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The 4th International Electronic Conference on Cancers

06–08 March 2024 | Online

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The 4th International Electronic Conference on Cancers

The 4th International Electronic Conference on Cancers

6–8 March 2024 | Online

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Welcome from the Chairs

Dear Colleagues,

It is a great pleasure to welcome you to the 4th International Electronic Conference on Cancers (IECC 2024), which will be held from 6 to 8 March 2024. The conference is organized by the MDPI open-access journal Cancers (Impact Factor 5.2). It allows scientists from all over the world to present their latest research in Cancers, receive direct feedback, and engage in discussions with the wider scientific community.

In recent years, we have witnessed remarkable breakthroughs in basic cancer research, where discoveries in the genetic and epigenetic tumor make-up and tumor microenvironment have provided valuable insights into the molecular mechanisms underlying cancer initiation, progression, and therapeutic response. This newfound knowledge has laid the groundwork for novel treatment strategies and personalized approaches that hold the potential to revolutionize cancer care. This conference aspires to bring together clinicians and scientists with diverse expertise and perspectives in cancer research to interact, exchange ideas, and form new collaborations that may lead to new advancements in scientific understanding and ultimately impact patient outcomes.

This year's conference is dedicated to following sessions:

Session A. Brain Metastases
Session B. Cancer Biomarkers
Session C. Cancer Immunology and Immunotherapy
Session D. Tumor Microenvironment
Session E. Molecular Cancer Biology
Session F. Cancer Epidemiology and Prevention
Session G. Cancer Therapy
Session H. Cancer Pathophysiology

The IECC 2024 will be an online-only proceeding, which allows participation from all over the world with no requirement for travel or related expenditures. An electronic conference provides a platform for rapid and direct exchanges about the latest research findings and novel ideas.

We are committed to equality and inclusion principles. Therefore, we ask authors to ensure that the papers and presentations are highly accessible to the wider and more diverse scientific community. We encourage submissions from scientists at all career stages and backgrounds and aim for an equal gender balance.

The conference will provide 6 awards including **Best Oral Presentation Award** and **Best Poster Award**.

We look forward to receiving your contributions to this scientific event and would like to thank you in advance for your active support.

We hope that the community will share this enthusiasm and help make this conference a success.

Prof. Dr. Angeliki Magklara
Conference Chair

Dr. Shinji Kawabata
Conference Chair

Prof. Vasso Apostolopoulos
Conference Chair

Prof. Dr. Alfredo Conti
Conference Chair

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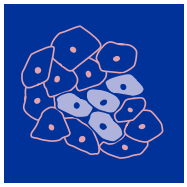


cancers

an Open Access Journal by MDPI

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.

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

Keynote Speakers

Prof. Magdalena Plebanski
School of Health and Biomedical Sciences, RMIT University, Melbourne, Australia

Prof. Kulmira Nurgali
Institute for Health and Sport, Victoria University, Melbourne, Australia

Invited Speakers

Dr. Michela Croce
IRCCS Ospedale Policlinico San Martino, Genova, Italy

Dr. Giovanni Nassa
Department of Medicine, Surgery and Dentistry "Scuola Medica Salernitana", University of Salerno, Baronissi (Salerno), Italy

Dr. Bruno Simoes
Breast Biology Group, Manchester Breast Centre, Division of Cancer Sciences, Faculty of Biology, Medicine and Health, University of Manchester, United Kingdom

Dr. Annamaria Gullà
Candiolo Cancer Institute-IRCCS-FPO, Italy

Dr. Giuseppina Augimeri
Department of Pharmacy, Health and Nutritional Sciences, University of Calabria, Italy

Dr. Zachary R Hunter
Bing Center for Waldenström Macroglobulinemia, Dana Farber Cancer Institute, USA
Department of Medicine, Harvard Medical School, USA

Dr. Marilena V Iorio
Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy

Professor Banafshé Larijani
Centre for Therapeutic Innovation, Cell Biophysics Laboratory, Faculty of Science, University of Bath, UK

Professor Rajamaran Eri
Associate Dean, School of Science/STEM RMIT University, Australia

Professor John Trant
Department of Chemistry and Biochemistry University of Windsor, Canada

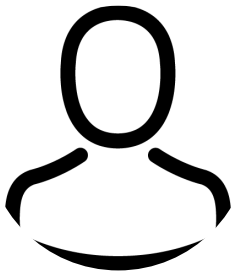
Professor Andreas Tzakos
Department of Chemistry University of Ioannina, Greece

Assoc. Prof. George Alexiou
Department of Neurosurgery University of Ioannina, Greece

Prof. Dr. Vivek Chavda
L.M. College of Pharmacy, India

Dr. Schleiermacher Gudrun
Recherche Translationelle en Oncologie Pédiatrique (RTOP), INSERM U830 Cancer, Heterogeneity, Instability and Plasticity, Department of Translational Research, Institut Curie Research Center, PSL Research University, France, SIREDO Integrated Pediatric Oncology Center, Institut Curie Hospital Group, France

Professor Ramin Massoumi
Department of Laboratory Medicine, Translational Cancer Research, Faculty of Medicine, Lund University, Sweden



Dr. Cirino Botta
Hematology Unit, Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties (PROMISE), University of Palermo, Palermo, Italy

Program at a Glance

The 4th International Electronic Conference on Cancers
6–8 Mar 2024, Online

	6 March 2024 (Wednesday)	7 March 2024 (Thursday)	8 March 2024 (Friday)
Morning	Session G. Cancer Therapy	Session C. Cancer Immunology and Immunotherapy	Poster Session
	Break	Break	Break
Afternoon	Session H. Cancer Pathophysiology	Session B. Cancer Biomarkers	Session D. Tumor Microenvironment Session E. Molecular Cancer Biology Session F. Cancer Epidemiology and Prevention

IECC 2024 Program

6 March 2024 (Wednesday)
Session G. Cancer Therapy

CET (Central European Time - UTC+1)	CST Asia (China Standard Time - UTC+8)	Speaker	Title
9:00–9:15	16:00–16:15	Welcome from the conference chairs - **Dr. Shinji Kawabata** and **Dr. Ulrich Preffer**	
9:15–9:35	16:15–16:35	Invited Speaker **Michela Croce**	Epigenetic drugs to improve efficacy of immune checkpoint blocker therapy
9:15–9:35	16:15–16:35	Invited Speaker **Giovanni Nassa**	Targeting chromatin remodelers to overcome endocrine therapy resistance in breast cancer
9:15–9:35	16:15–16:35	Break	
10:05–10:20	17:05–17:20	Selected Speaker **Yoshiki Fujikawa**	Exploring BNCT as a Novel Approach for Metastatic Spinal Tumor Management
10:20–10:35	17:20–17:35	Selected Speaker **Yantao Tian**	Impact of Removal of Lymph Nodes on Survival in Stage I-III Gastric Signet-ring Cell Cancer: The More, the Better?
10:35–10:50	17:35–17:50	Selected Speaker **Kohei Tsujino**	Evaluation of the safety of folate receptor-targeted boron carrier in boron neutron capture therapy (BNCT) for malignant gliomas using CED administration

6 March 2024 (Wednesday)
Session H. Cancer Pathophysiology

CET (Central European Time - UTC+1)	CST Asia (China Standard Time - UTC+8)	Speaker	Title
15:00–15:10	22:00–22:10	Welcome from session chairs - **Dr. Nicola Amodio** and **Prof. Giuseppe Viglietto**	
15:10–15:30	22:10–22:30	Invited Speaker **Annamaria Gullà**	Dissecting the path to immunogenic chemotherapy in multiple myeloma
15:30–15:50	22:30–22:50	Invited Speaker **Bruno Simoes**	Targeting cancer stem cells in hormone-resistant breast cancer
15:50–16:10	22:50–23:10	Invited Speaker **Giuseppina Augimeri**	A hybrid cell population generated through engulfment of mesenchymal stem cell by breast cancer cells enhances chemoresistance and metastasis
16:10–16:20	23:10–23:20	Break	
16:20–16:40	23:20–23:40	Invited Speaker **Marilena V Iorio**	ncRNA deregulation as a flag of drug resistance in HER2-positive breast cancer
16:40–17:00	23:40–00:00	Invited Speaker **Cirino Botta**	The Dynamic myeloma microenvironment: implications for cancer evolution and therapy resistance
17:00–17:20	00:00–00:20	Invited Speaker **Zachary R. Hunter**	Multi-omic Analysis of Clonal Evolution and the Subtypes of Waldenstrom's Macroglobulinemia

CET (Central European Time - UTC+1)	CST Asia (China Standard Time - UTC+8)	Speaker	Title
17:20–17:35	00:20–00:35	Selected Speaker **Valentina Serratore**	Deciphering the role of USP16 in lung cancer

7 March 2024 (Thursday)
Session C. Cancer Immunology and Immunotherapy

CET (Central European Time - UTC+1)	CST Asia (China Standard Time - UTC+8)	Speaker	Title
8:00–8:05	14:00–14:05	Welcome from session chairs - **Prof. Dr. Vasso Apostolopoulos**	
8:05–8:25	14:05–14:25	Keynote Speaker **Magdalena Plebanski**	Personalised immunotherapy and earlier diagnosis in ovarian cancer
8:25–8:40	14:25–14:40	Invited Speaker **John Trant**	Cancer Immunotherapy three ways
8:40–8:55	14:40–14:55	Invited Speaker **Rajamaran Eri**	Role of NLRP3 Inflammasome Colitis-Associated Colorectal Cancer
8:55–9:05	14:55–15:05	Break	
9:05–9:20	15:05–15:20	Invited Speaker **Andreas Tzakos**	Targeting Gliomas
9:25–9:35	15:25–15:35	Invited Speaker **George Alexiou**	New Theragnostic Agent Against Glioma Based on Gemcitabine
9:35–9:50	15:35–15:50	Invited Speaker **Vivek Chavda**	CAR T-Cell therapy for the management of mantle cell lymphoma
9:50–10:05	15:50–16:05	Selected Speaker **Ramya Ephraim**	Differential Gene Expression of Checkpoint Markers and Cancer Markers in Mouse Models of Spontaneous Chronic Colitis
10:05–10:20	16:05–16:20	Selected Speaker **Nyanbol Kuol**	Cholinergic signaling influences the expression of immune checkpoint inhibitors, PD-L1 and PD-L2, and tumor hallmarks in human colorectal cancer tissues and cell lines

7 March 2024 (Thursday)
Session B. Cancer Biomarkers

CET (Central European Time - UTC+1)	CST Asia (China Standard Time - UTC+8)	Speaker	Title
15:00–15:10	22:00–22:10	Welcome from session chairs - **Prof. Dr. Mario Capasso**	
15:05–15:25	22:05–22:25	Invited Speaker **Ramin Massoumi**	Unlocking the Future of Lung Cancer Treatment: Biomarkers and Preclinical Insights
15:25–15:40	22:25–22:40	Selected Speaker **Ella Markalunas**	Correlational Analysis of Genetic Mutations and Galectin Levels in Breast Cancer Patients
15:40–15:55	22:40–22:55	Selected Speaker **Alejandro Cepero**	Predictive Value of FDG PET Radiomics for Early Response to Chemoradiation in Locally Advanced Cervical Cancer
15:55–16:05	22:55–23:05	Break	
16:05–16:20	23:05–23:20	Invited Speaker **Schleiermacher Gudrun**	
16:20–16:40	23:20–23:40	Invited Speaker **Banafshé Larijani**	The Fusion of Quantitative Molecular Proteomics and Immune-Oncology: A Step towards Precision Medicine in Cancer Therapeutic

8 March 2024 (Friday)
Poster Session

CET (Central European Time - UTC+1)	CST Asia (China Standard Time - UTC+8)	Speaker	Title
9:00–9:05	16:00–16:05	Welcome from the conference chairs	
9:05–11:05	16:05–18:05	Poster Session	The Poster Sessions will take place in Zoom break-out rooms. The list of names and titles are the posters can be found here.

8 March 2024 (Friday)
Session D. Tumor Microenvironment
Session E. Molecular Cancer Biology
Session F. Cancer Epidemiology and Prevention

CET (Central European Time - UTC+1)	CST Asia (China Standard Time - UTC+8)	Speaker	Title
15:00–15:05	22:00–22:05	Welcome from session chairs - **Prof. Dr. Robert-Alain Toillon**	
15:05–15:25	22:05–22:25	Invited Speaker **Prof. Dr. Robert-Alain Toillon**	Microenvironment and Breast Cancer
15:25–15:40	22:25–22:40	Selected Speaker **Kamila Wolnica**	Infrared Molecular Responce of Craniofacial Squamous Cell Carcinoma—Pilot Study
15:40–15:55	22:40–22:55	Selected Speaker **Vincenzo Aievola**	Noncoding Regulatory Mutations as a Driving Event for the Oncogenic Core Regulatory Circuitries of Neuroblastoma
15:55–16:10	22:55–23:10	Selected Speaker **Teresa Maiorino**	Post-GWAS Functional Analysis of the 11p11.2 Risk Locus Identifies *HSD17B12* as a Neuroblastoma Susceptibility Gene Involved in Lipid Metabolism
16:10–16:25	23:10–23:25	Selected Speaker **Maciej Maciejczyk**	Polycyclic Aromatic Hydrocarbons (PAHs) in Grilled Marshmallows

Poster List

Poster Session	
Name	**Title**
Binson V A	Unveiling the Smell of Health: E-Nose-Based Volatile Organic Compound Analysis of Exhaled Breath in Early Lung Cancer Detection
Kritika Chugh	Hidden Gems in the Genome: Pseudogenes Unleashing Revolution in Hepatocellular Carcinoma Detection and Therapy
Rohan Kaushikan	Predictive Modeling and Mutational Biomarker Identification for Invasive Ductal Carcinoma Recurrence using Machine Learning
Honghong Zheng	Application of a Preoperative Nomogram Based on the Gastric Cancer Integrated Oxidative Stress Score in Predicting Overall Survival and Chemotherapy Benefits in Gastric Cancer Patients
Devendra Kumar Mishra	Metabolic Strategies of Treg Cells in the Tumor Microenvironment: Implications for Immune Metabolism-Based Precision Medicine
Nada Akouh	A report of a rare case of a sinonasal mucosal melanoma not expressing PS100 initially diagnosed as plasmocytoma
Liana Lachinani	Two novel miRNAs encoded by oncogene MSI1
Maria Victoria Niklison-Chirou	Suppression of Medulloblastoma Cell Migration by clinically Significant Doses of Simvastatin through Mevalonate Pathway Targeting
Daoudi Chaimae	Desmoplastic fibroma of the mandible: case report
Muna Ali Mugibel	Cancer Distribution Among Patients Registered at Hadhramout National Oncology Center During 2015–2020
Tinashe Adrian Mazhindu	Pulmonary tuberculosis: A comorbidity or misdiagnosis of primary lung cancer in Africa?
Yogeshwaran M	Synthesis and Preliminary Investigation of Metal Nanoparticles from the Stem Extract of *Bacopa* sp. for the Treatment of Lung Cancer
Deepesh Kumar Verma	Machine Learning Strategies for Drug Discovery in AML: Focus on RUNX1 Bioactivity
Dharshana K	Development of Letrozole-Loaded Magnetic Nanoemulsion Used for Breast Cancer Treatment
Madhumethra R G	Optimization and Development of Magnetically Triggered Letrozole Nanoliposomes for Breast Cancer Targeting
Diana I Salnikova	Development of synergetic combinations of a novel apoptosis inducer with AKT and Hsp90 selective inhibitors targeting hormone-sensitive and hormone-resistant breast cancer cells
Keyan Xie	Comparative Study of Long-Term Efficacy and Safety of neoadjuvant chemotherapy before radical surgery versus concurrent chemoradiotherapy for FIGO 2018 stage IB3/IIA2 cervical squamous cell carcinoma: a propensity score-matched analysis
Tong Chen	
HongXin Huang	Hippocampus-sparing volume-modulated arc therapy (HS VMAT) for patients with World Health Organization grade II gliomas: a feasibility study
Charles Nnadi	Cancer Stem Cells as Potential Targets of Phytotoxic Alkaloids: Drug-likeness Prediction and Molecular Docking Studies
Tahreem Arshad Butt	The role of Exostosin Glycosyltransferase 1 (EXT1) in ovarian cancer
Mohammed El Magroud	A Bone Marrow Biopsy Revealing an Exceptional Complication of Multiple Myeloma
Salvatore Audia	Atypical immunogenetic and molecular characteristics of a 15-Years-Old male affected by ETP-ALL (Early T-precursor acute lymphoblastic leukemia)

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About Us

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Abstracts

Session B. Cancer Biomarkers

sciforum-084940: Hidden Gems in the Genome: Pseudogenes Unleashing Revolution in Hepatocellular Carcinoma Detection and Therapy

Kritika Chugh

University of Texas at Dallas

Hepatocellular Carcinoma (HCC), a formidable global health challenge, continues to claim numerous lives due to its asymptomatic nature in the early stages and limited treatment options. In this ever-evolving landscape of cancer research, pseudogenes, once relegated to the genetic sidelines as 'non-functional', have emerged as intriguing players. Contrary to their historical dismissal, pseudogenes are now recognized for their intricate roles in modulating gene expression and contributing to the complex molecular milieu of cancer. This comprehensive review delves into the uncharted territory of pseudogenes and their potential to revolutionize HCC detection and treatment. From deciphering the molecular connections between pseudogenes and HCC to exploring their utility as diagnostic biomarkers, prognostic indicators, and therapeutic targets, this article aims to solvethe enigma of pseudogenes in hepatocellular carcinoma.

sciforum-085377: Predictive Modeling and Mutational Biomarker Identification for Invasive Ductal Carcinoma Recurrence using Machine Learning

Rohan Kaushikan

Menlo-Atherton High School, 555 Middlefield Road, Atherton, CA 94027, USA

Invasive Ductal Carcinoma (IDC) constitutes approximately 80% of breast cancer cases. After treatment, there is a 3–15% chance that IDC will recur. The aim of this study was to accurately predict IDC recurrence with a low false negative rate and to identify mutated genes associated with IDC recurrence. We hypothesize that IDC recurrence can be predicted using genomic, clinical, and phenotypic patient data and that certain genes, when mutated, are highly influential in the recurrence of IDC. To attain an understanding for the underlying causes of IDC recurrence, genomic data such as gene expression and mutation variant, in addition to clinical and phenotypic data, were aggregated. An XGBoost framework was utilized for the classification task of predicting a patient's status as disease free or cancer recurrent. The XGBoost framework and the XGBClassifier algorithm employ sequential learning and an ensemble of weaker learning models such as individual decision trees, both of which allow for continuous correction of errors made by previous models and identification of complex relationships between features. The XGBClassifier algorithm predicted IDC recurrence with over 99% accuracy and 0% false negative rate across nearly 2200 IDC patient samples, approximately half of which were recurrent cases. These results were obtained after model fine tuning upon examination of generated ROC Curves, Precision-Recall Curves, and Confusion Matrices. Feature importance scores, in this case representing the significance of mutated genes in IDC recurrence, were calculated by the XGBoost model for the 40 most commonly mutated genes among IDC patients. GATA3, CDH1, and BRCA1 genes were given the highest feature importance scores despite relatively low mutation occurrences, indicating that our model did not simply associate gene importance with mutation frequency. Our results prompt further inspection both of genes given high importance scores with low occurrences and of genes given low importance scores with high occurrences using ontological tools. The feature importance scores can aid in biomarker identification, cancer diagnoses, and drug development. Our study can be generalized to other cancers to determine common biomarkers and deepen understanding of general cancer recurrence.

sciforum-084394: A Modified Systemic Prognostic Score Based on Oxidative Stress and Immunoinflammatory Indicators: A Novel Tool for Predicting Gastric Cancer Outcomes—A Multicenter Study

Honghong Zheng and Lingkang Zhang

Fujian Medical University Union Hospital

Background

Oxidative stress and immunoinflammation are two important areas in the field of cancer research. At present, no studies have confirmed that both can accurately predict the progression and long-term prognosis of gastric cancer (GC).

Methods

In this study, univariate and multivariate Cox proportional hazards regression analyses were used to analyze oxidative stress and immunoinflammatory indicators in the training set, and the best biomarkers for the establishment of an improved systemic prognosis score (mSPS) were screened. The Area Under the Curve (AUC) and Concordance Index (C-index) were used to evaluate the predictive ability of our model for long-term efficacy. Kaplan–Meier (K-M) survival analysis was conducted to assess survival outcomes. Univariate and multivariate Cox proportional hazards regression analyses were performed to investigate the impact of the model on tumor progression, lymph node metastasis, and overall prognosis. These findings were subsequently validated using both internal and external validation sets.

Results

A total of 3788 GC patients were included in this study, including 2339 in the training set, 1003 in the internal validation set, and 446 in the external validation set. The Receiver Operating Characteristic (ROC) curve analysis revealed that the AUC for mSPS in predicting overall survival (OS) among GC patients significantly surpassed that of all other markers related to oxidative stress and immunoinflammatory indicators ($p < 0.001$). Compared to the low mSPS group, patients in the high mSPS group were predominantly male and were more likely to be aged over 65, exhibit a higher BMI, possess a higher ASA grade, display a greater prevalence of vasculature and neuroinfiltration, exhibit deeper tumor invasion, have a higher incidence of lymph node metastasis, be diagnosed at a more advanced tumor stage (Stage III), and receive a higher proportion of chemotherapy ($p < 0.05$). Logistic regression analysis demonstrated that elevated mSPS was an independent risk factor for tumor invasion and lymph node metastasis in patients with GC. COX regression analysis further indicated that high mSPS independently contributed to a poorer prognosis among GC patients. The association between mSPS and pathological stage, as well as long-term prognosis, was validated through both internal and external sets, using the same cut-off value. The results aligned consistently with the training set effect.

Conclusions

As a newly developed prognostic score based on oxidative stress and immunoinflammatory indicators, mSPS can independently and effectively predict the tumor burden of advanced gastric cancer, and further distinguish the long-term prognosis of GC patients based on a pTNM staging system.

sciforum-084277: Application of a Preoperative Nomogram Based on the Gastric Cancer Integrated Oxidative Stress Score in Predicting Overall Survival and Chemotherapy Benefits in Gastric Cancer Patients

Honghong Zheng and Lingkang Zhang

Fujian Medical University Union Hospital

Background

Oxidative stress in blood is associated with gastric cancer (GC) prognosis, but the predictive value of an integrated oxidative stress score comprising multiple indicators remains uncertain.

Methods

Between 2009 and 2017, clinicopathological data from GC patients were split 7:3 for developing and validation cohorts. Using COX proportional hazards regression, we analyzed oxidative stress indicators to construct a Gastric Cancer Integrated Oxidative Stress Score (GIOSS). GIOSS and other indicators were evaluated for overall survival (OS) prediction using the AUC and C-index. Kaplan–Meier analysis assessed 5-year OS in high/low GIOSS groups, stratified by pTNM stage. A Cox proportional hazards regression model identified preoperative factors influencing OS, leading to a preoperative nomogram (preope-Nomogram). The model accuracy was assessed via the ROC, calibration curve, and decision curve analysis (DCA), validated in the validation cohort. The Kaplan–Meier analysis and log-rank tests compared survival among risk groups.

Results

The study included 3498 patients. GIOSS in the training cohort outperformed any single indicator in predicting 5-year OS (AUC = 0.605; C-index = 0.590). Low GIOSS values were associated with better 5-year survival, applicable across different pTNM stages (p0.05). The preope-Nomogram, incorporating GIOSS, age, cT, and cN, aligned with the pTNM stage. The ROC, calibration curve, and DCA all demonstrated the model's excellent performance, consistent across validation and training cohorts. High GIOSS patients in pTNM II (p = 0.010) and III (p0.001) showed higher 5-year OS with adjuvant chemotherapy.

Conclusions

High GIOSS independently predicts 5-year OS in GC patients after surgery. The preope-Nomogram distinguishes patient prognosis in different pTNM stages and successfully identifies high-risk patients who would benefit from adjuvant chemotherapy.

sciforum-085041: 5Correlational Analysis of Genetic Mutations and Galectin Levels in Breast Cancer Patients

Ella Markalunas [1], Avery Funkhouser [2], David Arnold [2], Julie Martin [3], Michael Shtutman [4], William Jeffery Edenfield [3] and Anna Blenda [2,3]

[1] Brown University
[2] University of South Carolina School of Medicine—Greenville
[3] Prisma Health Cancer Institute
[4] University of South Carolina College of Pharmacy

Background

Galectins are immune system regulators, associated with disease progression in cancer. This research aims to investigate the correlation between mutated cancer-critical genes and galectin levels in breast cancer patients to determine whether galectins and genetic profiles can be used as biomarkers for disease and potential therapy targets.

Materials and Methodology

Prisma Health Cancer Institute's Biorepository provided sixty-five breast cancer patient samples, including all four stages as well as major molecular subtypes of breast cancer. Hotspot mutation statuses of cancer-critical genes were determined using multiplex PCR in tumor samples from the same patients.

The galectin levels of patients' sera were analyzed using an enzyme-linked immunosorbent assay (ELISA) to measure the concentrations of galectins-1, -3, and -9. Two-sample *t*-tests ($\alpha = 0.05$) were performed using JMP software.

Results

Our analysis indicates that KIT mutations correlate with elevated levels of galectin-1 and -9, while TP53 mutations correlate with elevated galectin-3 levels. In patients with the Luminal A subtype, FLT3 mutation is correlated with lower galectin-1 and -9 levels, TP53 mutations correlate to higher galectin-3 levels, and MET mutations correlate to higher galectin-9 levels. Patients with Invasive Ductal Carcinoma had significantly higher levels of galectin-3 than patients with Ductal Carcinoma in Situ.

Patients with both TP53 and KIT mutations exhibit elevated galectin-3 levels, while patients with one or neither mutation show no significant differences in galectin-3 levels. Similar trends were observed for patients with both TP53 and PIK3CA mutations compared to those with one or neither mutation.

In addition, metastatic breast cancer samples were more likely to have KIT or PIK3CA mutation compared to primary breast cancer samples.

Conclusions

The relationship between genetic mutations and galectin levels will potentially identify appropriate candidates for combined therapy which targets genetic mutations and galectins, aiding the search for biomarkers used for breast cancer diagnosis, disease progression, and prognosis.

sciforum-082395: Effects of Tumor Marker Regression Load Score on Long-Term Prognosis of Gastric Cancer Patients Undergoing Radical Surgery after Neoadjuvant Chemotherapy

Ling-Kang Zhang

Department of Gastric Surgery, Fujian Medical University Union Hospital, Fuzhou 35001, China

Background

Serum tumor markers have been shown to correlate with the prognosis of gastric cancer (GC); however, the effects of the dynamics of serum tumor markers (cancer antigen (CA)72-4, carcinoembryonic antigen (CEA), CA19-9, CA125, and alpha-fetoprotein (AFP)) on the prognosis of GC before and after neoadjuvant chemotherapy (NACT) remain unclear.

Methods

Data from 334 patients with **GC** who underwent NACT followed by radical gastrectomy between January 2016 and December 2021 were included in the present study. Tumor marker regression load (ΔTMRL) indicator, including ΔCA72-4, ΔCEA, ΔCA19-9, ΔCA125, and ΔAFP, is defined as [(postNACT marker − preNACT marker)/preNACT marker]. Based on the results of Cox regression analysis, the tumor marker regression load score (TMRLS) was composed of ΔCA72-4, ΔCEA, and ΔCA125. The predictive performance of the nomogram-TMRLS was evaluated using the area under the receiver operating characteristic (ROC) curve (AUC), decision curve analysis (DCA), and C-index.

Results

The patients were divided into two groups, TMRLS-low and TMRLS-high, based on the optimal breakpoint of TMRLS determined in R using the maxstat package. Survival analysis revealed a higher 3-year overall survival (OS) in the TMRLS-low than in the TMRLS-high group (69.8% vs. 34.8%, respectively; $p = 0.001$). Those in the TMRLS-high group who received postoperative adjuvant chemotherapy (AC) showed a significantly higher 3-year OS rate than those who did not (52.3% vs. 8.3%, respectively; $p = 0.020$). Multivariate Coxregression analysis indicated that TMRLS was an independent prognostic factor for OS. A nomogram for predicting OS based on TMRLS, ypT stage, ypN stage, and AC showed a significantly higher C-index and AUC than the traditional ypTNM stage (C-index, 0.794 vs. 0.697, respectively; $p = 0.001$; AUC, 0.827 vs. 0.678, respectively; $p = 0.001$).

Conclusions

TMRLS appears to be a novel independent prognostic factor for patients with GC who underwent NACT and a radical gastrectomy. Furthermore, the TMRLS-high group, who received postoperative AC, achieved better survival outcomes. Of note, the predictive performance of the nomogram-TMRLS significantly outperformed that of the ypTNM stage.

sciforum-083986: Predictive Value of FDG PET Radiomics for Early Response to Chemoradiation in Locally Advanced Cervical Cancer

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Purpose

FDG-PET is often used in the assessment, treatment planning, and monitoring of locally advanced cervical cancer (LACC), contributing to improved patient care and management. The aim of this study is to examine the utility of FDG-PET radiomics in discriminating between patients with LACC who demonstrated an early response to treatment and those who did not.

Methods

The study uses FDG-PET scans of 21 patients obtained from The Cancer Imaging Archive (TCIA) Cervical Cancer Tumor Heterogeneity (CCTH) collection. Among the study cohort, 12 patients responded to chemoradiation treatment while the remaining 9 did not. A total of 59 radiomics texture features were extracted from the gross tumor volumes (GTVs). Top radiomics features in terms of differentiating response status were selected using sequential feature selection (SFS) algorithm. The top two features were used to build a support vector machine (SVM) predictive classifier, with performance assessed by a receiver operating characteristic (ROC) curve analysis.

Results

The top two radiomics features being selected consisted of the gray level co-occurrence matrix (GLCOM)-based cluster prominence and gray level run length matrix (GLRLM)-based length nonuniformity. The SVM predictive classifier built using the top two features had an area under the ROC curve (AUC) of 0.88, showing strong discriminative power between responders and non-responders.

Conclusions

The radiomic features extracted from FDG-PET scans showed discriminative ability to discern patients with LACC who would have an early response to treatment. This knowledge could have clinical implications for adjusting treatment strategies for patients who might not show an early response.

sciforum-085217: 8Role of Oxidative/Nitrosative Stress in the Development and Progression of Clear Cell Renal Cell Carcinoma

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It is believed that oxidative stress plays a role in the development and progression of renal cell carcinoma (RCC). Identifying oxidative and nitrosative modifications in proteins and defining their roles in clear cell RCC (ccRCC) may be helpful in the elaboration of targeted therapeutic approaches to mitigate protein damage. The study aimed to investigate the status of oxidative/nitrosative stress and to explore its role in development and progression. The studied group consisted of 48 newly diagnosed ccRCC and 30 healthy controls. Serum levels of oxidative stress markers, such as advanced oxidation protein products (AOPPs), thiol groups, Amadori products, 3-nitrotyrosine, nitrate/nitrite, malondialdehyde (MDA), 4-hydroxy-2-nonenal, and total antioxidant capacity (TAC), were determined. Additionally, associations between tumor stage assessed according to TNM classification, histological grade, and the effect of the presence of angioinvasion on the level of stress markers were evaluated. The levels of Amadori products, 3-nitrotyrosine, and nitrate/nitrite were elevated, while the levels of thiol groups and TAC decreased in the ccRCC group. The levels of AOPP, Amadori, and 3-nitrotyrosine increased, and thiol group and TAC levels decreased with the increasing clinical stage of the tumour. In the case of the advanced histological assessment of the tumour, we found decreasing levels of thiol groups and increasing levels of MDA. In patients with angioinvasion, nitrate/nitrite and MDA levels were significantly elevated in those without angioinvasion. Moreover, we found weak significant positive correlations of AOPP and MDA with age. Furthermore, the concentration of thiol groups and the TAC were inversely correlated with age. Surprisingly, there was not any correlation between markers of oxidative stress and sex of patients and their body mass index. Oxidative stress increased with the progression of the disease assessed according to the TNM and histological grade. These results demonstrate systemic oxidative stress in ccRCC, suggesting the therapeutic application of antioxidants.

sciforum-085112: Unveiling the Smell of Health: E-Nose-Based Volatile Organic Compound Analysis of Exhaled Breath in Early Lung Cancer Detection

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Lung cancer remains a formidable global health challenge, necessitating the exploration of innovative diagnostic approaches for early detection. This review paper delves into the burgeoning field of exhaled breath analysis using electronic nose (e-nose) technology for the identification of volatile organic compounds (VOCs) as potential biomarkers for lung cancer diagnosis. An electronic nose inspired by the human olfactory system comprises an array of sensors that can detect and differentiate complex odor profiles. This paper elucidates the principles behind e-nose technology and its application in capturing the unique VOC signatures present in exhaled breath, which serve as indicators of underlying physiological conditions. A significant portion of this review is dedicated to elucidating the methodology and advancements in e-nose-based VOC analysis, providing insights into the potential of this non-invasive approach for disease diagnosis. The exploration extends beyond general applications to specifically spotlight the utilization of e-nose technology in the realm of early lung cancer detection. E-nose-based disease diagnosis, and more specifically, lung cancer detection, is discussed in detail, with an emphasis on the recent studies and advancements. The potential of VOC profiling as a reliable and early diagnostic tool for lung cancer is explored, addressing both the promises and challenges associated with this cutting-edge approach. This comprehensive review amalgamates the current state of knowledge in the field, offering a roadmap for future research opportunities and the realization of e-nose technology's promise in revolutionizing lung cancer diagnosis.

Abstracts

Session C. Cancer Immunology and Immunotherapy

sciforum-083130: A Report of a Rare Case of a Sinonasal Mucosal Melanoma Not Expressing PS100 Initially Diagnosed as Plasmocytoma

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Background

Sinonasal mucosal melanoma is a rare and highly aggressive malignant neoplasm with a very unfavorable prognosis. It can exhibit various histological patterns, potentially mimicking other diagnoses. Therefore, complementary immunohistochemical studies are crucial alongside morphological analysis.

We present an unusual case of locally advanced sinonasal melanoma, negative for PS100 and displaying a plasmacytoid morphology with focal aberrant expression of CD138.

A 74-year-old patient experienced epistaxis, decreased visual acuity, and treatment-resistant headaches in August 2022. A brain scan revealed a large tumor in the left nasal fossa. Initial biopsy suggested nasal plasmacytoma based on the presence of disorganized, plasmacytoid cells, CD138 positivity, and PS100 negativity. Radiotherapy was administered, but symptoms worsened. A subsequent scan showed an extensively advanced maxillo-ethmoido-sphenoidal left-sided tissue mass with distant metastases. An initial bone marrow biopsy, cervical adenectomy, and another mass biopsy were performed.

Results

Received tissue fragments appeared brownish-black.

Histologically, the tumor proliferation comprised large, markedly atypical cells arranged in diffuse sheets, with nuclei exhibiting eccentricity, dense or vesicular chromatin, and prominent nucleoli. Melanin pigments were diffusely present in the cytoplasm.

Immunohistochemical analysis revealed diffuse positive staining for two melanocytic markers, HMB45 and MelanA. PS100 was initially very focally positive on the second biopsy, contrasting with its complete negativity in the medullary and nodal areas. CD138 was negative, avoiding confusion with melanin pigments.

Based on these findings, a diagnosis of melanoma was established.

Discussion and Conclusion

Mucosal melanoma constitutes 0.3% to 2% of melanomas. Tumors displaying focally melanin pigments with unique histomorphology pose diagnostic challenges. Key melanocytic markers are PS100, HMB45, and MelanA.

In this case, initial and metastatic biopsies were entirely PS100-negative, except for a weak, focal positivity in the later biopsy. Such immunohistochemical profile variations underscore intratumoral immunophenotypic heterogeneity.

The absence of PS100 expression and focal CD138 expression should not lead to diagnostic errors. A comprehensive panel, including at least two plasmacytic and two melanocytic markers, is mandatory for a conclusive diagnosis.

sciforum-084662: Cancer Immunotherapy Three Ways

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Cancer immunotherapy and immunology increasingly focuses on antibody development; however, there are multiple ways to re-engage the immune system in assisting with clearing cancer. The Trant Lab at the University of Windsor, Canada is working on three complementary methods (both to each other and to the antibody paradigm) to improve cancer immunotherapeutics. These include the preparation of anticancer vaccines based on modified and stabilized carbohydrates; the development of molecules able to modulate the tumour microenvironment to render it less pleasant for tumour cells, and more favourable for healthy tissue looking to resist tumour invasion and metastasis; and the design of new small molecules to stimulate the invariant natural killer T-cell system. Through cross-fertilization, these disparate disruptive projects inform each other to drive innovation in cancer immunotherapy. This presentation will provide an overview of these methods with a focus on recent results, and a discussion on what needs to be considered in these fields to avoid common pitfalls.

sciforum-084666: CAR T-Cell Therapy for the Management of Mantle Cell Lymphoma

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Mantle cell lymphoma (MCL) is a subtype of Non-Hodgkin lymphoma (NHL) of mature B-cells characterized by translocation, which is typically due to excess expression of Cyclin D1. However, with the progress in our knowledge of the causes of MCL and available treatments for MCL, this cancer is still incurable. Age, male gender, rapid advancement, significant nodal involvement, elevated serum lactate dehydrogenase level, and prognostic indications including increased expression of Ki-67 and presence of TP53 mutation, are symbols of poor outcome. Advanced immunotherapy using chimeric antigen receptor (CAR)-T cells is advantageous for patients suffering from B-cell malignancies and MCL. Targeting B-cell antigens on the cell surface is a feasible approach in re-occurring (R/R) MCL because of significant responses obtained in other B-cell cancers. USFDA has approved brexucabtagene autoleucel (Tecartus, KTE-X19), a novel CAR T-cell therapy to be used in patients with MCL who have not responded to previous treatments or have relapsed. The FDA approved this new treatment depending on the outcomes of the ZUMA-2 clinical trial. Serious adverse reactions, moderate anti-tumor activity, allergen withdrawal, antigen escape, limited tumor infiltration, and trafficking are major barriers to successful CAR T-cell therapy. This review is a brief synopsis of the development of CAR T-cell therapy for MCL.

sciforum-084667: Cholinergic Signaling Influences the Expression of Immune Checkpoint Inhibitors, PD-L1 and PD-L2, and Tumor Hallmarks in Human Colorectal Cancer Tissues and Cell Lines

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Background

Cancer cells express immunosuppressive molecules, such as programmed death ligands (PD-L)1 and PD-L2, enabling evasion from the host's immune system. Cancer cells synthesize and secrete acetylcholine (ACh), acting as an autocrine or paracrine hormone to promote their proliferation, differentiation, and migration.

Methods

We correlated the expression of PD-L1, PD-L2, cholinergic muscarinic receptor 3 (M3R), alpha 7 nicotinic receptor (α7nAChR), and choline acetyltransferase (ChAT) in colorectal cancer (CRC) tissues with the stage of disease, gender, age, risk, and patient survival. The effects of a muscarinic receptor blocker, atropine, and a selective M3R blocker, 4-DAMP, on the expression of immunosuppressive and cholinergic markers were evaluated in human CRC (LIM-2405, HT-29) cells.

Results

Increased expression of PD-L1, M3R, and ChAT at stages III-IV was associated with a high risk of CRC and poor survival outcomes independent of patients' gender and age. α7nAChR and PD-L2 were not changed at any CRC stages. Atropine and 4-DAMP suppressed the proliferation and migration of human CRC cells, induced apoptosis, and decreased PD-L1, PD-L2, and M3R expression in CRC cells via inhibition of EGFR and phosphorylation of ERK.

Conclusions

The expression of immunosuppressive and cholinergic markers may increase the risk of recurrence of CRC. These markers might be used in determining prognosis and treatment regimens for CRC patients. Blocking cholinergic signaling may be a potential therapeutic for CRC through anti-proliferation and anti-migration via inhibition of EGFR and phosphorylation of ERK. These effects allow the immune system to recognize and eliminate cancer cells.

sciforum-084668: Differential Gene Expression of Checkpoint Markers and Cancer Markers in Mouse Models of Spontaneous Chronic Colitis

Ramya Ephraim [1], Sarah Fraser [1], Jeannie Devereux [1], Rhian Stavely [2], Jack Feehan [1,3], Rajaraman Eri [4], Kulmira Nurgali [1,5,6] and Vasso Apostolopoulos [1,3]

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The presence of checkpoint markers in cancer cells aids in immune escape. The identification of checkpoint markers and early cancer markers is of utmost importance to gain clarity regarding the relationship between colitis and progressive inflammation leading to cancer. Herein, the gene expression levels of checkpoint makers, cancer-related pathways, and cancer genes in colon tissues of mouse models of chronic colitis (Winnie and Winnie-Prolapse mice) using next-generation sequencing are determined. Winnie mice are a result of a Muc2 missense mutation. The identification of such genes and their subsequent expression and role at the protein level would enable novel markers for the early diagnosis of cancer in IBD patients. The differentially expressed genes in the colonic transcriptome were analysed based on the Kyoto Encyclopedia of Genes and Genomes pathway. The expression of several oncogenes is associated with the severity of IBD, with Winnie-Prolapse mice expressing a large number of key genes associated with development of cancer. This research presents a number of new targets to evaluate for the development of biomarkers and therapeutics.

sciforum-082942: Metabolic Strategies of Treg Cells in the Tumor Microenvironment: Implications for Immune Metabolism-Based Precision Medicine

Devendra Kumar Mishra [1], Sandeep Yadav [1], Sumit Chaudhari [1], Ila Dixit [1], Lavkush Tiwari [1], Khalid Abdul Waheed [1], Shubham Shukla [2] and Savita Upadhyay [1]

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In recent years, the complex relationship between immune cells and the area around the tumour has become an important factor in how cancer grows and how well treatment works. Regulatory T cells (Tregs), a specific type of CD4+ T cell, are very important for keeping the immune system in balance, but tumours can also use them to weaken the immune system. To improve precision medicine approaches in cancer immunotherapy, we need to know more about the metabolic strategies used by Tregs in the tumour microenvironment. This review looks at the changes that Tregs' metabolism goes through when they enter a tumour, showing how their metabolism is different from that of effector T cells. We look into how Tregs use glycolysis, oxidative phosphorylation, and fatty acid metabolism to help them stay alive and keep other cells from attacking. We also talk about how the metabolism of Treg cells changes in response to environmental cues and immune checkpoint inhibitors. We also talk about what Treg metabolic plasticity means for the development of new strategies in immune metabolism-based precision medicine. In conclusion, this review shows how important it is to understand how Treg cells work in the area around a tumour because it could lead to more personalised and effective cancer immunotherapy. The new information from these studies opens up new ways to treat cancer that might tip the balance in favour of the body's immune system. This could start a new era in the fight against cancer.

sciforum-084664: New Theragnostic Agent Against Glioma Based On Gemcitabine

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Introduction

One of the main causes of death worldwide is cancer. The capacity of theranostic prodrugs to provide simultaneous diagnosis and therapy has drawn more and more attention in recent years. Here, we present the development of a novel theranostic molecule, called GF, based on the fluorescent dye 5(6)-carboxyfluorescein and the nucleoside anticancer drug gemcitabine.

Material and Methods

By using confocal microscopy to assess the synthesized GF's mode of cell uptake and cellular localization, a clathrin-mediated endocytosis was also revealed. Furthermore, three distinct human cancer lines—A549 (lung cancer), U87 and T98 (glioblastoma) were used to investigate the in vitro cytotoxicity and its pharmacokinetic profile in mice. Lastly, the effectiveness of the treatment in vivo was assessed using zebrafish and xenografted mice.

Results

GF has the ability to effectively enter tumor cells and locate in the lysosomes, which are the site of drug release and anticancer action. In mice, GF demonstrated improved pharmacokinetics as compared to gemcitabine. Higher concentrations of GF had notable anti-proliferative effects; yet, at all tested concentrations in all cell lines, GF was shown to be less cytotoxic than gemcitabine.

Conclusion

These findings suggest that GF, as a prodrug, can be a highly effective cytotoxic agent against glioblastoma. Additionally, as a potential gemcitabine prodrug, GF demonstrated less cytotoxic action than gemcitabine

sciforum-084661: Role of NLRP3 Inflammasome Colitis-Associated Colorectal Cancer

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NLRP3 inflammasome remains controversial with both protective and harmful effects reported in experimental colitis and colitis associated colorectal cancer (CAC) murine models. To address this controversy, we designed the world first murine model deficient in NLRP3 in a spontaneous chronic colitis mouse model Winnie [1]. Our results of WinniexNlrp3$^{-/-}$ at 12 and 16 weeks, shows spontaneous multiple colonic tumours with significant colonic shortening, increased activity of myeloperoxidase, Nitric Oxide and serum C-reactive protein. Histopathology revealed high-grade dysplasia and adenocarcinoma regions with increased DNA damage, oxidative stress, Ki-67, VEGF and Survivin biomarkers. Colon tissue culture supernatants identified differential expression of cytokines and chemokines. Protein analysis of colonic tumours showed upregulation of Wnt/β-catenin and PI3K/AKT pathways while qPCR identified upregulation of CAC biomarkers. Faecal microbiota analysis revealed significant increase in colitogenic members in the phylogenetic architecture in WinniexNlrp3$^{-/-}$ mice while metabolomics profiling revealed upregulation of key metabolites and short chain fatty acids. In addition, we looked at the therapeutic effect of specific small molecule NLRP3 inhibitor, MCC950 in Winnie mice. Oral administration of MCC950 significantly improved colonic length, disease activity index, histopathology and significantly reduced proinflammatory cytokines ameliorating colitis [2]. Our results show genetic ablation of NLRP3 gene in a chronic colitis model lead to CAC. However, chemical inhibition of an overactive NLRP3 inflammasome in chronic colitis attenuates severity of the disease. Altogether our results stresses the need for careful investigation of temporal therapeutic strategies for NLRP3 inhibitors in the gut at different disease phases in clinically relevant experimental models.

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sciforum-083390: Sanguinarine Impedes Human Oral Cancer via Attenuating Reactive Oxygen Species and PI3K/Akt/MAP Kinase Pathway

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Purpose

Oral squamous cell carcinoma (OSCC) personifies a worldwide problem for public health. Indeed, squamous cell carcinoma is the most common cancer in the oral cavity and one of the top ten cancers across the globe. According to GLOBOCAN 2020, 264211 new cases of oral cancer were reported, and 125022 individuals died as a result of the disease. Oral cancer had an all-inclusive incidence and mortality rate.

Materials and Methods

An MTT assay was used to assess the proliferation effects of Sanguinarine in oral cancer. A scratch assay was performed using sanguinarine to evaluate the migration effects in oral cancer. To determine the effects of sanguinarine on the characteristics of OSCC colonization, a colony formation assay was performed. In oral cancer, Western blotting was used to measure EMT-attenuating protein expression as well as major pathway protein expression induced by TGF- treatment.

Results

The MTT assay revealed a dose-dependent inhibition of cell proliferation in oral cancer. The results of the scratch assay revealed that sanguinarine played a significant role as a migration impeder in oral cancer. The results of the colony-forming assay demonstrated that sanguinarine has the ability to inhibit the development of colonies. Sanguinarine inhibited cadherin switching in oral cancer based on Western blotting results for EMT-regulating protein expression after TGF- treatment. Furthermore, after TGF treatment, the expression of pathway proteins involved in the EMT process, such as Smad, PI3K/Akt, and MAP kinase, was significantly disguised.

Conclusions

Our findings aided inunderstanding the inhibitoryrole of sanguinarine in OSCC tumorigenesis and its effects on impeding migration and metastasis by following the Smad and PI3K/Akt/MAP kinase pathways.

sciforum-084663: Targeting Gliomas

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The prognosis for patients with GBM remains poor and novel therapeutic approaches to address this unmet clinical need are urgently required. In this work we will present our recent efforts to develop compounds to target and tackle gliomas. Furthermore, we will illustrate other approaches that we are following to develop novel theranostic compounds that could be able to target the specific tumor microenvironment.

Abstracts

Session D. Tumor Microenvironment

sciforum-082398: Different Longitudinal Changes in the Neutrophil-to-Lymphocyte Ratio during Neoadjuvant Chemotherapy in Gastric Cancer Are Associated with Short- and Long-Term Prognosis: A Group-Based Trajectory Analysis

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Background

Systemic inflammatory factors can predict the survival prognosis of gastric cancer (GC) patients after neoadjuvant chemotherapy (NACT). However, whether longitudinal changes to systemic inflammatory factors over time are related to short-term and long-term prognosis has not been reported.

Methods

Prospective collection retrospective analysis of 216 GC patients who received NACT in our department from January 2011 to April 2019. Comparing receiver operating characteristic (ROC) curves for screening suitable inflammatory markers. Group-based trajectory modeling (GBTM) was used to analyze longitudinal changes in inflammatory markers during NACT to identify different potential subgroups. The endpoints were postoperative complications, recurrence-free survival (RFS), and overall survival (OS).

Results

Finally, Neutrophil-Lymphocyte Ratio (NLR) was the best predictor of the prognosis of the area under the curve (AUC) value compared with other common inflammatory markers and was included in the GBTM analysis. Three trajectories of NLR were obtained, and named the stable group (SG) (n = 89), the ascent–descent group (ADG) (n = 80) and the continuous descent group (CDG) (n = 47). Compared with SG OR = 0.333 (95% CI: 0.141–0.788) and ADG OR = 0.284 (95% CI: 0.119–0.675), the CDG had significantly higher postoperative serious complications. The risks of tumor recurrence and death in ADG were HR = 1.989 (95% CI: 1.157–3.419) and HR = 1.830 (95% CI: 1.127–2.969), while for CDG they were HR = 2.031 (95% CI: 1.098–3.757) and HR = 1.913 (95% CI: 1.092–3.351), respectively. The median RFS and OS of SG were better than those of ADG and CDG (median RFS 81 months vs. 44 and 22 months, and median OS 69 months vs. 41 and 30 months).

Conclusions

There were different trajectories of NLR during NACT, and these potential trajectories were significantly associated with severe postoperative complications, recurrence, and mortality in patients with GC.

sciforum-085312: Infrared Molecular Responce of Craniofacial Squamous cell Carcinoma—Pilot Study

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Introduction

Squamous cell carcinoma (SCC) occurring in the craniofacial region poses significant challenges due to its location and aggressive nature. This study explores the application of Fourier transform infrared spectroscopy (FTIR) as an innovative approach to unravel molecular responses within craniofacial SCC. This technique holds clinical promise for early diagnosis, personalized treatment, intra-operative diagnosis, and preventive screening.

Infrared spectroscopy reveals molecular vibrations, providing unique fingerprints of biological tissues. In craniofacial SCC, FTIR plays a key role in distinguishing cancerous from non-cancerous tissue by identifying characteristic spectral markers. These markers correspond to changes in vibrational modes of biomolecules like lipids, proteins, nucleic acids, and carbohydrates. Notably, alterations in lipid content and protein conformation reflect changes in the tumor microenvironment, cell proliferation, and differentiation.

Aim

The study aims to evaluate the protocol for differentiating SCC tissue from non-SCC tissue based on the infrared spectroscopic response.

Materials and methods

Samples were collected from craniofacial SCC patients at the Department of Cranio-Maxillo-Facial Surgery. FTIR investigations utilized an Agilent Cary 640 spectrometer, with data analyzed through chemometric analysis focusing on 2 and 3 main components.

Results

The study demonstrates a statistically significant separation of cancerous and healthy tissue, varying among patients. Even in cases with subtle differences, speculation arises about the presence of cancerous lesions or tumor markers in healthy sections. PCA analysis highlights pronounced differences in amide groups of proteins, particularly alpha and beta structures, and in phospholipid moieties.

Conclusions

Infrared spectroscopy emerges as a powerful tool for probing molecular responses in squamous cell carcinoma. Providing unique molecular information, it aids in early diagnosis, real-time monitoring of treatment efficacy, and precise tumor margin assessment. Continued research and technological advancements could integrate this method into routine clinical practice, ultimately enhancing the management and outcomes for SCC patients.

sciforum-083052: Single-Cell RNA Sequencing Revealed That the Enrichment of TPI1$^+$ Malignant Hepatocytes Was Linked to HCC Metastasis and Immunosuppressive Microenvironment

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Background

Background: Tumor metastasis is the leading cause of high mortality in hepatocellular carcinoma (HCC). Moreover, the HCC microenvironment is characterised by high heterogeneity. Single-cell RNA sequencing (scRNA-seq) may aid in determining specific cell clusters that could regulate the immune microenvironment of HCC.

Methods

The scRNA-seq data of 10 HCC samples were collected from the Gene Expression Omnibus (GEO) database GSE124395. Subcluster analyses were conducted to identify malignant hepatocytes. Correlations between key gene expression and clinicopathological data were determined using public databases. Immune cell infiltration analysis was performed and verified by immunohistochemistry and immunofluorescent staining.

Results

Nine malignant hepatocyte clusters with different marker genes and biological functions were identified. C3_Hepatocyte-SERF2 and C6_Hepatocyte-IL13RA2 were mainly involved in the regulation of the immune microenvironment, which was also a significant pathway in regulating HCC metastasis. Key genes in malignant hepatocyte clusters that were associated with HCC metastasis were further screened by LASSO regression analysis. TPI1, a key gene in C6_Hepatocyte-IL13RA2, presented a significant role in regulating the HCC immune microenvironment in the Cancer Genome Atlas (TCGA) and Tumor Immune Estimation Resource (TIMER) databases. Moreover, immunohistochemistry analysis demonstrated that TPI1 expression was positively correlated with HCC metastasis and poor prognosis, while it was negatively correlated with CD8$^+$ T cell infiltration. The negative correlation between TPI1 expression and CD8$^+$ T cell infiltration was further confirmed by immunofluorescence staining. Conclusion: In summary, a cluster of TPI1$^+$ malignant hepatocytes was associated with the suppression of CD8$^+$ T cell infiltration and HCC metastasis, providing new insights into novel biomarkers and immunotherapeutic targets for HCC.

Conclusions

As a newly developed prognostic score based on oxidative stress and immunoinflammatory indicators, mSPS can independently and effectively predict the tumor burden of advanced gastric cancer, and further distinguish the long-term prognosis of GC patients based on a pTNM staging system.

Abstracts

Session E. Molecular Cancer Biology

sciforum-085207: Noncoding Regulatory Mutations as a Driving Event for the Oncogenic Core Regulatory Circuitries of Neuroblastoma

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Introduction

Neuroblastoma (NB) is a pediatric tumor composed of adrenergic (ADRN) and mesenchymal-like (MES) cells which derive from the dysregulation of normal cell differentiation imposed by NB Core Regulatory Circuitries (CRCs). We hypothesize that somatic single-nucleotide variants (SNVs) in active CRCs transcription factor binding sites (aTFBSs) may underlie such perturbation, promoting NB tumorigenesis. We aim to investigate such patterns of regulatory elements and identify putative driver SNVs, exploring their role in NB.

Methods

MES and ADRN aTFBSs were identified by integrating 42 ChIP-seq and 12 ATAC-seq experiments in 7 ADRN and 2 MES NB cell lines. Using the Fisher test, we tested these regions for an enrichment of somatic SNVs obtained from the WGS data of 397 NB patients. SNVs were selected based on their impact on CRC TF binding through the FABIAN-variant tool. Next, aTFBS target genes were identified by analyzing the promoter capture HiC (CHiC) in 2 ADRN and 2 MES NB cell lines and their expression values were correlated with clinical and survival data of a second cohort of 498 NBs.

Results

We found six aTFBS sets of significantly enriched TFs (FDR ≤ 0.1) in SNVs, i.e., 5 ADRN (GATA3, HAND2, ISL1, MYCN, and TBX2) and 1 MES (FOSL2), with 689 mutations impacting the binding of CRC TFs (Fabian $\neq 0$). Mutated aTFBSs were found to interact with genes of neuronal differentiation pathways and proliferated MES cells , suggesting the potential impact of SNVs on NB cell identities. By focusing on genes of developmental and differentiation processes interacting with aTFBSs carrying SNVs with the highest (cut-off ≥ 0.1) or lowest (cut-off ≤ -0.1) Fabian score, we found targets (*ROBO2, CACNB1, PIK3R1, MDGA1, HES6, LDLRAD4, DGUOK, IRX1*, and *SPOCK2*) whose expression significantly correlated with worse NB outcomes (FDR ≤ 0.05).

Conclusions

These results demonstrated that somatic noncoding SNVs may act synergistically to affect NB CRCs and thus contribute to tumorigenesis.

sciforum-085436: Aberrantly Expressed Long Non-Coding RNAs and MRNAs in Breast Cancer and Their Interaction

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According to the latest global statistics for 2020, breast cancer (BC) has taken first place in the incidence of epithelial tumors, ahead of lung cancer, and is the main cause of mortality from cancer pathology among women around the world. Recently, the critical role of non-coding RNAs (ncRNAs) in the regulation of genes and signaling pathways in cancer pathogenesis, particularly apoptosis, has been identified.

The aim of our work was to identify new aberrantly expressed long non-coding RNAs and mRNAs in BC, as well as to study their possible interactions in BC.

Materials and Methods. Total RNA was isolated from paired breast cancer samples according to the standard method. Reverse transcription was performed using the MMLV RT kit # SK021 (Evrogen, Moscow, Russia), and qPCR was performed on a Bio-Rad CFX96 Real-Time PCR Detection System (Bio-Rad, Hercules, CA, USA) using the qPCRmix kit -HS SYBR (Evrogen, Moscow, Russia) according to the manufacturer's protocol. Data were analyzed using relative quantification based on the ΔΔCt method. Changes in the expression levels of lncRNAs and mRNAs were considered less than 2 times ($|\Delta\Delta Ct| \leq 2$) as 'no changes'. qPCR was performed in three technical replicas.

Results. Changes in the expression level of the lncRNA ADAMTS9-AS1, OIP5-AS1, and mRNA of genes associated with apoptosis, such as APAF1, BAX, BAK1, BIM, and BCL2, were studied in breast cancer. We found decreased expression levels of ADAMTS9-AS1, OIP5-AS1, and APAF1 and BAX in 60 breast tumor samples compared with paired norms ($p = 0.05$). The level of BCL2 expression is significantly ($p = 0.001$) higher in breast tumors compared to the paired norm. A high statistically significant correlation was established between the expression of BIM and BAX (Rs = 0.48, $p = 0.01$). This result may indicate that the mRNA pairs may be involved in common processes of breast carcinogenesis. A highly significant positive correlation of expression was established for the pairs ADAMTS9-AS1–BAX (Rs = 0.67, $p = 0.01$), OIP5-AS1–BAK1 (Rs = 0.52, $p = 0.01$), and OIP5-AS1–BIM (Rs = 0.51, $p = 0.01$), suggesting a direct or indirect activating interaction of these pairs in breast cancer. The obtained data on coexpression are confirmed by the data obtained from correlation analysis carried out on a dataset showing differential expression levels of lncRNAs in breast cancer, selected from and complementary to the TCGA Tumor/TCGA Normal libraries.

Conclusions. LncRNAs and mRNAs that are differentially expressed in breast cancer have been identified; a positive correlation has been established in mRNA-mRNA and mRNA-lncRNA pairs in breast cancer, which indicates their participation in common signaling pathways in breast cancer. Determining new lncRNAs involved in the pathogenesis of BC and in the deregulation of apoptosis genes is one of the priority tasks of modern molecular oncology.

This work was supported by the Russian Science Foundation grant no. 22-75-00132.

sciforum-085171: Differential Expression Analysis in Genes Associated with the Mitochondrial Metabolism Reveals a Potential Influence on the Progression of Glioblastoma from Astrocytoma

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The most common forms of primary brain tumors are low-grade astrocytoma (ACT) tumors and their progression to the glioblastoma multiforme (GBM), in a high-aggressiveness form. Understanding mechanisms of progression is necessary, and mitochondrial mechanisms are not yet as well elucidated and may be a factor in this disease. Therefore, in this study, we analyzed differential gene expression (DGE) between GBM and ACT, using the MitoXplorer 2.0 to screen nuclear genes involved in mitochondrial metabolism, totaling 1193 genes. The analysis used ACT (n = 195) and GBM (n = 157) samples made available by The Cancer Genome Atlas (TCGA) database. As a complement, we checked the expression of differentially expressed genes (DEGs) in normal tissues using the GTEx Portal, as well as checking disease-free survival (DFS) using GEPIA2. DGE showed five potential DEGs, three of which were downregulated (ACSM2A, ACSM2B, and PRODH2) and two were upregulated (TERT and FBP2). In non-cancerous tissues, upregulated DEGs are normally expressed basally in brain tissue and TERT is normally expressed in tissues such as testis and small intestine, while FBP2 is expressed in the stomach, skeletal muscle, testis, pancreas, and adrenal glands. Alternatively, downregulated DEGs normally show basal or zero expression in brain tissues and are normally expressed in the liver and kidneys. DFS analysis showed that the high expression of the TERT is associated with poor survival, and is the only gene found to be significant among the five DEGs (p-value 0.05). Briefly, our analyses showed five mitochondrial DEGs as potential markers of GBM progression in relation to ACT. Four of the five DEGs have not been reported as factors that can influence the GBM cascade until this work, while the TERT gene has already been indicated as a potential biomarker of brain cancer, having an essential function in the protection of the mitochondrial genome.

sciforum-084318: Exposure to Mycovirus-Containing *Aspergillus flavus* Alters Transcription Factors in Normal and Leukemia Cell Lines

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Abstract: Transcription factors bind specific DNA motifs to regulate the expression of target genes in order to maintain normal hematopoiesis. The dysregulation of these factors can lead to hemopoietic disorders, including leukemias. Mutations, translocations, or the aberrant expression of several transcription factors in various leukemias have been well documented. Mycoviruses are known to alter the genetics of their fungal host and transform their biological characteristics. We have evaluated the effects of the products of a certain mycovirus-containing *Aspergillus flavus* (MCAF), which we have isolated from the home of a patient with leukemia, on the transcription factors of acute lymphoblastic (ALL), acute myelogenous leukemia (AML) cell lines, and controls. This organism does not produce any aflatoxin. Our previously published studies have shown that patients with B-cell ALL, unlike controls, have antibodies to MCAF, and the exposure of the mononuclear leukocytes from ALL patients in complete remission to its products results in the re-development of genetic and cell-surface markers characteristic of ALL. In additional investigations, ALL and AML cell lines and controls were exposed to incremental doses of the supernatant of the culture of MCAF. Prior to and after exposure, the levels of PAX-5 and Ikaros (75 and 55 kDa) in ALL cell lines, and AML-1,c/EBP-a and PU.1 in AML cell lines, as well as NF-κB(p65) transcription factors in both cell lines, were assessed. Cellular viability was also evaluated. The exposure of the 'normal' cell line to the MCAF resulted in apoptosis, and the downregulation of all tested transcription factors, with no detectable levels remaining. In leukemia cell lines, exposure to MCAF also caused cell death; however, while there was a downregulation of all tested transcription factors, some residual levels were retained. The genetic alterations caused by MCAF are novel findings and of significance. Further studies on the possible role of mycovirus-containing *Aspergillus flavus* in leukemogenesis are warranted.

sciforum-085068: Post-GWAS Functional Analysis of the 11p11.2 Risk Locus Identifies *HSD17B12* as a Neuroblastoma Susceptibility Gene Involved in Lipid Metabolism

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Introduction

Genome-wide association studies (GWASs) have contributed to the study of neuroblastoma (NB) genetics by identifying common risk variants that activate cancer-related processes associated with NB susceptibility.

Aim

This study aims to functionally characterize the 11p11.2 predisposition locus identified in our GWAS on 2101 cases and 4202 controls, evaluating how the regulatory variant and its target gene can influence NB development.

Methods

To identify functional variants, we annotated 72 candidate SNPs with functional data from public NB databases and validated the functional SNP's regulatory activity vialuciferase assays in NB cells. The candidate SNP was predicted to map inside a GATA3 binding motif and differential GATA3 allele binding was evaluated using ChIP-qPCR. eQTL analysis and CRISPR/Cas9 genome editing allowed us to identify the target gene of the functional SNP. To evaluate its role in NB tumorigenesis, we correlated gene expression with clinical features using RNA-seq data from 498 tumors and performed MTT and invasion assays after gene silencing in NB cells. Targeted lipidomic assays were performed to study the involvement of the target gene in lipid metabolism.

Results

rs2863002T>C represents the candidate functional SNP of the risk locus. The rs2863002-C allele correlated with high expression levels of its target gene *HSD17B12* and showed a lower binding affinity for the transcription factor GATA3 in NB cells, suggesting that it may alter the GATA3 binding motif. High *HSD17B12* expression levels correlated with poor prognosis and survival in NB tumors, and gene silencing in NB cells reduced proliferation and invasiveness, supporting the oncogenic role of *HSD17B12* in NB. Lipidomic results showed that *HSD17B12* silencing in NB cells altered lipid metabolism, affecting lipid molecules related to energy production and cellular membrane chemical—physical properties.

Conclusions

This study highlights the importance of the post-GWAS functional characterization of risk loci to identify new susceptibility genes and new biological mechanisms underlying NB predisposition.

sciforum-086823: Suppression of Medulloblastoma Cell Migration by Clinically Significant Doses of Simvastatin through Mevalonate Pathway Targeting

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Aims

Medulloblastoma (MBs), the most prevalent malignant paediatric brain tumour, exhibits distinct subgroups—Wingless (WNT), Sonic Hedgehog (SHH), Group 3 (G3), and Group 4 (G4)—each characterized by unique molecular signatures and clinical outcomes. Despite being the most aggressive, Group 3 (G3) and Group 4 (G4) remain the least understood. Current treatments, involving surgical resection, radiation, and chemotherapy, are associated with significant morbidity and adverse effects. This study aims to explore the potential of clinically significant doses of simvastatin, known for its ability to penetrate the blood-brain barrier, as a targeted and less toxic therapy for aggressive MBs.

Method

In-silico gene expression analysis assessed mevalonate pathway (MVP) enzyme expression in MBs, corroborated by immunocytochemistry and RT-PCR in SHH, G3, and G4 cells. The anti-cancer and anti-metastatic properties of low doses of simvastatin were investigated through both 2D and 3D cell culture methods.

Results

Our findings reveal that clinically significant doses of simvastatin effectively reduces the migration of MBs cells in both 2D and 3D in vitro cultures.

Conclusions

This study establishes simvastatin as a promising therapeutic candidate for mitigating MBs cell invasion, offering a potential avenue for the development of novel and less invasive treatment strategies for MBs tumours.

sciforum-086326: Two Novel miRNAs Encoded by Oncogene MSI1

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Introduction

The RNA-binding protein Musashi1 (*MSI1*), well known for its increased expression level in several malignancies, has been reported as a prognostic biomarker. Since miRNAs are among the very stable non-coding RNAs in body fluids and are considered to be more efficient biomarkers in several biological processes, we were interested to find out if any novel miRNAs are encoded by *MSI1* genes, which could be considered as novel biomarkers in future studies. Both experimental and computation-based methods were used to find the most reliable structures.

Methods

Several types of bioinformatics software were used to predict novel miRNA precursors based on RNA secondary structure criteria and evaluate the probability of producing mature miRNAs using Drosha/Dicer processing. For experimental confirmation, candidate miRNA precursors were transfected into HEK293T cells and their ability to produce mature miRNAs was assessed via RT-qPCR and sequencing. Additionally, we analyzed the endogenous expression of miRNAs in cancer cell lines and breast cancer samples.

Results

Two structures within the intron 4 of the *MSI1* gene, named MSM2 and MSM3, which possessed the most characteristics of miRNA precursors, were selected for further studies. In HEK293T cells, the MSM3 precursor generated two mature miRNAs, MSM3-3p and MSM3-5p, while MSM2 generated only one mature miRNA, MSM2-5p. The significant endogenous expression of MSM2-5p and MSM3-3p was detected in MCF-7 and SH-SY5Y cell lines, but not the MSM3-5p. Interestingly, the expression of novel miRNAs was only detected in breast clinical samples with increased expression levels of *MSI1*.

Conclusions

Our RT-qPCR and sequencing results confirmed the presence of two novel miRNAs within the intronic region of the *MSI1* gene. The expression of these novel miRNAs was confirmed in cancer cell lines and breast cancer samples. However, additional studies are necessary to fully understand the precise roles of these novel miRNAs in various cancers and assess their potential as biomarkers.

Abstracts

Session F. Cancer Epidemiology and Prevention

sciforum-084838: Cancer Distribution among Patients Registered at Hadhramout National Oncology Center during 2015–2020

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Background

Cancer has become a significant public health issue and is one of the world's leading causes of death. This study reports on the types and distribution of cancer using data from the Hadhramout Oncology Center (HNOC) from 2015 to 2020. This study aims to estimate the cancer incidence among patients registered at (HNOC) from 2015 to 2020.

Method

Retrospective descriptive study of patients diagnosed with cancer at (HNOC) in the period of 2015–2020 in Yemen.

Results

The results obtained from the Hadhramout National Oncology Center during the period 2015–2020 showed a total of 2591 cases. Of these, 1279 cases (49.4%) were males and 1312 (50.6%) were females, with a female-to-male ratio of 1.02. There has been an increase in the number of cases from 2015 to 2020 with a peak occurring in 2018. The mean ages of diagnosis were 52.29 and 50.45 years for males and females, respectively. For all cancer types, cancers of blood were the most common type, followed by breast cancer and colorectal cancer. Breast cancer (28.9%) and blood cancer (18.84%) were the most common types in females and males, respectively. Among all the cases registered at (HNOC), Hadramout had the highest reported cases with 1787 (68.9%), followed by Shabwa 518 (20%) and Almahra 105 (4.1%).

Conclusions

The findings of this study demonstrated that cancer incidence has increased over the past few years. Therefore, it is essential to establish a high-quality regional cancer registry to allow for the surveillance of cancer and facilitate the development of effective programs for cancer control and prevention in Yemen.

sciforum-083871: Polycyclic Aromatic Hydrocarbons (PAHs) in Grilled Marshmallows

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Introduction

Grilling more and more sophisticated dishes is a popular activity. Marshmallows are confectionery products, popular among children and teenagers all over the world, available in many well-known supermarkets ready to be grilled. Grilled marshmallows can be a source of exposure to harmful compounds, including carcinogenic polycyclic aromatic hydrocarbons (PAHs).

Method

The procedure of PAHs formed in marshmallows grilled under different conditions includes the dilution stage with deionized water and liquid—liquid extraction with cyclohexane and solid-phase extraction (SPE on silica gel columns). PAH fractions were initially analyzed via planar chromatography (HPTLC) using densitometry, and PAH concentrations were determined via GC-MS/MS using the selective reaction monitoring (SRM) mode. The authors' designed survey, in relation to the consumption of grilled marshmallows, was also conducted among approximately 300 children and adolescents.

Results

Preliminary results of TLC and GC-MS/MS analysis indicate that "raw" marshmallows do not contain PAHs. However, obtained data suggest a high exposure of young people to carcinogenic PAHs from grilled marshmallows. Carcinogenic BaP was determined in all investigated samples, constituting 36% of total PAH4 content, on average.

Conclusions

The profile of PAH concentrations in extracts isolated from grilled various types of marshmallows was very similar ($R > 0.8$), regardless of the grilling method. The higher concentrations of PAHs were determined in multicolour marshmallows than in white ones. The lack of social awareness in relation to the exposure to carcinogenic substances is frightening.

sciforum-080524: Association between Oral Microbiome and Seven Types of Cancers in East Asian Population: A Two-Sample Mendelian Randomization Analysis

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Background

The oral microbiome has been intricately linked to various pathological conditions, notably cancer, though clear causal links remain elusive.

Objective

This study aimed to investigate the potential causal relationships between the oral microbiome and seven major cancers: breast, lung, pancreatic, colorectal, gastric, ovarian, and prostate cancers, leveraging Mendelian randomization (MR).

Methods

A two-sample MR analysis was conducted using genome-wide association study (GWAS) data specific to oral microbiota in individuals of East Asian descent. Single nucleotide polymorphisms (SNPs) independent of confounders served as instrumental variables (IVs) to deduce causality. MR methodologies such as the inverse variance weighted (IVW) method, weighted median (WM) method, and Mendelian randomization-Egger (MR-Egger) method were employed. The study utilized datasets encapsulating a multitude of cancer cases and controls, focusing on Asian populations.

Results

Our analysis revealed intricate associations between specific bacterial genera of the oral microbiome and diverse cancers. Notably, *Fusobacterium* showed mixed associations with various cancers, while genera like *Prevotella* and *Streptococcus* exhibited nuanced roles across malignancies. The genus *Aggregatibacter* demonstrated a multifaceted influence, positively correlating with some cancers while inhibiting others.

Conclusions

Our findings underscore the profound implications of the oral microbiome in systemic malignancies, suggesting potential modulatory roles in cancer etiology. These insights, though preliminary, accentuate the need for deeper exploration and could pave the way for novel therapeutic strategies.

sciforum-085131: Desmoplastic Fibroma of the Mandible: Case Report

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Introduction

Desmoplastic fibroma is an extremely rare and locally aggressive benign tumor. It can affect all bones of the body but most frequently the mandible, followed by long bones (the femur, radius, and tibia) and the bones of the pelvis.

Objective and Importance

A unique aspect of our study is the rare focus on desmoplastic fibroma in children. Furthermore, reports of this pathology are exceedingly rare.

Presentation of the Case

We studied a 3-year-old patient, with no notable pathological history, who presented with swelling in the cheek area that has been developing since birth without pain or inflammatory signs.

The radiological examination showed a multilocular lesion breaking the bony cortex and reaching the jugal soft tissues.

A biopsy of the mass was performed intraorally.

Results

Histologically, it is a tumoral proliferation made of bundles of regular and uniform myofibroblastic cells. The stroma is collagenous, the seat of a few congestive capillaries aligned parallel to the bundles. This proliferation is non-encapsulated and infiltrates the surrounding muscle and bone tissue.

The absence of cytonuclear atypia, atypical mitoses, and necrosis.

An immunohistochemical study was carried out showing:

- The positive marking of tumor cells using β-cathenin and AML.

By combining clinical, radiological, histological, and immunohistochemical data, the diagnosis of a desmoplastic fibroma was made.

Discussion

Desmoplastic fibroma is an exceptional tumor that constitutes less than 0.1% of all primary bone tumors. It mainly affects adolescents and young people with a peak age between 20 and 30 years old and there is no gender predominance.

Clinically, desmoplastic fibroma is manifested by a painless swelling, difficulty in opening the mouth, and displacement of teeth. Sometimes, the tumor is asymptomatic and the discovery is incidental.

Radiologically, desmoplastic fibroma manifests as a well-defined, multilocular, and radiolucent lesion. Intralesional trabeculations are often present. Large lesions can destroy the bone cortex and infiltrate the surrounding soft tissue, which is clearly shown by MRI displaying a lesion with T1 and T2 hyposignal.

Histologically, it is a sparsely cellular-infiltrating tumor proliferation arranged in bundles of monomorphic spindle cells resting on the abundant collagenous stroma. It is characterized by the absence of necrosis and very rare mitoses. This proliferation may show positive cytoplasmic staining using β-cathenin and AML. The main differential diagnoses are fibrous dysplasia, low-grade central osteosarcoma, low-grade myofibrodysplasia, myoepithelial tumors, follicular dendritic tumors, and synovialosarcoma.

We selected surgical resection with wide resection margins as the treatment. Aggressive curettage may be used. Tumoral surgical margins were associated with higher recurrence rates.

Conclusions

Desmoplastic fibroma is an extremely rare, benign, and locally aggressive tumor that most frequently affects the mandible. It generally occurs in children and young adults in the form of an osteolytic mass. The positive diagnosis of histological and molecular biology is recommended to eliminate differential diagnoses. Treatment is based on surgery and the prognosis is characterized by recurrences in the case of excision with tumoral margins.

sciforum-083870: Exceptional Peritoneal Metastasis of Small Cell Carcinoma of Pulmonary Origin

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Background

Lung carcinoma is the leading cause of cancer-related mortality, with 50% of cases presenting metastases at the time of diagnosis. Metastatic peritoneal localisation of lung carcinoma is an exceptionally rare situation, accounting for 3% of lung cancers. The rarity is heightened when dealing with small cell lung carcinoma cases, making reported instances even more exceptional.

Accurate diagnosis and proper disease staging are crucial in determining whether the disease is metastatic or non-metastatic, influencing subsequent management.

A 58-year-old patient with a history of non-metastatic small cell lung carcinoma diagnosed in October 2021 (2 years ago) underwent radiotherapy and achieved remission. In February 2023, the patient experienced abdominal pain and hematemesis with melena. Esophagogastroduodenoscopy revealed an ulcerative, polypoid gastric process. Biopsy confirmed moderately differentiated gastric adenocarcinoma. A whole-body CT scan identified new peritoneal nodules.

Laparoscopy with biopsy was performed, and specimens were sent for histopathological examination.

Results

Histologically, the specimen showed a diffuse tumor proliferation consisting of generally small, highly mitotic cells, displaying irregular, hyperchromatic nuclei and scant, basophilic cytoplasm. Immunohistochemical analysis revealed the following:

- Positive staining of tumor cells for TTF1 and CK7 and negative staining for CK20, indicating a pulmonary origin and ruling out gastric origin.
- Tumor cells expressed chromogranin A and synaptophysin, with a high proliferative index (Ki67) estimated at 60%.

Considering all data, the diagnosis retained is a secondary localisation of undifferentiated carcinoma, with immunohistochemical profiling primarily aligning with small cell lung carcinoma.

Discussion and Conclusions

Small cell carcinoma, a therapeutic emergency, poses a significant health problem due to its high incidence and mortality. Diagnosis relies on histology supported by immunohistochemistry. Patients often present acute symptoms due to the rapid local growth of intrathoracic tumors, especially at the pulmonary hilum, or distant extrapulmonary dissemination in 40% of cases involving lymph nodes, liver, adrenal glands, bones, or brain.

Peritoneal metastasis is exceptionally rare, with the most common histological type being pulmonary adenocarcinoma (80% of cases), and the least common scenario is the one reported in this abstract: small-cell carcinoma.

Thorough morphological and immunohistochemical studies, guided by the suspected histological type and patient history, are mandatory for a conclusive diagnosis.

sciforum-079532: Pulmonary Tuberculosis: A Comorbidity or Misdiagnosis of Primary Lung Cancer in Africa?

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Background

Globally, over 2 million new cases of lung cancer are diagnosed annually, representing about 11% of all cancers. In males and females, it is the leading cause of cancer-related deaths in 87 and 26 countries, respectively. Only 1% of lung cancer deaths are reported in Africa. In Zimbabwe, lung cancer accounts for less than 4% of annual cancer incidence. Investigating patients for probable lung cancer needs a high index of suspicion by physicians practicing in a high HIV/TB burden country and requires specialized radiology, pathology, surgery and oncology services in diagnosis and treatment. In this setting, the misdiagnosis and/or delayed diagnosis of primary lung cancer is highly probable as Africa goes through the disease burden transitional phase. This study was carried out to determine the prevalence of initial misdiagnosis of primary lung cancer as pulmonary tuberculosis and the resultant time delay in establishing a histological diagnosis.

Methods

A retrospective descriptive study reviewing medical records of patients who presented with pathologically confirmed primary lung cancer from January 2014 to 31 December 2018 was carried out at Parirenyatwa Group of Hospitals Radiotherapy and Oncology Centre. This is the largest cancer treatment centre in Zimbabwe.

Results

A total of 73 patients were eligible for review and males accounted for 58% of all new cases. A pulmonary TB diagnosis in the preceding 12 months before a diagnosis of primary lung cancer was identified in 53% of patients. The median time delay to diagnosis was 8.37 months (range: 1–37 months). Only 11 patients (15.1%) had lung cancer diagnosed within 3 months of the initial presentation to a health care centre. A diagnosis of tuberculosis (TB) is associated with a delay of >7 months in lung cancer diagnosis ($p = 0.001$). At the time of diagnosis, 77% of patients had stage IV disease.

Conclusions

Most lung cancer patients are initially misdiagnosed as having TB, and this results in a significant time delay to diagnosis. The majority of patients had distant metastases at diagnosis. There is a relationship between the prevalent lung cancer misdiagnosis and the high burden of HIV/TB in Zimbabwe

sciforum-085129: Two Cases of Plunging Goiter Revealing Primary Thyroid Lymphoma

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Introduction

Thyroid lymphoma is a rare tumor that accounts for 5% of all thyroid neoplasms and 1 to 2% of extranodal lymphomas. The predominant histological type is diffuse large B-cell lymphoma. It mainly affects women in their sixth decade and it is manifested by a rapidly progressive cervical mass. The diagnosis is histological and treatment is essentially based on chemotherapy.

Case Presentation

Case 1: a 50-year-old female patient, with no notable pathological history, who presented with cervical swelling that has been present for 6 months and is associated with dysphagia, dyspnea, and respiratory difficulty.

The clinical examination found the patient conscious and stable on the hemodynamic and respiratory levels. Cervical examination reveals cervical swelling that is painful on palpation and mobile on swallowing.

The biological assessment found TSH at 8.71 mIU/L, free T4 at 8.64 mIU/L, and free T3 at 3.68 mIU/L, suggesting peripheral hypothyroidism. Anti-thyroperxydase antibodies were elevated at 177.88 IU/mL.

Cervical ultrasound found a diffuse heterogeneous goiter associated with right supraclavicular lymphadenopathy, measuring 20 $\times$ 10 mm.

Cervicothoracic CT found a heterogeneous plunging goiter without suspicious lesions.

Case 2: a 75-year-old female patient, followed for hypertension under monotherapy, admitted for cervical swelling.

The clinical examination found the patient conscious and stable on the hemodynamic and respiratory levels. Cervical examination revealed a cervical swelling that was painful on palpation and mobile on swallowing.

The biological assessment showed a thyroid assessment without abnormalities.

Cervico-thoracic CT revealed a plunging and compressive nodular goiter starting from the left lobe associated with sub-centimeter laterocervical and mediastinal lymphadenopathy.

Both patients underwent surgical biopsy of the mass.

Results

Histologically, the two biopsies corresponded to malignant tumor proliferation occurring mainly in diffuse layers. The tumor cells were dyscohesive, atypical, and large with hyperchromatic nuclei and clear-appearing cytoplasm. We also noted the presence of numerous mitotic figures.

The immunohistochemical study showed the following:

- Strong and diffuse positive marking of tumor cells by the anti-CD20 antibody.
- A tumor proliferation index estimated at 85% for the first case and 75% for the second case.
- Negative staining of tumor cells via anti-CK antibody and anti-CD3 antibody.

By combining clinical, radiological, histological, and immunohistochemical data, a diagnosis of diffuse large thyroid B-cell lymphoma was made for both cases.

Discussion

Primary thyroid lymphoma (PLT) is defined as lymphoma developing from the thyroid gland and not from another area and arriving at the thyroid by contiguity or metastasis. It is generally a non-Hodgkin lymphoma, of which diffuse large B-cell lymphoma accounts for 70%, followed by B-cell non-Hodgkin lymphoma of

mucosa-associated lymphoid tissue (MALT), follicular lymphoma, mantle cell lymphoma , Burkitt lymphoma, and finally angioblastic lymphoma.

A history of Hashimoto's thyroiditis is a well-recognized risk factor for developing PTL, with a relative risk of 67 compared with people without thyroiditis.

This pathology is generally manifested by rapidly progressive cervical swelling associated with signs of compression including dysphagia, dyspnea, and superior vena cava syndrome, with a deterioration in general condition and night sweats. The biological assessment found euthyroidism in patients followed for Hashimoto's thyroiditis treated with levothyroxine, and hypothyroidism in the other patients. Anti-thyroperoxidase antibodies were elevated in 60% of patients.

The use of ultrasound (US) scans can suggest a diagnosis, as the mass may be nodular, diffuse, or mixed. Common ultrasound findings include a hypoechoic solid lesion associated with hypervascularity and a diversity that characterizes its outline. Therefore, a thorough investigation is indicated in any patient with autoimmune thyroiditis who has suspicious findings on ultrasonography.

Fine needle aspiration (FNA) has become an essential tool in the management of thyroid diseases, but it has shown inconsistent results in the diagnosis of primary thyroid lymphomas; for this, core or surgical biopsies are necessary to establish a definitive diagnosis.

Histologically, LBDGC is characterized by a diffuse architecture with large B cells of variable appearance (centoblasts and immunoblasts). Tumor cells typically express CD20, PAX5, and CD79a. The tumor proliferation index (Ki67) is greater than 40%.

Primary thyroid lymphomas respond well to chemotherapy and radiotherapy. The chemotherapy regimen includes cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP). Radiation therapy is usually given after three to six cycles of chemotherapy. The prognosis depends on the stage of the disease at the time of presentation.

Conclusions

Primary thyroid lymphoma is a rare cause of thyroid malignancy. It mainly affects women and is manifested by rapidly progressive cervical swelling. The diagnosis is histological and treatment is based on chemo-radiotherapy.

sciforum-085213: Use of Proton Pump Inhibitors and Risk of Gastric Cancer in Patients Requiring Gastric Acid Suppression

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Background

Proton-pump inhibitors (PPIs) have raised concerns regarding an increased risk of gastric cancer.

Aim

This study aims to evaluate the association between PPI use and the risk of gastric cancer.

Methods

A systematic search of Medline/PubMed, Embase, and Scopus databases was conducted to identify both randomized and non-randomized studies examining the link between PPIs and gastric cancer. Histamine-2 receptor antagonist (H2RA) users were chosen as controls to minimize confounding by indication and focus on patients requiring gastric acid suppression. Two authors independently extracted data and assessed bias risks. Maximally-adjusted relative risk (RR) estimates were extracted, and random- and fixed-effect models calculated summary estimates. Heterogeneity and small-study effects were examined, and GRADE was used to evaluate evidence certainty.

Results

Of 8375 records, 12 non-randomized studies (>6 million patients; 11,554 gastric cancers) and two randomized clinical trials (498 patients; 1 gastric cancer) met eligibility criteria. Randomized evidence provided very-low certainty evidence. Meta-analysis of six adequately adjusted non-randomized studies (2.5 million patients; 7372 gastric cancers) revealed no association between PPIs and gastric cancer (RR_random = 1.07, 0.97–1.19; RR_fixed = 1.05, 0.98–1.12), with low certainty of evidence. No convincing evidence of dose-response or increased risk with long-term use was found. Lack of or minimal adjustment for confounding was associated with larger effect sizes.

Conclusions

Non-randomized studies with adequate confounding control found no association between PPIs and gastric cancer. Previous published studies indicating an increased risk of gastric cancer associated with PPIs may suffer residual confounding.

Abstracts

Session G. Cancer Therapy

sciforum-083973: Exploring BNCT as a Novel Approach for Metastatic Spinal Tumor Management

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Background

Boron neutron capture therapy (BNCT) is a particle beam therapy that enables the precise targeting of tumors at the cellular level. Building on the success observed in nuclear reactors, BNCT exhibits potential as a therapeutic approach for managing invasive brain tumors, including malignant gliomas and high-grade meningiomas. Metastatic spinal tumors have been treated by surgical removal, radiation therapy, and a variety of other multidisciplinary therapies. However, none of them has been successful in overcoming this metastatic disease. This study aimed to assess the efficacy of BNCT in treating metastatic spinal tumor using a mouse model.

Methods

In vitro experiment: neutron irradiation was applied to A549 human lung carcinoma cells with (BNCT group) or without p-boronophenylalanine (BPA) 10 μg Boron/ml for 24 h exposure before irradiation (hot control group) for 0 to 30 min. The cell killing effect was assessed by a colony forming assay. In vivo experiment: an A549 subcutaneous tumor was removed and implanted into the lumbar lamina, where it was partially resected. A few weeks later, metastatic spinal tumor models were successfully established. For the biodistribution of boron, after 2.5, 6, or 24 h of intravenous BPA administration (250 mg/mouse body weight), the metastatic spinal tumor models were sacrificed and the boron concentration of the tumor and each organ measured using Inductively Coupled Plasma Atomic Emission Spectroscopy (ICP-AES).

Results

In vitro neutron experiment: the BNCT group showed a greater cell killing effect than the hot control group. The highest boron accumulation in the tumor was observed at 2.5 h after BPA administration (8.6 μg B/g), and the tumor to normal spinal cord ratio (T/N) was 2.7 and the tumor to blood ratio (T/Bl) was 2.8.

Conclusions

The findings may indicate that BNCT represents an effective approach in the management of metastatic spinal tumor. We will perform an in vivo neutron irradiation experiment on this model to evaluate the effects of BNCT on survival and neurological function.

sciforum-084853: Pharmacological Network Study on the Effect of Quercetin on Gastric Cancer Using Computerized Databases

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Gastric cancer (GC) is the second most common cause of death of any cancer-related cases in the world, and is also in the top 5 most common malignancy cancers in general. There are plenty of well-distributed treatments , offering better hygiene, more robust and complete nutrition, and the eradication of pathogens such as *Helicobacter pylori.* Currently, there is still the need for more treatments, especially those of lower cost, like those coming from already easily available products. Quercetin (QRC) is a natural phenolic compound present in a wide variety of products, e.g., in plants like *Hibiscus sabdariffa*, onions, grapes, broccoli, and citrus fruits. This product has been shown to have great potential therapeutic effects, and it has also been suggested that it could be useful in combating different types of cancer; however, information regarding the targets or mechanisms that QRC has on cancer cells is still unclear. Therefore, this study aims to identify the targets that QRC has, like anti-cancer treatment for GC using different bio-informatic tools and databases. From MalaCards and SwissTargetPrediction, both QRC and GC molecular targets were defined, and then they were matched with the Venny 2.1.0 platform. From this, 31 genes were gathered, and then they were analyzed using the ShinnyGo0.77 and DAVID-Bioinformatic Resources. Furthermore, StringDB was used to identify the protein—protein interactions, and Citoscape 3.6.0 12 hub genes were obtained. Those hub genes were then subject to Gene Expression Profiling Interactive Analysis and TISIDB. Finally, molecular docking studies were performed using the SwissDock database. The results suggest that, according to the gene ontology data, QRC has a relationship with the regulation of cell death, response to stress, cell motility, response to amyloid-beta, cellular response to reactive oxygen species, and apoptotic processes. Some genes like EGFR were correlated with an abundance of CD8 and Neutrophil infiltration, but didn't show to improve the survival rate. Furthermore, molecular docking results show that QRC can bind to multiple molecules of interest. These results complement some of the currently available information alluding to the effectiveness of plants rich with QRC as part of the treatment used for different kinds of cancer, but it also suggests a plethora of new targets that this molecule has in GC, while at the same time giving a clearer idea of the mechanisms that are affected in GC by QRC. However, as with any other study that primarily uses bioinformatic tools, these final results are to be used for more direct and precise research, especially if experimental protocols are used.

sciforum-082407: Appraisal of the Surgical Outcomes and Oncological Efficiency of Intraoperative Adverse Events in Robotic Radical Gastrectomy for Gastric Cancer

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Background

Surgical quality control is a crucial determinant for evaluating tumor efficacy.

Objective

To assess the ClassIntra grade for quality control and oncological outcomes of robotic radical surgery for gastric cancer (GC).

Methods

Data of patients undergoing robotic radical surgery for GC at a high-volume center were retrospectively analyzed. Patients were categorized into two groups, the iAE (intraoperative adverse event) group and the non-iAE group, based on the occurrence of intraoperative adverse events. The iAEs were further classified into five sublevels (ranging from I to V according to severity) based on the ClassIntra grade. Surgical performance was assessed using the Objective Structured Assessment of Technical Skill (OSATS) and the General Error Reporting Tool.

Results

This study included 366 patients (iAE group: n = 72 [19.7%] and non-iAE group: n = 294 [80.3%]). The proportion of ClassIntra grade II patients was the highest in the iAE group (54.2%). In total and distal gastrectomies, iAEs occurred most frequently in the suprapancreatic area (50.0% and 54.8%, respectively). In total gastrectomy, grade IV iAEs were most common during lymph node dissection in the splenic hilum area (once for bleeding [grade IV] and once for injury [grade IV]). The overall survival (OS) and disease-free survival (DFS) of the non-iAE group were significantly better than those of the iAE group (Log rank p 0.001). **Univariate analysis showed that tumor location, surgical procedure, tumor size, cT, cN, and OSATS scores were significantly associated with an increased risk of iAE (all p 0.05). A further multivariate analysis showed that BMI $\geq$ 28 (OR = 4.70), $cT_{2\text{-}4}$ (OR = 4.15), and cN_{+} (OR = 3.28) were independent risk factors for an increased incidence of iAE (all p 0.05), whereas a high OSATS score was an independent protective factor for iAE (OR = 0.62, p 0.001).**

Conclusions

iAEs in patients who underwent robotic radical gastrectomy significantly correlated with the occurrence of postoperative complications and a poor long-term prognosis. **Postoperative complications not only affect the postoperative recovery outcome but also the choice of the next treatment plan, due to the presence of serious and prolonged complications. The iAE group had advanced tumor stages, and high-risk factor analysis showed that they were more likely to experience iAEs.** Therefore, the utilization and inclusion of ClassIntra grading as a crucial surgical quality control and prognostic indicator in the routine surgical quality evaluation system are recommended.

sciforum-085223: Cancer Stem Cells as Potential Targets of Phytotoxic Alkaloids: Drug-likeness Prediction and Molecular Docking Studies

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Targeting cancer stem cells (CSCs) in anticancer discovery is very difficult due to the resistance of CSCs to conventional drugs, their low proliferation rate, improved DNA damage repair, and the overexpression of anti-apoptotic proteins and multidrug resistance transporters. Different CSC targets, such as the ABC cassette, surface markers, signal cascade, and tumour microenvironment, are involved in the interruption of cell signaling pathways that are critical for the survival and functioning of the CSC population. The study aims to identify potential drug-like phytotoxic alkaloids with anticancer activity from the toxic plants-phytotoxins (TPPTs) database. A total of 1586 phytotoxins were filtered to obtain 653 alkaloids. Lipinski's properties and the TPSA of alkaloids were predicted for drug likeness and toxicity based on various organ endpoints. Compounds that obeyed Lipinski's rule of five, with moderate or no toxicity and an LD_{50} of >2000 mg/kg, were selected. The 12 drug-like phytotoxic alkaloids obtained from the filtering were docked on an isomerase-perdeuterated E65Q-TIM protein (ID: 7AZA; resolution = 1.10 Å) cocrystallized with phosphoglycolohydroxamate. The best binding poses were ranked using their binding energies (E) and inhibition constants (Ki). An evaluation of the protein—ligand's best conformational poses allowed us to identify three alkaloids (norcoclaurine, palustridiene, and apovincamine) with Ki 1.00 μM and E −9.00 kcal/mol. All the docked ligands could bind more efficiently to the isomerase-perdeuterated E65Q-TIM protein than the co-crystallized phosphoglycolohydroxamate. Significant protein—ligand binding interactions also occurred for (-)-eburnamonine (E = −8.03 kcal/mol; Ki = 1.30 μM) and retamine (E = −7.81 kcal/mol; Ki = 1.89 μM). The efficient inhibition of perdeuterated E65Q-TIM in CSCs usingphytotoxic alkaloids provided more insights into understanding the mechanisms of the anticancer activity of phytotoxic alkaloids.

sciforum-085117: Chordoma Treatment with Boron Neutron Capture Therapy (BNCT): Experimental Insights

Yoshiki Fujikawa [1], Shinji Kawabata [1], Kohei Tsujino [1], Hideki Kashiwagi [1], Yusuke Fukuo [1], Ryo Hiramatsu [1], Hiroki Tanaka [2], Naonori Hu [3], Toshihiro Takami [1] and Masahiko Wanibuchi [1]

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Background

Boron neutron capture therapy (BNCT) is a particle beam therapy that enables the precise targeting of tumors at the cellular level. Drawing on the success observed in nuclear reactors, BNCT holds promise as a therapeutic approach for addressing invasive brain tumors, such as malignant gliomas and high-grade meningiomas.

Chordomas are rare bone tumors characterized by locally invasive, frequent recurrence, and relative radioresistance. Recently, treatment modalities, including proton or carbon ions particle irradiation, have been developed; however, conclusive evidence supporting their efficacy is yet to be established. This experimental study aimed to evaluate the effectiveness of BNCT in the treatment of chordoma.

Methods

The U-CH1 and JHC7 human chordoma cell lines were employed in this study. In the in vitro experiment, both cell lines were exposed to p-boronophenylalanine (BPA) at a concentration of 10 μg boron/ml for duration of 3, 6, and 24 h. Subsequently, the measurement of cellular boron uptake was conducted using Inductively Coupled Plasma Atomic Emission Spectroscopy (ICP-AES). After 24 h of exposure, the medium was replaced with a boron-free medium, and the subsequent investigation was focused on boron clearance. Neutron irradiation was then applied to these two cell lines, BNCT with BPA (10 μg Boron/mL for a 24-h exposure before irradiation) (BNCT group), and neutron irradiation without BPA (hot control group), for 0 to 30 min. Assessment of the cell-killing effect was carried out using a colony forming assay. In the in vivo experiment, subcutaneous tumor-bearing mice were intravenously administered BPA (250 mg/mouse body weight). After 1 h, the mice were sacrificed, and the boron concentrations in both the tumor and each organ were measured using ICP-AES.

Results

In the in vitro BPA exposure experiment, U-CH1 exhibited an increase in cellular boron uptake with prolonged BPA exposure time, whereas JHC7 demonstrated a consistent uptake unaffected by exposure time. Both cell lines showed a rapid decrease in cellular boron concentration after incubation with boron-free medium. Neutron irradiation revealed that the BNCT group demonstrated a more pronounced cell-killing effect than the hot control group in both cell lines. In the in vivo biodistribution of boron, the tumor accumulation was 5.7 μg B/g with a tumor-to-blood ratio (T/Bl) of 1.3 in U-CH1, while JHC7 showed a tumor accumulation of 9.3 μg B/g, with a T/Bl of 1.5.

Conclusions

Despite the relatively low intracellular boron uptake compared to other malignant tumors, these findings suggest that BNCT may represent an effective approach in the management of chordoma. Future efforts will include in vivo neutron irradiation experiments to more fully assess the effects of BNCT on survival and neurological function.

sciforum-085295: Combining Avoidance Structure and Jaw-Tracking Techniques to Reduce the Dose to Lens in Radiotherapy for Sinonasal Cancer

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Purpose

To assess the effectiveness of avoidance structure (AS) techniques, alone and in combination with jaw-tracking (JT) techniques, in the treatment of sinonasal cancer, with the aim of minimizing radiation exposure to the lens.

Methods

Thirty patients were included in the study, and three sets of intensity-modulated radiation therapy (IMRT) plans were designed in an Eclipse treatment planning system: (1) original plans (O-Ps) with seven non-coplanar fields were optimized to meet clinical criteria; (2) duplicated O-Ps were re-optimized using the AS technique (AS-P), specifically for lens structures while keeping other optimization conditions consistent; and (3) utilizing both AS and JT techniques to generate a third set of plans (AS-JT-P). Dosimetric parameters, including dose to target volume and organs at risk (OARs), were evaluated. Additionally, the Lyman—Kutcher—Burman (LKB) model was utilized to predict the normal tissue complication probability (NTCP) of OARs. The data from three sets of treatment plans were collected and compared.

Results

Compared to O-P, the average reduction of $D_{2\%}$ for the lens in AS-JT-P was approximately 2–3 Gy, with a corresponding average NTCP reduction of 0.1–0.3%. The AS-P reduced the $D_{2\%}$ of the contralateral lens by approximately 1Gy. The differences mentioned above were statistically significant (p 0.05). Additionally, the AS technique resulted in a slight deterioration in dose uniformity and conformity for the target volume, with minimal impact on other OARs.

Conclusions

The combination of AS and JT techniques can effectively minimize the radiation exposure to the lenses, reducing the risk of radiation-induced cataract. The use of AS and JT techniques is recommended in clinical practice for the treatment of sinonasal cancer.

sciforum-085321: Comparative Study of Long-Term Efficacy and Safety of Neoadjuvant Chemotherapy before Radical Surgery versus Concurrent Chemoradiotherapy for FIGO 2018 Stage IB3/IIA2 Cervical Squamous Cell Carcinoma: A Propensity Score-Matched Analysis

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Introduction

Cervical cancer remains a significant public health problem affecting middle-aged women, particularly in less resourced countries. Three-dimensional conformal radiotherapy (3DCRT) is still a commonly used radiotherapy technique in countries with fewer resources. This study was conducted to compare the long-term efficacy and safety of neoadjuvant chemotherapy before radical surgery (NCRS) and concurrent chemoradiotherapy (CCRT) for FIGO 2018 stage IB3/IIA2 cervical squamous cell carcinoma in a resource-limited setting where only a 3DCRT radiotherapy technique was accessible.

Methods

This retrospective study encompassed a cohort of 300 patients diagnosed with FIGO 2018 stage IB3/IIA2 cervical squamous carcinoma, who received treatment at Tianjin Central Hospital of Gynecology Obstetrics (Tianjin, China) from January 2011 to December 2016. The primary data utilized in this study can be accessed online without any restrictions. The clinical outcomes and incidence rates of adverse effects in 137 patients with stage IB3/IIA2 cervical squamous cell carcinoma who underwent neoadjuvant chemotherapy followed by radical surgery (NCRS) with those of 163 patients who underwent concurrent chemoradiotherapy (CCRT) were compared. None of these patients had received adjuvant chemotherapy or adjuvant radiotherapy after surgery or CCRT. Propensity score matching analysis was used to match the two groups, considering factors such as age, anemia, tumor diameter, degree of pathological differentiation, and clinical stage, to enable further statistical comparisons. Survival analysis was conducted using Kaplan—Meier curves, log-rank tests, and Cox proportional hazards regression analyses. Additionally, chi-squared tests were employed to compare the incidence rates of recurrence and adverse effects between the two groups.

Results

Propensity score matching identified 103 matched pairs of patients. The NCRS and CCRT groups displayed 5-year overall survival (OS) rates of 85.4% and 91.2%, respectively, with no statistically significant difference ($p = 0.19$). Additionally, the NCRS and CCRT groups exhibited 5-year disease-free survival (DFS) rates of 76.7% and 89.3% ($p = 0.02$), and the recurrence rates were 20.4% and 9.7% ($p = 0.03$), respectively. Notably, the CCRT group exhibited a higher incidence of early adverse events (including myelosuppression, gastrointestinal, and urinary complications) compared to the NCRS group. This difference was observed in both any-grade adverse events (79.6% vs. 35.9%, p 0.001) and grade-3 adverse events (15.5% vs. 0.03%, $p = 0.005$). There was no statistically significant disparity observed between the two groups in relation to late adverse events. In the multivariate analysis of clinicopathologic characteristics for OS, stage IIA2 (HR 8.51; $p = 0.037$) emerged as an independent risk factor, while histologic grade 2–3 (HR 4.88; $p = 0.03$) and anemia (HR 2.76; $p = 0.025$) were identified as independent risk factors for DFS.

Conclusions

Although the incidence of early side effects was increased in patients treated with CCRT, patients had significantly higher DFS rates and lower recurrence rates compared to those treated with NCRS. In patients with FIGO 2018 stage IB3/IIA2 squamous cervical cancer, CCRT seems to be a better option compared to NCRS in a resource-limited setting where only a 3DCRT radiotherapy technique was available.

sciforum-085300: Design and Synthesis of Novel Triarylethylenes as Proteasomal Inhibitors and Anti-Cancer Agents

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Protein homeostasis or proteostasis is achieved through a dynamic balance between protein synthesis and degradation. The ubiquitin proteasome pathway is responsible for the breakdown of approximately 80% of intracellular proteins. The protein is firstly tagged by ubiquitin molecules, and then targeted for degradation by the proteasome. Abnormalities in protein synthesis, folding, transportation, degradation, chromosomal imbalance, oncogenic activation, and translation errors can lead to an imbalance in the protein homeostasis and result in a wide range of human illnesses and diseases, such as cancer, autoimmune diseases, and neurodegenerative disorders.

Proteasome inhibition has emerged as a powerful strategy for anti-cancer therapy. The constitutive proteasome, commonly referred to as the 26S proteasome, is a large, multicatalytic enzyme complex of approximately 2.5 MDa, consisting of a 20S catalytic core particle made up of seven α subunits (α 1-7) and seven β subunits (β 1-7), with catalytic protease activity residing in the β1, β2, and β5 subunits. The 20S core is associated with one or two regulatory particles, which could be 19S (PA700), which is ATP-dependent, as well as 11S (PA28, PA26, REG) or PA200 which are ATP-independent.

Proteasome inhibitors mediate their apoptotic effect in tumor cells via the inhibition of NFκB activity, inhibition of angiogenesis and DNA repair, altered degradation of cell-cycle-related proteins, altered pro-apoptotic and anti-apoptotic protein balance, and endoplasmic reticulum stress.

Ridaifen (RID) compounds are tamoxifen (TAM) analogues, with RID-F featuring two homopiperidine moieties on rings B and C. RID-F was the most effective in inhibiting all three proteasome functions, which are chymotrypsin-like (CT-L), trypsin-like (T-L), and caspase-peptidyl glutamyl peptide hydrolase (PGPH).

Besides the established role of proteasome inhibitor (PI) drugs in the treatment of hematological malignancies such as multiple myeloma and mantle cell lymphoma, PIs have emerged as promising drug candidates for other conditions, including neurodegenerative disorders, inflammation, immune diseases, ischemic stroke, and tuberculosis.

In light of this, we report the design and synthesis of novel ridaifen analogues that target the proteasome enzyme. The synthesized analogues maintained the triphenylethylene scaffold of ridaifen, while varying the substituents on rings A, B and C.

sciforum-085397: Development of Letrozole-Loaded Magnetic Nanoemulsion Used for Breast Cancer Treatment

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Introduction

Emulsions are attractive delivery systems for hydrophobic drug molecules compared to hydrophilic drug molecules. An emulsion is a biphasic liquid preparation, containing two immiscible liquids. In the delivery of therapeutically active compounds, nanoemulsions have gained considerable interest because approximately 50% of new chemical entities are hydrophobic. Nanoemulsions are a group of dispersed particles which are used as pharmaceutical biomedical aids and vehicles that show great promise for the future of cosmetics, diagnostics, drug therapies, and biotechnologies. To achieve targeted drug delivery and to reduce side effects, we have prepared a magnetic nanoemulsion.

Methods

Using both high-and low-energy methods, we will prepare the nano emulsion. Microfluidization, ultrasonication, and high-pressure homogenization are examples of high-energy methods, whereas we will also use low-energy techniques like the phase inversion emulsification method and the self-nanoemulsification method. We also may use the self-nanoemulsification method for the preparation and formulation of letrozole magnetic nanoemulsion.

Results

The pseudo ternary phase diagram explains the optimal concentration of excipients. The studies reported that the formulation was stable under the magnetic field. In vitro characterization studies have reported that the average globule size of the LMNEs was 49.63 nm, with a charge of 26.9 eV and a polydispersity index of 0.428. FT-IR results showed that citric acid successfully stabilized the magnetic nanoparticles and confirmed that interaction between the drug and liposomes. The report also found the rheological properties of LMNEs.

Conclusions

The nanoemulsion formulation parameters were evaluated to indicate that the results were obtained within an acceptable range. From in vitro data, it can be concluded that the developed magnetic nanoemulsion has great potential with better pharmaceutical and therapeutical properties. Letrozole magnetic nanoemulsion is a suitable module used for controlled and targeted drug delivery in order to combat breast cancer. The formulation of a letrozole-loaded magnetic nanoemulsion was performed and in vitro cell line studies and pre-clinical studies may be performed in the future.

sciforum-085385: Development of Synergetic Combinations of a Novel Apoptosis Inducer with AKT and Hsp90 Selective Inhibitors Targeting Hormone-Sensitive and Hormone-Resistant Breast Cancer Cells

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Introduction

The design and development of antitumor compounds based on an isatin core led to the synthesis of 1-substituted isatin-5-sulfonamides with potent antiproliferative activity. This investigation is aimed at new 1-substituted isatin-5-sulfonamides with pro-apoptotic properties alone and in combination with AKT and Hsp90 inhibitors on hormone-sensitive and hormone-resistant breast cancer cells.

Methods

The synthesis of target 1-substituted isatin-5-sulfonamides involved 3 stages. The alkylation of isatin-5-sulfonamide via various benzyl chlorides allowed us to synthesize previously unknown series of 1-substituted isatin-5-sulfonamides. 4-Hydroxytamoxifen (HT) was used to develop a MCF7-resistant subline (MCF7/HT) via the long-term incubation of MCF7 cells with HT. MCF7 cells were transfected with the p53 luciferase reporter plasmid to obtain MCF7/p53-LUC cells.

Results

1-(4-((trifluoromethyl)thio)benzyl)isatin-5-sulfonamide (LCTA-3344) exhibited the highest antiproliferative activity, suppressing tumor cells at low micromolar concentrations. After the development of the resistant subline, the IC_{50} values of HT were 5.1 $\pm$ 0.3 μM (MCF7) and 10.2 $\pm$ 0.4 μM (MCF7/HT), and a resistance index (RI) of 2 was found. Compound LCTA-3344 showed higher antiproliferative activity in MCF7/HT (IC_{50} = 1.4 $\pm$ 0.1 μM), than in MCF7 (2.6 $\pm$ 0.3 μM). A search for effective combinations with AKT Inhibitor IV (6-(2-benzothiazolyl)-1-ethyl-2-[2-(methylphenylamino)ethenyl]-3-phenyl-1H-benzimidazolium, monoiodide), AKT Inhibitor X (10-DEBC; 2-chloro-N,N-diethyl-10H-phenoxazine-10-butanamine), and Hsp90 Inhibitor (luminespib, NVP-AUY922; 5-[2,4-dihydroxy-5-(1-methylethyl)phenyl]-N-ethyl-4-[4-(4-morpholinylmethyl)phenyl]-3-isoxazolecarboxamide) was performed. The combinations of LCTA-3344 and AKT Inhibitor IV on MCF7 and MCF7/HT were synergetic with combination index (CI) values equal to 0.8 and 0.4 (a higher effect), correspondingly. For comparison, combinations of LCTA-3344 with 10-DEBC and luminespib did not demonstrate such a high effect with a minimal value of CI 0.9. MCF7/p53-LUC cells were used to assess p53 activity. LCTA-3344 did not increase luciferase activity in MCF7/p53-LUC cells, whereas doxorubicin has been identified as its strong inducer.

Conclusions

A leading 1-substituted isatin-5-sulfonamide LCTA-3344 was 1.9 times more effective against MCF7/HT, than parental cells. The most effective drug combination was LCTA-3344 with AKT Inhibitor IV on the MCF7/HT subline, CI 0.4. The isatin-5-sulfonamide LCTA-3344 induced apoptosis with the p53-independent

mechanism, which may provide a basis for novel therapeutic strategies in the treatment of hormone-resistant breast cancers.

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sciforum-085206: Evaluation of the Safety of Folate Receptor-Targeted Boron Carrier in Boron Neutron Capture Therapy (BNCT) for Malignant Gliomas Using CED Administration

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Introduction

Knowing how to accumulate boron into the tumor cells is a crucial aspect of boron neutron capture therapy (BNCT), which can be targeted at the cellular level, and the development of novel boron agents other than BPA, which is used in clinical practice, is urgently needed. Our previous work demonstrated the efficacy of BNCT in malignant gliomas using PBC-IP, a pteroyl-*closo*-dodecaborate-conjugated 4-(p-iodophenyl) butyric acid with folate receptor targeting. Administered through convection-enhanced delivery (CED), PBC-IP resulted in long-term survival equivalent to cure, surpassing BPA outcomes. While the local administration method has been employed for the treatment of brain tumors using this drug, its applicability extends to cancers in other organs throughout the body through intravenous administration. Consequently, this report emphasizes the safety of BNCT treatment with this drug, examining both local dosing in the brain and intravenous administration in the experimental investigation. This study focuses on assessing PBC-IP's safety in CED procedures and implications for clinical application.

Methods

PBC-IP was administered intravenously or via CED to normal Fischer rats. At the predetermined time, each organ was collected and boron concentration was measured via Inductively Coupled Plasma-Atomic Emission Spectroscopy (ICP-AES). The intravenous administration of PBC-IP aimed to evaluate toxicity in cases where the tip of the CED catheter was implanted in the normal brain or accidentally inserted into a blood vessel. Additionally, CED administration of PBC-IP to normal rats aimed to evaluate the extent of drug clearance from normal tissues. PBC-IP concentrations were set at a maximum of 5000 μg B/mL for intravenous administration and 1500 μg B/mL for CED.

Results

Upon PBC-IP administration intravenously, no indications of apparent toxicity were observed in post-administration assessments. Furthermore, the boron concentration in each organ was within acceptable limits. The maximum boron concentration was 10.3 ± 0.8 μg B/g in the liver at a dose of 200 μL of PBC-IP 5000 μg B/mL. The boron concentration in the brain on the same side as PBC-IP CED administration exhibited a gradual decrease, while boron concentrations in other organs were minimal (the boron concentrations in each organ were less than 1 μg B/g).

Conclusions

Safety assessments revealed no apparent toxicity with intravenous administration, and acceptable boron concentrations in organs. CED administration exhibited gradual brain boron reduction, minimizing concentrations in other organs. Furthermore, the potential of BNCT with intravenous administration of this drug for cancers in organs other than the brain has been explored, and the safety of the drug in such scenarios has been established. PBC-IP emerges as a non-toxic, swiftly cleared boron agent, offering promise for BNCT applications. Future clinical prospects are encouraging, positioning PBC-IP as a potential breakthrough in boron neutron capture therapy.

sciforum-085313: Exploring the Antimicrobial and Anticancer Potential of a Bioactive Peptide from *T. radiatus*: A Comprehensive Study

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Therapeutic peptides have emerged as a promising frontier in the development of anti-cancer agents, classified into three main groups: antimicrobial/pore-forming peptides, cell-permeable peptides, and tumor-targeting peptides. This classification, delineates the diverse cellular targets of these peptides, offering a comprehensive perspective on their potential applications in cancer treatment. Antimicrobial/pore-forming peptides (AMPs) represent a subset of these therapeutic peptides with natural occurrences across living organisms, integral to the innate immune defense mechanism. This study focuses on a bioassay-guided fractionation approach to purify a bioactive peptide (PAP) from the soft body tissue of marine gastropod *T. radiatus*, highlighting its multifaceted properties, utilizing sequential procedures such as ammonium sulfate precipitation, cation exchange chromatography, and gel filtration chromatography. The purified antibacterial peptide (PAP), exhibited exceptional efficacy against both Gram-positive and Gram-negative bacteria, particularly demonstrating sensitivity towards *E. faecium*, *K. pneumoniae*, and *S. dysenteriae*. Further characterization revealed PAP's stability across broad pH and temperature ranges, serum stability, and the ability to form membrane pores, as evidenced by SEM analysis. PAP displayed stability across diverse conditions and the ability to form membrane pores, suggesting a potent antimicrobial mechanism. Significantly, PAP demonstrated noteworthy anticancer activities by inhibiting proliferation in lung cancer cell lines (A549 and NCI-H460) in a concentration-dependent manner, while exhibiting non-cytotoxicity to normal cells. This selective anticancer effect was further evidenced by the promotion of angiogenesis in chick embryos. The amino acid sequence of PAP (MSMGSFGFALAVMVLAVLVASAAGAPNTNLVSSACNGNKIPSGNPFFNNLGALLVDLEK) and its three-helix structure with an extended loop were determined through MALDI-TOF-MS/MS analysis and in-silico modeling, respectively. In conclusion, this research unveils the multifaceted nature of the bioactive peptide from *T. radiatus*, emphasizing its dual-action as a potent antimicrobial agent and a selective anticancer drug candidate. These findings underscore the potential therapeutic significance of marine peptides in addressing global health challenges, particularly in the context of antimicrobial resistance and cancer treatment.

sciforum-084474: Hippocampus-Sparing Volume-Modulated Arc Therapy (HS VMAT) for Patients with World Health Organization Grade II Gliomas: A Feasibility Study

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Introduction

Radiotherapy can improve the survival rates of patients with gliomas; meanwhile, the impaired cognitive functions have been brought to the forefront, with the offending organ, radiosensitive hippocampus. Moreover, there is no further research exploring whether we can minimize the radiation dose to the hippocampus using volumetric-modulated arc therapy (VMAT) as the treatment for gliomas. This study aimed to assess the feasibility of hippocampus-sparing volumetric-modulated arc therapy (HS VMAT) in patients with WHO Grade II gliomas.

Materials & Methods

Hippocampus-sparing VMAT plans and non-hippocampus-sparing VMAT plans were generated using a computed tomography (CT) dataset of 10 patients with WHO grade II gliomas who underwent postoperative radiotherapy. The gross target volume (GTV), organs at risk (OARs), and hippocampus were localized based on the CT images and modified according to the pre-treatment MRI images in fusion. The prescribed dose for both radiotherapy plans was 54 Gy/30 F to primary tumor volume (PTV). The dose volume histogram (DVH), homogeneity index (HI), conformity index (CI), and irradiated dose of the hippocampus and other OARs were analyzed.

Results

The HI (0.057 ± 0.014 vs. 0.046 ± 0.009, $p = 0.011$) and CI (0.91 ± 0.02 vs. 0.92 ± 0.02, $p = 0.071$) for both HS VMAT plans and NHS VMAT plans were clinically acceptable. Regarding the protection of OARs, HS VMAT plans were equally capable and even lowered the radiation dosages to the brainstem (35.56 ± 16.67 vs. 41.74 ± 16.18, $p = 0.017$) and spinal cord (1.34 ± 0.77 vs. 1.43 ± 0.80, $p = 0.006$). The HS VMAT plans substantially reduced radiation doses to the hippocampus. The ipsilateral hippocampal Dmin, Dmean, Dmax, and D40% for NHS VMAT plans and HS VMAT plans were 22.33 ± 19.12 vs. 7.80 ± 4.20 ($p = 0.005$), 35.20 ± 19.58 vs. 18.60 ± 8.52 ($p = 0.005$), 45.37 ± 16.84 vs. 34.28 ± 12.79 ($p = 0.013$), and 36.73 ± 19.52 vs. 19.98 ± 9.63 ($p = 0.005$). While the contralateral hippocampal Dmin, Dmean, Dmax, and D40% of the two plans were 9.68 ± 6.51 vs. 3.38 ± 1.12 ($p = 0.005$), 16.86 ± 8.86 vs. 4.86 ± 0.91 ($p = 0.006$), 29.13 ± 13.88 vs. 8.41 ± 1.38 ($p = 0.001$), and 17.30 ± 9.14 vs. 4.89 ± 0.94 ($p = 0.005$), respectively.

Conclusions

The use of the HS VMAT plan is feasible, which can effectively reduce the dosage delivered to the hippocampus while not significantly exacerbating the HI, CI, and OARs. Consequently, it may help mitigate the risk of cognitive impairment to a certain extent.

sciforum-083389: Homoharringtonine Impedes Hypoxic Colorectal Carcinoma Cell-Induced Angiogenesis via Inhibiting HIF-1α/VEGF Signalling

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Abstract: Hypoxia is a key component of the tumour microenvironment, and it is linked to cell proliferation, angiogenesis, metabolism, and the tumour immune response. All of these variables may accelerate tumour growth, increase tumour aggressiveness, raise tumour metastatic potential, and result in a poor prognosis. The goal of this trial was to determine if the pharmaceutical substance Ometaxine mepesuccinate, commonly known as Homoharringtonine or (HHT), is effective. Cephalotaxus fortunei is the source of natural plant alkaloids. HHT is a chemical derived from traditional Chinese medicine that has been licenced by the Food and Drug Administration for the treatment of leukaemia. Previous research has suggested that HHT might limit protein synthesis and promote apoptosis by upregulating the proapoptotic protein Bax and triggering the caspase-3-mediated cleavage of PARP. Aside from hematologic tumours, HHT has also been shown to be useful in renal cell carcinoma, colon rectal cancer, and non-small cell lung cancer. The impact of HHT on CRC, as well as the underlying HIF-1/VEGF-associated mechanisms of action, have not been explored. Tube formation was used to measure in vitro angiogenesis. A cell viability assay, scratch assay, real-time PCR, enzyme-linked immunosorbent assay and immunoblotting were used to analyse the gene and protein expressions of hypoxia-inducible factor-1 (HIF-1) and vascular endothelial growth factor (VEGF). The development of hypoxic HUVEC cell tubes is inhibited by HHT. In CRC SW480 cells, HHT reduced hypoxia-induced VEGF overexpression at both the mRNA and protein levels. Furthermore, HHT suppressed HIF-1a-induced angiogenesis in vitro via inhibiting HIF-induced ERK phosphorylation. Hypoxia raised HIF-1 mRNA and protein levels, which were all suppressed by HHT. Hypoxia significantly elevated ERK and AKT phosphorylation in CRC cells, which HHT reduced. By reducing HIF-1/VEGF-mediated intercellular communication between CRC cells and endothelial cells, HHT decreased hypoxic CRC cell-induced angiogenesis. We think that HHT could be an ideal candidate for CRC tumour inhibition and needs more investigation for further study.

sciforum-082655: Impact of Removal of Lymph Nodes on Survival in Stage I-III Gastric Signet-Ring Cell Cancer: The More, the Better?

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Background

There is an ongoing debate over the prognostic value of the number of examined lymph nodes (ELNs) in cases of gastric signet-ring cell cancer (GSRCC). In this study, we sought to evaluate the correlation between the number of ELNs and the prognosis of GSRCC and identify the optimal number of ELNs.

Methods

A total of 1020 patients diagnosed with GSRCC between 2011 and 2018 in the National Cancer Center (NCC) database were identified. Clinicopathological characteristics were retrospectively collected, and the optimal cutoff values of ELNs were calculated using X-tile. The impact of different ELNs on overall survival (OS) was compared using Kaplan-Meier curves. We used univariate and multivariate Cox and subgroup analyses to explore the relationship between ELNs and OS. Furthermore, nonlinear correlations were investigated using restricted cubic splines (RCSs).

Results

X-tile showed that the optimal cutoff value of ELNs was 22. The 5-year OS was higher for patients with ELNs > 22 (vs. ELNs $\leq$ 22, 66.9% vs. 74.9%, p = 0.026). Multivariate Cox analyses showed that high ELNs were associated with superior OS (HR = 0.56, 95% CI = 0.43-0.74, p 0.001). In subgroup analyses, the significant association between tumor size > 4 cm and TNM III stage was still observed. The RCS regression model showed a U-shaped nonlinear dose–response relationship between ELNs and OS; the inflection point, as well as the lowest risk points, corresponded to 44-52 ELNs.

Conclusions

A U-shaped nonlinear correlation, with inflection points of 44-52 ELNs, between ELNs and prognosis in GSRCC was identified.

sciforum-085429: Machine Learning Strategies for Drug Discovery in AML: Focus on RUNX1 Bioactivity

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Acute myeloid leukemia (AML) is an aggressive blood cancer where immature stem cells in the bone marrow multiply rapidly, disrupting blood cell production and leading to infections, anemia, and bleeding. This devastating disease claims around 85,000 lives annually and is projected to double by 2040, highlighting its critical importance for research and improved treatment strategies. The RUNX1 transcription factor, a critical gene for hematopoiesis, is highly prevalent in AML and linked to poor patient outcomes. Mutations disrupt RUNX1's function, essentially acting as a "bad switch" that promotes aggressive leukemia growth and significantly reduces survival chances. Targeting this master regulator holds promise for developing novel therapies to improve patient outcomes in AML.

In the current study, we utilized a Computational drug discovery approach, involving bioactivity data retrieval for Human RUNX1 "CHEMBL2093862" from the CHEMBL database, where RUNX1 is the target protein. Performed a chemical space analysis using Lipinski descriptors to identify whether the compounds have the properties of ideal drugs or not. Calculated molecular descriptors, specifically PubChem fingerprints, to see the unique structure of the compounds. Applied machine learning algorithms like Random Forest, Linear Regression, Decision Tree, and XGBoost to create a model to classify whether the compounds are active or inactive. Culminates in a user-friendly bioactivity prediction app using Streamlit so researchers can check for the bioactivity and potency of drugs in real-time for targeting RUNX1 in AML. This study introduces a comprehensive plan for drug development targeting RUNX1, offering potential interventions for AML mediated by RUNX1.

sciforum-085104: Oncolytic Viral Therapy with Gravity Approaching Zero to Ameliorate Glioblastoma Multiforme

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Glioblastoma multiforme (GBM) is the most common aggressive malignant primary brain tumor, afflicting approximately 3 in every 100,000 persons in the United States, with an incidence rate that is 1.6 times higher in males compared to females. Arising from the neural and/or glial progenitor/stem cells, GBM is commonly located in the supratentorial cortical region affecting the frontal lobes. The rapid local growth and spread of GBM leads to a dismal prognosis with a 5-year survival rate of 6.9%, despite multiple therapeutic interventions, including surgery, radiotherapy, and chemotherapy. To overcome the challenge to develop curative treatments of GBM, several promising experimental methods (immune therapy, gene therapy, simulated microgravity therapy, and oncolytic viral therapy) are under investigation. Potentially beneficial effects of microgravity on GBM include (A) the repression of survival signaling pathways, (B) the induction of the apoptosis of cancerous cells, and (C) the blocking of spherical colony formation and cellular proliferation via the downregulation of ATM/ATR and CDK1/2 proteins to block cellular phase 2 to progress to G2. We combined oncolytic viral therapy using an autonomous rat parvovirus H1 with simulated microgravity, in turn utilizing the potentially beneficial effects of microgravity on tumor cells (decreased cell proliferation, disrupted mitochondrial functions, and the induction of apoptosis) (Elshourbagy, T.; Brašić, J.R. Amelioration of glioblastoma multiforme via the combination of simulated microgravity and oncolytic viral therapy. Med. Sci. Forum. 2023; 20: 9. https://doi.org/10.3390/IECC2023-14219) and was limited by the use of simulated microgravity on earth. We now propose to conduct similar investigations on space stations where gravity approaches zero. We hypothesize that oncolytic viral therapy in space without gravity will (A) lyse tumor cells through the induction of apoptosis, decreased cell proliferation, and the induction of an immune response, and constitute the foundation of potentially curative treatments of GBM.

sciforum-085396: Optimization and Development of Magnetically Triggered Letrozole Nanoliposomes for Breast Cancer Targeting

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Background

Breast cancer is one of the most frequently diagnosed cancers and is the leading cause of death among women worldwide. Breast cancers are most common among women and they represent the second most common cancer condition. Moreover, breast cancers account for 14% of all cancers in women. The development of magnetic nanoliposomes as carrier-loaded drug delivery system promotes the active-site-targeted delivery of drug molecules with increased biocompatibility and reduced toxicity and side-effects.

Aim

The research work aims to develop and characterize magnetically letrozole nanoliposomes used for breast cancer targeting.

Methodology

The thin film hydration method is carried out in preparation of letrozole nanoliposomes. Citric-acid-coated magnetic nanoparticles are synthesized via the chemical co-precipitation method. The formulated nanosuspension is characterized through initial characterization studies.

Results

The characterization studies show that various physical, chemical, and morphological integrity of nanoliposomal suspension. In vitro characterization studies reported that the average hydrodynamic size of LET-MNLs was 89.23 nm with a charge of -24 mV and apolydispersity index of 0.395. The drug loading and encapsulation efficiency of the prepared formulation were studied at various stages to confirm the conjugation of letrozole with the magnetic nanoliposomal system, and the highest encapsulation efficiency was found to be 76.83%.

Conclusions

Liposomal nanocarriers promote targeted responses and iron oxide nanoparticles create an onsite action and lower the toxicity associated with unwanted biodistribution. Based on the results from pharmaceutical characterizations, the developed formulation is fit for targeted drug delivery applications. Further in vitro and in vivo studies will be carried out to assess the anticancer efficacy of developed formulation.

sciforum-085647: Synthesis and Preliminary Investigation of Metal Nanoparticles from the Stem Extract of *Bacopa* sp. for the Treatment of Lung Cancer

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Lung cancer is the third most common cancer in women and the most common cancer in males. Chemotherapy, allopathy, hormone therapy, radiation therapy, surgery, immune system, and targeted therapies are frequently used to treat lung cancer. These medications induce other diseases and have a variety of negative effects. Thus, we used a different strategy and sought to treat lung cancer with medicinal herbs. We selected the perennial creeping herb *Bacopa monnier*i, which belongs to the Scrophulariaceae family, among other medicinal herbs. It contains several active phytoconstituents, including sterols, alkaloids, flavanoids, terpenoids, and saponins. The primary component with anti-lung cancer efficacy is phytosterol, according to the components. According to the phytochemical investigation, this plant contained it. The literature review indicates that the problem is lessened by nanoparticle production. Thus, the novelty of our work is the manufacture of zinc oxide nanoparticles for the treatment of lung cancer using BM stem extracts. Researchers have been interested in ZnO material because of its huge band gap (3.37 eV) with n-type semi-conductivity and high excitonic binding energy (60 meV) with regards to the different semiconductor nanomaterials, such as TiO_2, SnO_2, GaN, CuO, GaAs, Si, and ZnO. Zinc oxide in bulk is economical and can be used for many different industrial processes, such as the creation of nanoparticles. Zinc acetate serves as the precursor and stem extract serves as the reducing agent in the synthesis. The absorbance peak between 300 and 400 nm in UV spectroscopy was used to characterize the ZnO nanoparticles that were produced from hydromethanolic BM stem extract. In later research, lung cancer treatment might be considered. Given that lung (A549) cell lines will be treated with phytosterol-containing hydromethanolic BM stem extract in the form of ZnO nanoparticles, which will cause cell death by reducing cell proliferation, DNA damage and apoptosis may occur.

Introduction

One of the main causes of illness and mortality worldwide is cancer. Among non-communicable diseases, cancer ranks second in terms of mortality, after cardiovascular disease. Globally, cancer is responsible for one in eight fatalities, which is more than the combined deaths from AIDS, TB, and malaria. Treatment options for this complex, multifactorial, heterogeneous disease include chemotherapy, hormone therapy, surgery, radiation, immune system, and targeted therapies. The disease's defining feature is the unchecked growth and spread of abnormal cells, which can be brought on by a variety of internal, external, genetic, and environmental factors.

Lung cancer is the second most common cancer in both men and women, and is a highly metastatic disease. When compared to other tumor types, lung carcinoma is the most common cause of cancer-related death and has the lowest economic impact. Lung cancer accounts for 1.6 million cancer deaths annually (roughly 20% of all cancer deaths) and an additional 1.8 million new cases worldwide each year, making it the leading cause of cancer mortality worldwide in both high-income and low- and middle-income countries.

Bacopa Species

A genus of 70–100 aquatic plants is called Bacopa. The term "water hyssop" is commonly used, although it is misleading because Bacopa is not closely related to hyssop despite having a very similar look. These have upright or decaying stems, and they can be annual or perennial. The leaves are sessile and twisted in the opposite direction. The leaf has a regular, round-to-linear blade with a palmate or pinnate vein. The stems might be smooth or hairy. Seeds and broken stems are dispersed throughout the area. The scent of crushed leaves strongly resembles lemon. Herbs have been shown in preliminary clinical work to improve memory.

Some of these plants are commonly utilized in warmer climates in freshwater ponds and aquariums.

Zinc Oxide Nanoparticles

In the industrial setting, bulk zinc oxide is inexpensive and useful for several processes, such as the creation of nanoparticles. As a result, it can withstand strong electrical fields, elevated temperatures, and high power usage. Wurtzite architecture is a predominant feature of ZnO nanocrystals, with lattice parameters of a = 0.3296 nm and c = 0.52065 nm. In its most basic form, ZnO exhibits tetrahedron geometry, where each ion is surrounded by four counterions that point in the direction of the tetrahedron's corners. Three main mechanisms have been identified by NPs to improve food and package consistency: the release of antimicrobial ions, the disruption of bacterial cell integrity, and the generation of reactive oxygen species (ROS) as a result of light exposure.

Aim

To prepare and investigate the ZnO nanoparticles with the stem extract of *Bacopa monnieri* for the treatment of Lung cancer.

Objectives

- To extract the components from the dried and powdered stem.
- To synthesize the ZnO nanoparticles.
- To screen the phytochemical components of the BM stem extract.
- To characterize the extracts and nanoparticles.
- To analyse the components present in it.

Results and Discussion

Cancer treatment has benefited greatly from the discovery of drugs derived from medicinal plants. Additionally, throughout the past 50 years, the majority of new therapeutic uses of plant derivatives and secondary metabolites have been developed to combat cancer. After that, the project research was conducted to examine the phytochemistry and anticancer potential of stem extract from *Bacopa monnieri* (L.).

Phytochemical Screening Test

Using established procedures, the phytochemical screening test was performed to verify that the stem extract included flavonoids, alkaloids, proteins, phytosterols, and carbs.

Characterisation of Zinc Oxide Nanoparticles

The creation of zinc oxide nanoparticles is confirmed by the absorbance peak seen between 300 and 400 nm. The optical characteristics of the produced ZnO NPs have been examined using UV—visible spectroscopy. Moreover, the heavy absorption band seen between 300 and 400 nm can be attributed to the intrinsic band gap absorption of ZnO due to the electron transitions from the valence band to the conduction band.

Conclusions

According to the aforementioned study, ZnO nanoparticles containing *Bacopa monnieri* stem extract contain phytosterols, which are used to cure lung cancer.

Following a battery of phytochemical screening assays, the hydromethanolic BM stem extract revealed the absence of quinoids, saponins, and phenols but the presence of proteins, carbohydrates, phytosterols, and flavonoids.

The next step is to create zinc oxide nanoparticles using a magnetic stirrer and a NaOH solution to modify the pH. The solution for white precipitate was made. Following centrifugation and drying, 23.2 mg of zinc oxide nanoparticles was produced.

UV—visible spectroscopy was used to describe the optical characteristics of the zinc oxide nanoparticles. In this case, the presence of zinc oxide nanoparticles was confirmed by the absorbance peak seen between 300

and 400 nm. We were unable to conduct FTIR analysis and detect the in vitro anti-cancerous activities of the synthesized ZnO NPs because of the pandemic conditions.

sciforum-084479: Thyroid-Sparing Volume-Modulated Arc Therapy (TS VMAT) in Patients with Non-Distant Metastatic Nasopharyngeal Carcinoma: A Feasibility Study

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Introduction

Radiotherapy is an important treatment for nasopharyngeal carcinoma (NPC), but it can cause damage to other normal organs while improving the survival rate of patients. The most common of these is an imbalance of thyroid hormones caused by radiation damage to the thyroid gland, which affects many important functions of the body, such as regulating body temperature, metabolism, cholesterol levels, and growth. Moreover, there is no further research exploring whether we can minimize the radiation dose to the thyroid using volumetric-modulated arc therapy (VMAT) as the treatment for non-distant metastatic NPC. This study aimed to assess the feasibility of thyroid-sparing volumetric-modulated arc therapy (TS VMAT) in patients with non-distant metastatic NPC.

Methods

This dosimetric feasibility study included 30 patients with non-distant metastatic NPC who were treated with radiotherapy at the Affiliated Cancer Hospital of Shantou University Medical College between 2020 and 2023. Computed tomography datasets of 30 patients and inverse-planning VMAT with Eclipse version 15.6 treatment planning systems were used to generate thyroid-sparing volume-modulated arc therapy (TS VMAT) plans and non-thyroid-sparing volume-modulated arc therapy (NTS VMAT) plans. These patients were divided into 3 groups, including the bilateral upper neck irradiation group (bilateral UNI group), the one-side lower neck irradiation group (one-side LNI group), and the bilateral lower neck iradiation group (bilateral LNl group) with 10 patients in each group. All target volumes and organs at risk (OARs) were delineated by the radiation oncologists, according to Guidelines of Chinese Society of Clinical Oncology (CSCO, version 2023) and the Chinese Guidelines for Radiation Therapy of Nasopharyngeal Carcinoma (version 2022). The two radiotherapy plans were evaluated using dose volume histograms, homogeneity index (HI) and conformity index (CI) of all PTVs, and irradiation doses to the thyroid and other OARs.

Results

There were no statistically significant differences in HI and CI between two plans in all groups. In comparison to the NTS VMAT plans, there was a significant reduction in radiation dose to thyroid in TS VMAT plans of all groups, both in terms of the mean dose (Dmean), the minimum dose (Dmin), and the volume irradiated with 40 Gy or more (V40). For the protection of OARs, TS VMAT plans in the bilateral UNI group showed lower radiation dosages to left parotids (30.63 ± 3.07 vs. 30.41 ± 3.08, $p = 0.025$*) and left eyeballs (23.63 ± 9.66 vs. 21.78 ± 9.05, $p = 0.006$*), and the irradiation doses to other OARs had no significant differences between the two plans in all groups, such as brainstem PRV, brainstem, spinal cord PRV, lens, optic nerves, pituitary, oral cavity, and larynx.

Conclusions

The use of TS VMAT plans appears to be a viable approach in radiotherapy planning for patients with non-distant metastatic NPC. TS VMAT plans effectively reduce radiation dose to the thyroid gland compared with NTS VMAT plans, thus mitigating patients' risks of developing hypothyroidism without exacerbating the homogeneity index (HI), conformity index (CI), and the irradiation doses to OARs. The encouraging results of

our study need to be further validated by clinical trials with larger sample sizes to establish a clear advantage in the protection of thyroid function in NPC patients treated with TS VMAT plans.

Abstracts

Session H. Cancer Pathophysiology

sciforum-085427: A Bone Marrow Biopsy Revealing an Exceptional Complication of Multiple Myeloma

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Introduction

Bone marrow necrosis (BMN) is a relatively rare discovery in bone marrow biopsies (BMB); it is estimated to be present in less than 1% of cases. BMN is defined as the destruction of both the myeloid tissue and the medullary stroma, with the preservation of bone structures.

BMN is most commonly attributed to malignancy and chemotherapy. That being said, heterologous causes such as medication and infection have been incriminated in BMN.

We describe the case of a patient diagnosed with multiple myeloma (MM) presenting initially with extensive necrosis of the bone marrow in their biopsy. A finding that, to the best of our knowledge, remains an exceptional manifestation of this condition, only being described in five cases in the literature previously.

Objective

The particular nature of our case lies in the rarity of this presentation, which renders BMB interpretation challenging to pathologists who are unfamiliar with this complication.

Materials and Methods

We report the case of Mrs A, a 67-year-old patient with a medical history of repeated transfusions for iron deficiency anaemia and a fracture of the femoral diaphysis. The patient presented initially with severe anaemic syndrome and an alteration of her general state, associated with ostealgia, epigastric tenderness and polyuria.

Blood count showed a non-regenerative normochromic normocytic anaemia that is associated with thrombopenia and myeloma. The biochemical profile of the patient showed a malignant hypercalcemia with an alteration in the renal function.

Imaging found multiple geographical osteolytic lesions of axial and appendicular topography.

Bone marrow aspiration was performed, showing a sample of poor cellularity and the presence of a population of suspicious lymphoid-like cells.

A bone marrow biopsy was performed and treated for histopathological study.

Results

A histological examination of the fragments obtained showed multiple regular osseous trabeculae bordering marrow spaces that contained extensive tumoral necrosis which took up approximately 80% of the entire sample. We also noted the presence of a tumoral proliferation of cells with hyperchromatic eccentric nuclei and an abundant basophilic cytoplasm evoking a plasmacytoid nature.

An immunohistochemical study was carried out showing a positive marking of plasmacytoid cells by the CD 138 antibody with Lambda monoclonality.

By combining the histopathological and immunohistochemical findings with the patient's history, clinical presentation and imaging results, the diagnosis of multiple myeloma was made.

Discussion and Conclusion

BMN is a rare finding in bone marrow biopsies and it is estimated that only around 300 cases have been reported in the literature. A detailed pathophysiology of this condition is yet to be properly established,

with the prevailing hypothesis involving elevated levels of TNF-alpha and interleukin-6 causing damage to endothelial cells in the microenvironment, which results in vascular occlusions and necrosis.

Clinically, patients present with ostealgia, fever, elevated alkaline phosphatase, markedly elevated LDH levels and peripheral cytopenias with typical findings of bone marrow necrosis, the extent of which allows for the grading of BMN: grade I with necrosis involving less than 20% of the bone marrow; necrosis occupies between 20 and 50% of the bone marrow in grade II; and eventually grade III where the necrosis extends beyond 50% of the bone marrow.

A ten-year study by Wool et al. showed that malignancy—both secondary to a metastatic tumour and haemato-lymphoid malignancy—was responsible for 90% of BMN cases. BMN was also associated with poor prognosis, with a mortality rate of 55% during follow-up; however, Zhu et al. reported two cases of BMN with MM who received prompt treatment and showed complete restoration of hematopoietic function.

BMN is an exceptional discovery in BMBs and its aetiology is largely dominated by malignancy. To the best of our knowledge, BMN in MM has only been described in five cases in the literature; as such, the rarity of this finding may pose difficulties for pathologists during interpretation. The importance of pathologists' awareness of this possibility is amplified by the understanding that BMN is not only associated with a poorer prognosis for patients, but also that prompt diagnosis and treatment have introduced the possibility of recovery.

sciforum-085425: Atypical Immunogenetic and Molecular Characteristics of a 15-Years-Old Male Affected by ETP-ALL (Early T-Precursor Acute Lymphoblastic Leukemia)

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ETP-ALL (early T-cell precursor acute lymphoblastic leukemia) is a high-risk subtype of early T-cell leukemia. The distinctive immunophenotype of ETP-ALL is characterized by CD1a-, CD8-, CD5-, or weak-positive 75%. The complex karyotype and genomic instability are well-known characteristics of ETP-ALL. Throughout all disease stages, we examined the karyotypes, protein expressions, immunophenotypes, and gene expression profiles. The relapse's karyotype analysis reveals new mutations not found during diagnosis, some of which are unprecedented in any ETP-ALL case reported in the literature. Alterations are present in chromosomes 4, 6, 16, and 18 (BCL-2 locus). Immunophenotype analysis shows drastic changes from diagnosis to relapse in ETP-ALL, including CD56 switch and unusual CD5 and CD8 switches. After comparing the patient's relapse-stage marrow with the healthy subject's control marrow and the non-ETP ALL subject at the same stage, protein analysis showed the IL23R-SGK1-RANBP1 asset is overexpressed, along with MARCH5 and BLC-2. Additionally, the expression of BIM, a negative regulator of BCL-2, decreases, as well as Mitofusin-2 (MFN2), which plays a role in mitochondrial fusion and network maintenance. A test conducted on ex vivo blasts confirms that Venetoclax is sensitive at different levels during the relapse phase but not in the early stages. This confirms that disease-related genetic changes led to blast expansion, dependent on BCL2, and is associated with the feedback regulation of transcript expression. Throughout the disease progression, we examined bone marrow and peripheral blood smears. These prove the failures of all therapeutic lines and HSCT, as well as the knockdown of leukemic blasts and the resumption of bone marrow activity (measured by neutrophil levels) with venetoclax administration. In summary, ourunderstanding of the BCL2 pathway's impact in ETP-ALL is limited, and the occasional use of venetoclax is not yet standardized in guidelines. Our results highlight the importance of assessing BCL2 expression in refractory ETP-ALL cases.

sciforum-085416: Deciphering the Role of USP16 in Lung Cancer

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Deubiquitylating enzymes are proteases that reverse the ubiquitination of proteins, an important process for maintaining normal homeostasis.

USP16 is a deubiquitylating enzyme that belongs to the family of ubiquitin-specific proteases (USPs) and is involved in cell cycle progression and chromatin remodeling.

To elucidate the role of USP16 in lung cancer progression, we first analyzed its expression in a cohort of biopsies obtained from patients with non-small lung cancer (N = 18). Real-time PCR analysis and Western blot analysis showed that USP16 is highly expressed in NSCLC tissues compared to normal tissues. To characterize the role of USP16, we used two lung cancer cell lines (NCI-H460 and A549), in which USP16 was knocked down by lentiviral RNA interference (shUSP16).

The knockdown of USP16 affects cancer cell behavior in terms of proliferation and drug sensitivity. The knockdown of USP16 reduces the proliferation of cancer cells (≈40%) compared to control cells, which is due to defects in mitotic cell phase. These effects could be attributed to the deubiquitinating effect on its substrates. Indeed, the silencing of USP16 decreased the protein stability of the transcription factor Myc and Polo like kinase-1 (PLK1). Conversely, we found that USP16 impaired the response of lung cancer cells to platinum-containing compounds. The reduction of USP16 expression impairs the cytotoxicity of cisplatin by approximately 50% compared to control cells. This could likely be due to the impaired recruitment of repair proteins in proximity of double-strand breaks (DSBs) in lung cancer cells. These results prompted us to perform further analysis to investigate the role of USP16 in DNA repair and drug sensitivity.

sciforum-085438: The Role of Exostosin Glycosyltransferase 1 (EXT1) in Ovarian Cancer

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Exostosin glycosyltransferase 1 (EXT1) is a glycosyltransferase involved in the elongation of the saccharide chain of heparan sulfate proteoglycans (HSPGs). HSPGs, also known as Heparanosome, are important components of the extracellular matrix (ECM) and the cell surface. The ECM profile has been extensively studied in high-grade serous ovarian cancer (HGSOC), but data on the involvement of HPSGs in platinum resistance are still incomplete.

HGSOC patients from the TCGA dataset (73 resistant and 107 sensitive) were stratified in terms of their response to platinum-based therapy. The copy number alterations (CNAs) that occurred in the TCGA patients, leading to altered mRNA expression, were analyzed using the PathScore algorithm. The biosynthesis of HSPGs was significantly (p 0.05) enriched in the resistant patients with a high percentage of amplifications of the Ext1 gene. EXT1 protein expression was analyzed by immunohistochemistry on a microarray of 25 resistant and 25 sensitive patients. EXT1 protein levels were elevated in 60% of resistant patients compared to 24% of sensitive patients (p 0.05). Ovarian cancer cells were transfected with an Ext1-expressing vector (COV318 and MDAH2774) and/or interfered by shRNAs targeting the Ext1 gene (shEXT1 OVCAR-5 and OVCAR-429) to investigate the deposition and distribution of HPSGs and to determine how they affect the signal transduction, cell motility and invasion, and drug sensitivity of cancer cells.

EXT1-overexpressing cells synthesized an increased amount of HSPGs and showed reduced sensitivity to platinum-based drugs, which could be restored by heparinase treatment. In contrast, cells which experienced EXT1 knockdown showed increased sensitivity to platinum-based drugs. Through the transcriptomics analysis of EXT1 knockdown cells, we detected significantly reduced expressions of the Lcn2, Cacna2d1, Edn1, and Tagln genes. In addition, the GO analysis of shExt1 knockdown cells revealed a lower enrichment of the EMT category, as reflected by reduced cell motility in vitro, which was analyzed by time lapse microscopy. These effects could be partly explained by the lower accumulation of INFg and TNFa in cells lacking EXT1. Our preliminary results suggest that Heparanosome architecture can alter the behavior of cancer cells and their response to external stimuli. These phenomena may play an important role in the development of recurrence in patients resistant to platinum-based drugs.

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