included high troponin levels, reduced left ventricular ejection fraction, and conduction abnormalities.

Conclusion: ICI-M is a severe complication with high mortality. Early recognition via proactive monitoring, prompt diagnosis using a multi-modal approach, and immediate, aggressive immunosuppression are critical. Future research should focus on predictive biomarkers and randomized trials to optimize management.



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sciforum-171763: Immunomagnetic Fluorogenic ELISA Enabled by HRP-Catalyzed Resorufin Generation for Sensitive Quantification of Carcinoembryonic Antigen in Cancer Cells

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Abstract

Sensitive and reliable quantification of tumor biomarkers at the cellular level remains a critical requirement for early cancer diagnosis and therapeutic monitoring. Here, we report a magnetically programmable fluorescence-based enzyme-linked immunosorbent assay (ELISA) that integrates immunomagnetic separation with enzyme-amplified fluorogenic detection for the quantitative analysis of carcinoembryonic antigen (CEA) in gastric cancer cells. The assay employs antibody-functionalized magnetic beads for efficient target capture and isolation, followed by a horseradish peroxidase (HRP)-labeled secondary antibody to enable signal amplification through enzymatic catalysis.

The detection mechanism is based on the HRP-mediated oxidation of the non-fluorescent substrate 10-acetyl-3,7-dihydroxyphenoxazine (ADHP) into highly fluorescent resorufin, providing a robust fluorescence readout with minimal background interference. Systematic optimization of key assay parameters—including incubation time, pH, substrate concentration, oxidant level, and magnetic bead loading—enabled high analytical performance under mild, biologically compatible conditions. The resulting platform exhibited a linear response to CEA concentrations from 3.0 to 60 ng/mL, with a detection limit of 1.5 ng/mL (3σ) and excellent reproducibility (RSD $\approx$ 1.2%).

Importantly, the method was successfully applied to quantify endogenous CEA in extracts of gastric cancer cells, yielding concentrations in the range of 16.5–28.3 ng/mL with recoveries between 94.7% and 107%, demonstrating strong accuracy and matrix tolerance. Compared with conventional ELISA formats, the proposed approach offers enhanced sensitivity, rapid magnetic separation, reduced sample handling, and improved adaptability to complex biological matrices.

This magnetically assisted fluorogenic ELISA provides a versatile and scalable analytical framework for tumor marker detection and can be readily extended to other clinically relevant biomarkers, supporting its potential integration into cancer diagnostics and bioanalytical platforms.



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sciforum-178294: Investigation of the Protein Corona on Polyvinyl Alcohol-Stabilized Polymeric Nanoparticles

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Nanoparticles based on poly(lactic-co-glycolic acid) (PLGA) are widely used for targeted drug delivery in oncology. Upon intravenous administration, these particles are coated by biomolecules, forming protein corona that determines biodistribution of nanoparticles. While polyvinyl alcohol (PVA) is commonly used in particle formulation, its influence on the corona remains poorly understood. In this study, we determined the impact of residual PVA concentration on the protein corona composition of polymeric nanoparticles.

In this work, paclitaxel-loaded PLGA nanoparticles were prepared with varying PVA concentrations: 0.5% (NP1), 1% (NP2), 2% (NP3) and 5% (NP4). Characterization showed that increasing PVA concentration resulted in smaller particle size and lower polydispersity: NP1 (247±1 nm, PDI 0.305±0.009), NP2 (180±1 nm, PDI 0.109±0.015), NP3 (171±1 nm, PDI 0.057±0.015), and NP4 (177±2 nm, PDI 0.063±0.025). All formulations exhibited negative ζ-potential (ranging from -15.4±0.6 to -11.2±0.5 mV).

To form protein corona, particles were incubated with fetal bovine serum as a model source of proteins. Adsorbed proteins were quantified using the bicinchoninic acid assay. Increasing PVA concentration correlated with a decrease in adsorbed proteins, with NP1 showing the highest protein concentration (163±21 µg/µg particles) and NP4 the lowest (6±2 µg/µg particles). The qualitative corona composition was analyzed using liquid chromatography–tandem mass spectrometry (LC-MS/MS). LC-MS/MS revealed 393 proteins of different identities in all examined particles. A Venn diagram revealed a core set of common proteins across samples, but NP4 contained the highest number of unique proteins, indicating that high PVA content alters corona composition.

These results demonstrate that residual PVA concentration significantly affects both quantitative and qualitative protein corona composition. This study provides a rational basis for optimizing nanoparticle formulations to control corona formation. Further studies are needed to determine whether these differences can be exploited to improve tumor targeting and reduce off-target accumulation, thereby enhancing the therapeutic efficacy of encapsulated anticancer drugs.



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sciforum-171729: Lipid Dysregulation in Normal Tissues Following Cancer Therapy: Implications for Toxicity and Treatment Resistance

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Introduction: This study explores a significant issue within the chosen field, providing a comprehensive overview of current challenges and recent developments. By analyzing relevant literature and existing data, the research aims to identify knowledge gaps and propose potential solutions. The importance of this topic is underscored by its impact on both theoretical understanding and practical applications. Through carefully designed methods, the study seeks to contribute valuable insights and advance ongoing discussions. The findings will inform future research directions and support evidence-based decision-making in this area.

Methods: We developed an integrated imaging and histologic approach to quantify intra-renal non-adipose tissue (IRNAT) lipid accumulation and to examine its association with normal tissue toxicity and tumor response. Non-contrast whole-body MRI was combined with Oil Red O lipid staining for spatial validation to monitor lipid changes following clinically relevant radiation and chemoradiotherapy longitudinally. Studies were performed in mouse models with follow-up up to 40 weeks. Renal and salivary gland injury, inflammation, fibrosis, cholesterol accumulation, and tumor response were evaluated in parallel, and lipid-modulating interventions were tested.

Results: Cancer treatment induced progressive accumulation of non-adipose lipids in the kidney and salivary glands, detectable by MRI and confirmed histologically. Increased IRNAT lipid burden correlated with tubular and glomerular injury, inflammatory remodeling, fibrosis, and functional decline. Elevated lipid dysregulation in normal tissues was also associated with reduced tumor sensitivity and treatment resistance. Targeting lipid pathways mitigated normal tissue injury and improved therapeutic responsiveness.

Conclusions: These findings identify lipid dysregulation as a mechanistic link between cancer, normal tissue toxicity, and treatment resistance. This MRI-based approach provides a practical, non-invasive strategy to quantify lipid changes in both normal tissues and tumors, with potential to enable early prediction of toxicity risk and resistance and to inform treatment planning that balances tumor control with normal tissue protection.



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sciforum-166835: Liver Tumor Prediction: A Lifestyle-Based Risk Assessment

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Modified Abstract:

Liver cancer represent a significant global health burden, with the hepatocellular carcinoma (HCC) type of liver cancer ranking among the leading causes of cancer-related mortality. The progression from healthy liver function to liver malignancy and cancer follows a well-established pathway through distinct stages, with Stage I representing lifestyle indicators that offer the greatest potential for prevention. Current diagnostic approaches often identify liver ailments leading to cancer, at advanced stages when therapeutic options are limited, emphasizing the need for early detection strategies.

This cross-sectional study analyzed lifestyle and clinical data from 1,700 participants aged 18-80 years to develop and validate a comprehensive risk assessment framework for Stage I liver disease detection to prevent the developing of cancers at later stage. Eleven primary features were assessed, including lifestyle factors (alcohol consumption, smoking status, physical activity, BMI category) and clinical indicators (diabetes and liver function tests).

Machine learning techniques, specifically Gradient Boosting with hyperparameter optimization, were employed to develop predictive models. The results acheived serve as input variables for the intermediate stage, where the subjects oundergo the diagnostics and therapeutics. For the patients at an advanced stage of liver disease, these Machine learning algorithms confirmed on the basis of the comprehensive risk assessment framework. The confirmation of the advancement of the liver disease to a new level that is close to liver tumor, the irreversible liver damage, on the basis of the output from stage 1, serve as variables, along with new liver tests results.

The encouraging results only serve as an indication of the early cause of tumor, only if the medical tests of the subjects confirm the liver tumor for these subjects and other subjects with similar or close to similar data including life style, medical tests and the medicine usage.



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sciforum-169588: Modelling the transition from growth to decay: A dynamical system approach to diffuse intrinsic pontine glioma (DIPG)

Shruti Ria Burra

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Diffuse Intrinsic Pontine Glioma (DIPG) remains one of the most devastating paediatric brain tumours, with a survival median of 9-18 months. This aggressive progression is driven by uncontrollable cellular doubling, making it a critical subject for dynamical system modelling. This project uses Python-based simulations to model the mathematical goal of treatment: transforming the rapid growth of DIPG into a predictable state of decay. Given the urgent need for models that can visualise treatment efficiency, I present the tumour cell population as a dynamic system governed by the equation $dx/dt = f(x)$.

My research compares a simple exponential growth model ($a > 0$) with a more realistic logistic growth model ($dx/dt = ax - bx^2$). I also looked at how even tiny changes in the rule parameters can lead to completely different results for patients. By adding a second variable to the math, I was able to show the hidden link between how a tumour grows and the epigenetic signals that drive it. My Python simulation shows that the real Mathematical Goal of any treatment is to flip the growth switch into a negative state ($a < 0$). This forces the tumour's "shooting upward curve" to turn around and become a falling exponential decay curve. This computer-based approach acts like a "mathematical microscope", allowing us to see exactly how a drug can break through a tumour's resistance and finally make the cell population shrink.



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sciforum-170956: NDS: A Novel Deep Learning-Based Systems Biology Framework for Identifying Prognostic Biomarkers in Hepatocellular Carcinoma

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Purpose: Hepatocellular carcinoma (HCC) is one of the most aggressive and prevalent forms of liver cancer, posing a serious threat to global health, affirming the urgent need for reliable biomarkers to improve diagnosis and prognosis. Existing approaches often fail to capture nonlinear gene interactions and face challenges of high dimensionality, which limits their clinical translation.

Methods: The differentially expressed genes (DEGs) were identified by analyzing the gene expression profiles of 445 HCC and normal tissues. These filter genes were fed to a deep autoencoder to reduce the dimensionality of the data, capture non-linear interactions, and extract informative latent features. Predictive gene features were selected through mutual information (MI) ranking and LASSO regression and subsequently evaluated using logistic regression (LR), random forest (RF), and support vector machine (SVM) classifiers with 5-fold cross-validation. The top 50 genes underwent Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analyses. Protein-protein interaction (PPI) networks were constructed to identify core hub genes, followed by gene-drug interaction, transcription factor analysis, and survival validation.

Results: Enrichment analysis revealed involvement in metabolic pathways, PI3K/Akt signaling, protein processing in the endoplasmic reticulum, fatty acid metabolism, cell cycle regulation, and viral carcinogenesis. Cross-validation showed stable and high performance across classifiers (accuracy = 0.969, F1 $\approx$ 0.97), with RF and SVM achieving slightly higher AUC ($\sim$ 0.983 and $\sim$ 0.982). Independent tests showed excellent performance across all classifiers ($\sim$ 1.0), confirming high feature discriminative power. Survival analysis showed that hub genes, including *HSP90AB1*, *TUBA1B*, *PKM*, *H2AZ1*, *YWHAZ*, *ACLY*, *RAN*, *ILF2*, *KPNA2*, and *TXNRD1*, were significantly associated with poor prognosis (HR > 1.5, p < 0.05), correlating with reduced overall, relapse-free, and disease-specific survival in HCC.

Conclusion: This integrative novel framework effectively identifies biologically relevant biomarkers, providing insights into HCC mechanisms and potential targets for precision therapy.



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sciforum-178464: Quantum Entanglement as a Physical Determinant of Genomic Instability in TP53

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Mutations in the TP53 gene, a key tumor suppressor involved in DNA repair and cell cycle regulation, are among the most frequent alterations in human cancers. While TP53 mutagenesis can involve biochemical mechanisms such as methylation and oxidative damage, recent theoretical studies have proposed that quantum mechanical properties of DNA, particularly quantum entanglement, may influence mutation susceptibility in general. Whether such quantum effects contribute to mutational patterns in specific genes such as TP53 remains unexplored. In this exploratory study, we applied a coupled quantum harmonic oscillator model to quantify site-specific von Neumann Entropy (VNE), a proxy for quantum entanglement, across the TP53 sequence. Our findings show that known mutation hot spots exhibited significantly elevated VNE compared to non-hot spot regions, suggesting enhanced local quantum coupling may reflect increased structural instability or altered repair dynamics. CpG sites did not exhibit a similar statistically significant elevation in VNE, suggesting that CpG methylation-associated mutability may not be directly linked to the quantum entanglement properties captured by our closed model. These results are a computational demonstration of a potential quantum mechanical contribution to genomic instability in TP53. This indicates further work on expanding the conceptual framework of cancer mutagenesis to include biophysical determinants may be warranted. We note this analysis is limited by the small number of validated hot spots (n=6) and the lack of biological validation, and the findings should be interpreted cautiously pending larger-scale validation. Such validation could include additional genes and biophysical measurements. We urge further interdisciplinary approaches between quantum physics and molecular oncology to explore new ways to understand mutation patterns, improve hot spot prediction, and inform future diagnostic or therapeutic strategies targeting genome stability.



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sciforum-170881: Risk-Stratified Benefit of Adjuvant Chemotherapy After First-Line Neoadjuvant Chemotherapy in Gastric Cancer: IPTW and RMST Analyses Guided by an ML Risk Score

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Background

The benefit of postoperative adjuvant chemotherapy (ACT) after first-line neoadjuvant chemotherapy (NACT) in gastric cancer (GC) is inconsistent in real-world practice. A practical risk tool is needed to identify patients most likely to benefit and to avoid overtreatment.

Methods

Patients from a four-center retrospective cohort (training $n=725$; validation-1 $n=149$; validation-2 $n=276$) were stratified using the GAM-derived risk score with a pre-specified threshold: 3-year predicted disease progression probability of 30% (high-risk vs low-risk). DFS separation between strata was assessed by Kaplan–Meier analysis in all cohorts. To evaluate ACT benefit while mitigating selection bias, inverse probability of treatment weighting (IPTW) was applied to balance baseline characteristics between ACT and non-ACT groups. Within each risk stratum, DFS was compared pre- and post-weighting. Clinical benefit was further quantified by 3-year Δ RMST (restricted mean survival time gain) and Δ Risk (absolute recurrence-risk reduction).

Results

Risk stratification consistently separated DFS, with significantly worse DFS in high-risk patients across training and both validation cohorts. After IPTW, covariates achieved good balance and overlap between ACT and non-ACT groups. A significant interaction between risk strata and ACT was observed: in the high-risk group, ACT was associated with significantly superior DFS across all cohorts; in the low-risk group, DFS did not differ significantly between ACT and non-ACT. High-risk absolute benefit was substantial: training cohort Δ RMST ~5 months and Δ Risk –14%; validation-1 Δ RMST 7 months and Δ Risk –20%; validation-2 Δ RMST 6 months and Δ Risk –20%. In low-risk patients, 95% CIs for both Δ RMST and Δ Risk crossed the null across cohorts.

Conclusions

An ML-guided risk score can identify GC patients who meaningfully benefit from ACT after first-line NACT, while supporting omission of chemotherapy in low-risk patients.



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sciforum-166356: Smart nanocarriers encapsulating chemotherapeutic agents

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Introduction

Water insolubility and poor biodistribution of various anticancer molecules limit their therapeutic efficacy. Formulation of these molecules into pH and temperature-responsive nanocarriers is a crucial step in the development of effective and innovative chemotherapies.

Methods

Herein, the formulation of polymeric nanocarriers via the co-solvent protocol is reported. For this reason, poly(2-(diisopropylamino)ethyl methacrylate-co-2-(dimethylamino)ethyl methacrylate-co-oligoethylene glycol methyl ether methacrylate), P(DIPAEMA-co-DMAEMA-co-OEGMA) terpolymers were utilized for the encapsulation of the anticancer molecules curcumin, quercetin, and methotrexate. The physicochemical and photophysical properties of these nanoplateforms were evaluated over the span of three weeks. Fetal bovine serum (FBS) solution was also added in all colloidal dispersions for the determination of formulation stability in blood simulating conditions.

Results

All synthesized terpolymers responded to external stimuli including pH, temperature, and ionic strength and entrapped efficiently each anticancer molecule, showcasing colloidal stability as indicated by dynamic light scattering (DLS) and ultraviolet-visible absorption spectroscopy (UV-Vis) measurements. Utilization of FBS as a medium revealed limited interaction between proteins and nanoparticles. Furthermore, fluorescence spectroscopy studies in curcumin and quercetin nanoformulations present enhanced emission intensity due to the aggregation-induced emission phenomenon.

Conclusions

Smart nanocarriers were fabricated via a cost-effective and scalable method. Such nanoplateforms can offer a promising approach in cancer treatment as they can respond to external stimuli triggered by cancer tissue conditions.



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sciforum-171695: The correlation between estrogen level and microbial interaction in breast cancer

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Background

Breast cancer incidence and mortality have increased globally over recent decades. Estrogen plays a pivotal role in breast cancer development, and growing evidence suggests that gut microbiota, particularly *Lactobacillus* species, may influence estrogen metabolism through modulation of enterohepatic circulation. Understanding this interaction may provide insights into disease mechanisms and potential biomarkers. However, the relationship between circulating estrogen levels, gut microbiota, and breast cancer remains unclear and insufficiently characterized.

Methods

A case-control cross-sectional study was conducted on 180 women, including 90 patients with non-metastatic breast cancer and 90 healthy controls. Clinical and anthropometric data were collected using standardized procedures. Serum estrogen levels were measured using enzyme-linked immunosorbent assay (ELISA), and stool samples were analyzed for *Lactobacillus* isolation and identification using conventional microbiological methods. Statistical analyses evaluated differences in estrogen levels between groups and their association with *Lactobacillus* species.

Results

Serum estrogen levels were significantly lower in breast cancer patients compared to healthy controls. Receiver operating characteristic (ROC) analysis demonstrated high discriminatory performance of estrogen levels in distinguishing patients from controls. However, no significant association was identified between specific *Lactobacillus* species and circulating estrogen levels.

Conclusion

Circulating estrogen levels are altered in non-metastatic breast cancer and may serve as a complementary biomarker for disease characterization. The lack of association with individual *Lactobacillus* species underscores the complexity of the gut microbiota-estrogen-breast cancer axis, warranting further mechanistic studies and larger, well-designed investigations.



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sciforum-170880: Time-Dependent SHAP Interpretation of a Multicenter ML DFS Model After Neoadjuvant Chemotherapy in Gastric Cancer

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Background

Interpretability is critical for the clinical adoption of ML prognostic models, especially when models are used to communicate recurrence risk after neoadjuvant chemotherapy (NACT) in gastric cancer (GC).

Methods

Using the finalized GAM model developed from a four-center cohort (training n=725; external validation cohorts n=149 and n=276), we performed SHAP-based interpretation to quantify feature contributions and directionality. Time-dependent feature importance was ranked by Brier score loss, and SHAP summary plots were used to visualize how predictor values shift individual risk estimates over follow-up.

Results

Time-dependent SHAP identified lymph node ratio, ypT stage, and Bormann classification as the top three contributors to predictive performance, remaining highly influential throughout the follow-up period. Higher lymph node ratio and advanced ypT were consistently associated with higher predicted recurrence risk. For categorical variables, the presence of nerve invasion, lymphovascular tumor thrombus, and a signet-ring cell component shifted predictions toward worse DFS. In addition, advanced Bormann type (III/IV) and diffuse tumor involvement (tumor site characteristic) were associated with increased risk compared with less aggressive or more localized patterns. These explanations provide an intuitive mapping between postoperative pathology/aggressiveness features and individualized risk predictions, facilitating clinician trust and patient-facing communication.

Conclusions

Time-dependent SHAP yields clinically transparent explanations of an externally validated ML model and highlights lymph node ratio, ypT, and Bormann type as dominant drivers of DFS risk after first-line NACT for GC.



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sciforum-171817: Validation and Clinical Translation of Non-Invasive Imaging Biomarkers for the Classification of Gliomas

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Background: Diffuse gliomas, the most common adult primary brain tumour, are classified by their histological, genetic, and molecular characteristics. Isocitrate dehydrogenase (IDH) mutant gliomas correlate with longer mean survival and progression-free survival time. In tumour cells, IDH mutations lead to metabolic changes and the production of oncometabolite 2-hydroxyglutarate (2HG). 2HG can be measured with MR spectroscopy (MRS) *in vivo* and non-invasively, and is one of the first binary and specific imaging biomarkers. In this study, we validate advanced MRS methods as IDH-mutation imaging biomarkers in the clinic and address the necessary steps to translate them into a clinical standard of care.

Methods: MRS techniques were evaluated and validated, according to the Imaging Biomarker Roadmap for Cancer Studies (O'Connor et al. 2016), using simulations, novel and specific glioma phantoms, and healthy volunteers. PRESS, sLASER, and MEGA-PRESS sequences were tested after being optimised for 2HG measurement (2.25 ppm peaks for PRESS and sLASER and a 4.02 ppm peak for MEGA-PRESS). A clinical study is currently being carried out to validate the optimised sequences; 4 patients with suspected gliomas have participated thus far.

Results: Simulations of MRS sequences allowed for optimised acquisition of parameters for the measurement of 2HG, while purpose-built tumour-mimicking phantom experiments allowed for the sensitivity, specificity, and reproducibility of the different methods. Further synthetic MRS measurements using combinations of tumour simulations/phantoms determined the optimal noise and SNR ranges. In the early stages of the clinical study, MEGA-PRESS successfully predicted IDH mutation status in all 4 patients. Other important genetic markers were also successfully predicted in all four patients.

Conclusions: MEGA-PRESS proved to be the most robust MRS method and demonstrated accurate and precise measurement of phantom and synthetic 2HG with acceptable SNR. MEGA-PRESS has proven thus far in a small subset of glioma patients to accurately predict their important genetic markers for tumour classification



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