1st BALKAN CONFERENCE on BIOMEDICAL AND CANCER RESEARCH

Balkan.BMCR 2026

ABSTRACT BOOK

KNJIGA SAŽETAKA

September 03–05, Foča, Bosnia and Herzegovina

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1st BALKAN CONFERENCE on BIOMEDICAL AND CANCER RESEARCH
Balkan.BMCR 2026

FACULTY OF MEDICAL SCIENCES UNIVERSITY OF KRAGUJEVAC (*Serbia*)
CENTER FOR MOLECULAR MEDICINE AND STEM CELL RESEARCH
ФАКУЛТЕТ МЕДИЦИНСКИХ НАУКА УНИВЕРЗИТЕТА У КРАГУЈЕВЦУ (*Србија*)
ЦЕНТАР ЗА МОЛЕКУЛСКУ МЕДИЦИНУ И ИСТРАЖИВАЊЕ МАТИЧНИХ ЋЕЛИЈА

UNIVERSITY OF EAST SARAJEVO (*Bosnia and Herzegovina*)
FACULTY OF MEDICINE FOČA
УНИВЕРЗИТЕТ У ИСТОЧНОМ САРАЈЕВУ (*Босна и Херцеговина*)
МЕДИЦИНСКИ ФАКУЛТЕТ ФОЧА

UNIVERSITY OF BELGRADE (*Serbia*)
INSTITUTE FOR BIOLOGICAL RESEARCH "SINIŠA STANKOVIĆ"
УНИВЕРЗИТЕТ У БЕОГРАДУ (*Србија*)
ИНСТИТУТ ЗА БИОЛОШКА ИСТРАЖИВАЊА „СИНИША СТАНКОВИЋ"

UNIVERSITY OF APPLIED SCIENCES MERSEBURG
(*Germany*)
УНИВЕРЗИТЕТ ПРИМЕЊЕНИХ НАУКА МЕРЗЕБУРГ
(*Немачка*)

ACADEMY OF SCIENCES AND ARTS OF THE REPUBLIC OF SRPSKA
(*Bosnia and Herzegovina*)
АКАДЕМИЈА НАУКА И УМЈЕТНОСТИ РЕПУБЛИКЕ СРПСКЕ
(*Босна и Херцеговина*)

PUBLIC HEALTH INSTITUTE KRAGUJEVAC
(*Serbia*)
ИНСТИТУТ ЗА ЈАВНО ЗДРАВЉЕ КРАГУЈЕВАЦ
(*Србија*)

FOREWORD

We present to you an abstract book of the 1st BALKAN CONFERENCE on BIOMEDICAL AND CANCER RESEARCH (Balkan.BMCR 2026), dedicated to the latest achievements, challenges, and perspectives in the fields of biomedicine and oncology. Held from September 03-05 2026, in Foca (Bosnia and Herzegovina), this meeting brought together leading scientists, clinicians, researchers, and young professionals from across the globe with a shared mission- to advance the fight against malignant diseases through the synergy of fundamental science and clinical practice.

The international character of this meeting, featuring participants from over 10 countries, underscores once again that cancer knows no borders. Global health challenges can only be overcome through collective efforts, open dialogue, and cross-border scientific collaboration. The exchange of ideas and the establishment of new research networks during this event represent an invaluable asset for the further advancement of medical science.

We believe that the conclusions we reach will make a significant contribution to our academic community.

The Organizing and Scientific Committees extend their deepest gratitude to all the authors for their exceptional scientific contributions, and to the institutions and sponsors whose support made this significant meeting possible.

Chair of the Scientific Committee

***Ivan Jovanović*, MD PhD**

Center for molecular medicine and stem cell research

Faculty of medical sciences

University of Kragujevac (Serbia)

Chair of the Organizing Committee

***Dejan Bokonjić*, MD PhD**

Faculty of Medicine Foča

University of East Sarajevo

(Bosnia and Herzegovina)

ПРЕДГОВОР

Представљамо вам збирку сажетака са научне конференције: 1st BALKAN CONFERENCE on BIOMEDICAL AND CANCER RESEARCH (Balkan.BMCR 2026), посвећене најновијим достигнућима, изазовима и перспективама у областима биомедицине и онкологије. Одржан од 3. до 5. септембра 2026. године у Фочи (Босна и Херцеговина), овај састанак је окупио водеће научнике, клиничаре, истраживаче и младе стручњаке из целог света са заједничком мисијом - да унапреде борбу против малигних болести кроз синергију фундаменталних наука и клиничке праксе.

Међународни карактер овог састанка, на којем учествују учесници из преко 10 земаља, још једном наглашава да „тумор не познаје границе“. Глобални здравствени изазови могу се превазићи само колективним напорима, отвореним дијалогом и међународном научном сарадњом. Размена идеја и успостављање нових истраживачких конекција током овог догађаја представљају непроцењиву предност за даљи напредак био-медицинских наука.

Верујемо да ће закључци до којих дођемо значајно допринети нашој академској заједници.

Организациони и Научни одбор изражавају најдубљу захвалност свим ауторима на њиховом изузетном научном доприносу, као и институцијама и спонзорима чија је подршка омогућила овај значајан скуп.

Председник Научног одбора

Проф. др Иван Јовановић

Центар за молекулску медицину и истраживање матичних ћелија

Факултет медицинских наука

Универзитет у Крагујевцу (Србија)

Председник Организационог одбора

Проф. др Дејан Бокоњић

Медицински факултет Фоча

Универзитет у Источном Сарајеву

(Босна и Херцеговина)

CONFERENCE PROGRAM/ ПРОГРАМ КОНФЕРЕНЦИЈЕ

03.09.2026. (Thursday/четвртак)
- Faculty of Medicine Foča/ Медицински факултет Фоча-

12:00-13:00 ACCOMMODATION OF CONFERENCE PARTICIPANTS IN ROOMS
СМЈЕШТАЈ УЧЕСНИКА КОНФЕРЕНЦИЈЕ У СОБЕ

13:00-14:00 CONFERENCE PARTICIPANTS REGISTRATION
РЕГИСТРАЦИЈА УЧЕСНИКА КОНФЕРЕНЦИЈЕ

14:00-15:00 OPENING OF THE CONFERENCE/ ОТВАРАЊЕ СКУПА

Working Presidency/ Радно предсједништво:
Ivan Jovanović, MD PhD, University of Kragujevac, Serbia
Dejan Bokonjić, MD PhD, dean of Faculty of Medicine, University of East Sarajevo, Bosnia and Herzegovina
Milan Kulić, PhD, rector, University of East Sarajevo
Nenad Lalović, PhD, managing director, University Hospital Foča,

03.09.2026. (Thursday/четвртак)

- Faculty of Medicine in Foča/ Медицински факултет у Фочи-

15:00-17:00 SESSION 1/ СЕСИЈА 1: *Tumor microenvironment/Туморска микросредина*

Working Presidency/ Радно предсједништво:
Sanja Mijatović, PhD, University of Belgrade, Serbia
Amedeo Amedei, PhD, University of Florence, Italy

15:00-15:30 *Amedeo Amedei, PhD, University of Florence (Italy)*
The intratumoral microbiome: present and future perspectives

15:30-16:00 *Andrei Turtoi, MD PhD, French National Institute of Health Montpellier (France)*
Fibroblast defensive signaling in the tumor microenvironment

16:00-16:30 *Haichuan Zhu, PhD, Hubei University of Technology (China)*
Transcription factors depletion enhances the anti-tumor efficacy of CAR T cells by limiting the progression exhaustion

16:30-16:50 *Nevena Gajović, MD PhD, Faculty of medical sciences University of Kragujevac (Serbia)*
Tirzepatide amplifies NK mediated antitumor response and inhibits breast cancer growth

16:50-17:00 *Florian Dietrich, University of Applied Sciences Merseburg (Germany)*
Development of novel hybrid antitumour agents based on a cisplatin scaffold with nateglinide immobilized into mesoporous nanostructured silica

17:00-18:30 POSTER SESSION 1/ ПОСТЕР СЕСИЈА 1

Working Presidency/ Радно председништво:
Nevena Gajović, MD PhD, University of Kragujevac (Serbia)
Ivan Ranđelović, PhD, National Institute of Oncology Budapest (Hungary)
Milena Jurišević, PhD, University of Kragujevac (Serbia)
Dragana Drakul, PhD, University of East Sarajevo, Bosnia and Herzegovina

18:30-20:00 COCKTAIL/ КОКТЕЛ (Café restaurant „dr Freud“)

04.09.2026. (Friday/ петак)

- Faculty of Medicine in Foca/ Медицински факултет у Фочи-

09:30-11:30 SESSION 2/ СЕСИЈА 2: *Nanomaterials in Biomedicine: From innovation to safety/ Наноматеријали у биомедицини: Од иновације до безбједности*

Working Presidency/Радно предсједништво:
Goran Kaluđerović, PhD, University of Applied Sciences Merseburg, Germany
Dušan Materić, PhD, Helmholtz Centre for Environmental Research, Leipzig, Germany

09:30-10:00	*Goran Kaluđerović, PhD, University of Applied Sciences Merseburg (Germany)* **Beyond the pore: Mesoporous silica SBA-15 as a strategic frontline in cancer nanomedicine**
10:00-10:30	*Miodrag Čolić, MD PhD, Serbian Academy of Science and Arts (Serbia)* **Interactions of nanomaterials with the immune system**
10:30-11:00	*Dušan Materić, PhD, Helmholtz Centre for Environmental Research, Leipzig (Germany)* **Global nanoplastics problem**
11:10-11:25	**SPONSORED LECTURE (*ELTA90MB*)** *Danijela Jovanović, MD PhD, University of Kragujevac, Faculty of Medical Sciences/ University clinical center Kragujevac (Serbia)* **Application of flow cytometry in hemato-oncology**

11:30-12:00 Coffee Break

04.09.2026. (Friday/ петак)

- Faculty of Medicine in Foca/ Медицински факултет у Фочи-

12:00-14:00 SESSION 3/ СЕСИЈА 3: Biology of inflammation/ Биологија инфламације

Working Presidency/ Радно предсједништво:
Danijela Maksimović Ivanić, PhD, University of Belgrade, Serbia
Sergej Tomić, MD PhD, Institute for the Application of Nuclear Energy, Serbia

12:00-12:20	*Sergej Tomić, MD PhD, Institute for the Application of Nuclear Energy (Serbia)* **Myeloid-derived suppressor cells as targets of dysregulated immune response and potential therapeutics**
12:20-12:40	*Vesna Otašević, PhD, Institute for Biological Research "Siniša Stanković", National Institute of Republic of Serbia, University of Belgrade (Serbia)* **Targeting ferroptosis in diabetic liver injury: the protective role of hydrogen sulfide and reactive sulfur species**
12:40-13:00	*Nevena Todrović, MD, University of Florence (Italy)* **From research to new applications on personalized medicine: microbiome profiling and faecal microbiota transplantation**
13:00-13:20	*Nikolina Elez Burnjaković, PhD, University of East Sarajevo, Faculty of Medicine Foča (Bosnia and Hercegovina)* **Tumor cell modulation by halogenated boroxine**
13:20-13:40	*Bojana Simović Marković, MD PhD, Faculty of medical sciences University of Kragujevac (Serbia)* **The IL-33/ST2 axis drives mucosal inflammation and epithelial injury during acute gastric damage**
13:40-13:50	*Milica Markelić, PhD, Faculty of Biology, University of Belgrade (Serbia)* **H2S Donors Attenuate Renal Injury in NOD Mice by Inhibiting Ferroptosis**

14:00-15:00 COCKTAIL/ КОКТЕЛ (Café restaurant „dr Freud“)

15:00-16:30 POSTER SESSION 2/ ПОСТЕР СЕСИЈА 2

Working Presidency/ Радно предсједништво:
Nevena Gajović, PhD, University of Kragujevac (Serbia)
Ivan Ranđelović, PhD, National Institute of Oncology Budapest (Hungary)
Milena Jurišević, PhD, University of Kragujevac (Serbia)
Dragana Drakul, PhD, University of East Sarajevo, Bosnia and Herzegovin

04.09.2026. (Friday/ петак)

- Faculty of Medicine in Foca/ Медицински факултет у Фочи-

16:30-17:00 Coffee Break

17:00-19:00 SESSION 4/ СЕСИЈА 4: New disease models and innovative therapeutic approaches /*Нови модели болести и иновативни терапијски приступи*

Working Presidency/ Радно предсједништво:
Nataša Radulović, PhD, University of Belgrade, Serbia
Tamara Saksida, PhD, University of Belgrade, Serbia

17:00-17:30 *Ivan Ranđelović, PhD, National Institute of Oncology Budapest (Hungary)*
Closing the Translational Gap: PDTX Models in Cancer Therapy Development

17:30-17:50 *Nataša Radulović, PhD, Institute for Biological Research "Siniša Stanković", National Institute of Republic of Serbia, University of Belgrade (Serbia)*
Targeting the Inflammatory Tumor Microenvironment in Colorectal Carcinoma Using Advanced 3D Organoid Models

17:50-18:10 *Tamara Saksida, PhD, Institute for Biological Research "Siniša Stanković", National Institute of Republic of Serbia, University of Belgrade (Serbia)*
Novel models of chronic obstructive pulmonary disease: unraveling immunological mechanisms driven by nitrosative stress

18:10-18:30 *Hanluo Li, PhD, Hubei University of Technology (China)*
From Hair to Repair: personalized therapeutic potentials of stem cells from hair follicles

18:30-18:40 *Suzana Jovanović-Šanta, PhD, Faculty of Sciences, University of Novi Sad (Serbia)*
Modified bile acids and androstanes–Novel promising inhibitors of human cytochrome P450 17A1

18:40-18:50 *Jovana Francuz, PhD, Faculty of Sciences, University of Novi Sad (Serbia)*
Synthesis and biological profiling of asperilactone B derivatives

18:50-19:00 *Jovan Jovanović, MD PhD, State University of Novi Pazar (Serbia)*
Repurposing Metformin for Pancreatic Cancer: Molecular Docking Insights into Comparison with Olomorasib and Gemcitabine

04.09.2026. (Friday/ петак)

19:00-19.30 CLOSING THE CONFERENCE/ ЗАТВАРАЊЕ СКУПА

Working Presidency/ Радно председништво:
Danijela Maksimović Ivanić, PhD, University of Belgrade, Serbia
Ivan Jovanović, MD PhD, University of Kragujevac, Serbia

- Restaurant Zlatna Dunja, Foca/ Ресторан Златна Дуња, Фоча-
20:30-23:30 BANQUET/ СВЕЧАНА ВЕЧЕРА

05.09.2026. (Saturday/ субота)

09:00-21:00 EXCURSION TO DUBROVNIK OLD TOWN/ ИЗЛЕТ У ДУБРОВНИК (СТАРИ ГРАД)

Keynote lectures

KL-01 The intratumoral microbiome: present and future perspectives

Amedeo Amedei

Department of Experimental and Clinical Medicine (University of Florence- Italy)

For decades, the tumor microenvironment (ITM) was showed as a strictly host-centric ecosystem. However, recent advances in spatial transcriptomics, single-cell microbiomics, and robust decontamination algorithms have solidified ITM as a crucial component of most human malignancies, including colorectal cancer (CRC) and Breast Cancer (BC). These bacteria, fungi, and viruses are now recognized as active modulators of oncogenesis and therapeutic efficacy.

To date, research has moved beyond descriptive taxonomic profiling toward a mechanistic understanding of the **"Oral-Gut-Tumor Axis."** Key findings in 2026 highlight that specific taxa, such as *Fusobacterium nucleatum* and *Bacteroides fragilis*, actively remodel the TME by:

- **Immune Modulation:** Inducing STING signaling pathways or, conversely, promoting T-cell exhaustion and myeloid-derived suppressor cell (MDSC) recruitment.
- **Metabolic Reprogramming:** Secreting metabolites (e.g. SCFA) that directly alter tumor cell signaling and chemoresistance (e.g., enzymatic degradation of gemcitabine).
- **Spatial Heterogeneity:** Utilizing high-resolution spatial mapping to reveal that microbes reside in niche "microniches" within the tumor, often co-localizing with immune-suppressive cells.

The future of oncology lies in **Microbe-Guided Precision Medicine.** As we look toward the late 2020s, the focus is shifting from "what is there" to "how we can manipulate it." Emerging frontiers include:

- **Engineered Probiotics & Phage Therapy:** The development of tumor-homing bacteria designed to deliver payloads (checkpoint inhibitors or cytokines) directly to the TME.
- **Microbiome-Based Diagnostics:** Utilizing microbial DNA signatures in liquid biopsies as early-detection biomarkers with higher specificity than traditional protein markers.
- **Standardization & AI:** The integration of AI-driven "decontamination pipelines" and organoid-based co-culture models to establish causality rather than just correlation.

ITM represents a paradigm shift in cancer biology. By transitioning from a host-only view to a "holobiont" perspective, we unlock a new layer of therapeutic targets. The challenge for the next decade will be the clinical standardization of these microbial signatures to personalize immunotherapy and overcome treatment resistance.

KL-02 Fibroblast Defensive Signaling in the Tumor Microenvironment

Andrei Turtoi

Montpellier Cancer Research Institute, University of Montpellier, French National Institute of Health (INSERM)

Among the diverse cellular components of the tumor microenvironment, cancer-associated fibroblasts (CAFs) have long been portrayed predominantly as drivers of tumor progression. Despite their central roles in cancer development and extracellular matrix organization, CAFs remain unexploited in currently approved cancer-targeting therapies. Indeed, therapeutic strategies aimed at targeting or depleting CAFs have largely failed, prompting a critical reassessment of their functional roles.

Accumulating evidence over the past decade supports a more nuanced paradigm in which CAF populations can also exert essential tumor-restraining functions during malignant transformation and disease progression. Our previous work has contributed to this emerging view by demonstrating how soluble factors produced by CAFs within the tumor “wound” can suppress tumor progression-and how these protective mechanisms notably deteriorate in advanced stages of disease.

We and others therefore propose that CAFs should be considered dynamic functional components of the tumor microenvironment that can be preserved, modulated, and therapeutically reprogrammed to control cancer progression. The successful translation of these concepts will depend on innovative drug design, as well as on our ability to further elucidate the regulatory networks governing these tumor-suppressive paracrine signals.

KL-03 Transcription factors depletion enhances the anti-tumor efficacy of CAR T cells by limiting the progression exhaustion

Qifang Wu[1,2+], Tao Luo[2+], Yuan Zhao[2], Yan Liu[4], Qi Dong[2], Jinli Duan[2], Zishan Ye[1], Zhiyi Zhou[2], Shuyue Guo[1], Jiangzhou Shi[1], Tongcun Zhang[1]*, Zijian Zhang[1]*, Yi Xiao[4]*, Haichuan Zhu[2,3]

[1]Institute of Biology and Medicine, College of Life and Health Sciences, Wuhan University of Science and Technology, Wuhan, China;
[2]National "111" Center for Cellular Regulation and Molecular Pharmaceutics, Key Laboratory of Fermentation Engineering (Ministry of Education), Cooperative lnnovation Center of Industrial Fermentation (Ministry of Education &Hubei Province), Hubei Key Laboratory of Industrial Microbiology, Hubei University of Technology, Wuhan, China;
[3]College of Life Science， Wuchang University of technology, Wuhan, China;
[4]Department of Hematology, Tongji Hospital, Tongji Medical College, Hua Zhong University of Science and Technology, Wuhan, China

Chimeric antigen receptor (CAR) T cell therapy has achieved remarkable success in hematological malignancies. However its efficacy against solid tumors remains limited due to T cell exhaustion, which is characterized by loss of effector function, poor persistence, and dysfunctional states during chronic antigen exposure. To identify key regulators of this process, we integrated single-cell RNA sequencing from CAR T cells of patients with B-cell acute lymphoblastic leukemia and pan-cancer $CD8^+$ T-cell datasets. We identified interferon regulatory factor 7 (IRF7) as a key transcription factor of CAR T cell exhaustion. *IRF7* was consistently upregulated in progenitor-exhausted T cells (TEX_{prog}) and the IRF7 locus maintained chromatin accessibility across multiple exhaustion models. Mechanistically, IRF7 directly bound regulatory regions of and transcriptionally activated exhaustion-associated genes, including *PDCD1*, *HAVCR2*, *CTLA4*, *LAG3*, and *TOX*. *IRF7* overexpression impaired CAR T cell proliferation, cytokine production, and anti-tumor activity, whereas *IRF7* knockout enhanced effector function and therapeutic efficacy in multiple syngeneic tumor models, including ovarian cancer. Clinically, lower IRF7 expression was associated with response to immune checkpoint blockade and a longer duration of B-cell aplasia after CAR T cell therapy. These findings establish *IRF7* as a key regulator of CAR T cell exhaustion and a promising target for enhancing CAR T cell therapy in solid tumors.

KL-04 Beyond the Pore: Mesoporous Silica SBA-15 as a Strategic Frontline in Cancer Nanomedicine

Goran N. Kaluđerović

Department of Engineering and Natural Sciences, University of Applied Sciences Merseburg, Merseburg, Germany

Mesoporous silica SBA-15 is increasingly recognized as more than a passive drug carrier. Owing to its highly ordered pore structure, large surface area, and tunable surface chemistry, SBA-15 actively influences drug delivery, intracellular trafficking, and therapeutic response. Recent studies demonstrate that SBA-15-based systems enhance the efficacy of metallodrugs, including cisplatin, platinum(IV) complexes, and organotin derivatives, while reducing systemic toxicity and improving tumor selectivity.

Our research shows that the interaction between SBA-15 and loaded anticancer agents creates a synergistic effect that extends beyond controlled release. Surface functionalization significantly affects cellular uptake and mechanisms of action, influencing processes such as apoptosis, senescence, autophagy, and resistance modulation. Importantly, several SBA-15 formulations induce loss of cancer stemness and promote differentiation toward less aggressive tumor phenotypes, highlighting their potential for tumor reprogramming.

These findings support a new paradigm in cancer nanomedicine in which SBA-15 acts as an active therapeutic partner rather than an inert scaffold. Future development of stimuli-responsive and multifunctional SBA-15 platforms may enable precision-guided therapies capable of simultaneously delivering drugs and modulating tumor biology. As such, SBA-15 represents a promising frontline strategy for next-generation personalized cancer treatment.

KL-05 The response of the immune system to nanomaterials

Miodrag Čolić

Serbian Academy of Sciences and Arts, Kneza Mihajla 35, 11000 Belgrade, Serbia;
Faculty of Medicine Foča, University of East Sarajevo, Studentska 5, 73300 Foča, Republic of Srpska, Bosnia and Herzegovina

The immune response to nanomaterials is a central issue in nanomedicine, because the same physicochemical properties that make nanoparticles useful for biomedical applications may also determine their immunological safety. Engineered nanomaterials can activate, suppress, or reshape immune responses by interacting with complement proteins, macrophages, dendritic cells, neutrophils, lymphocytes, and soluble mediators such as cytokines and chemokines. These effects may result in immunotoxicity, inflammation, hypersensitivity, altered antigen presentation, or, conversely, immune inhibition and tolerance induction, which can be exploited in autoimmune and transplant-related settings. The outcome depends on material composition, size, shape, surface charge, porosity, degradability, protein corona formation, dose, route of exposure, and especially surface functionalization. Different immune models and parameters may therefore lead to different conclusions, making standardized characterization and immunotoxicological testing essential. At the same time, controlled immunomodulation by nanomaterials holds significant diagnostic and therapeutic potential. Nanoparticles are increasingly investigated as contrast agents, biosensors, imaging probes, vaccine platforms, adjuvants, drug and gene delivery carriers, and components of cancer immunotherapy. In photothermal and photoimmunotherapy, nanomaterials can promote tumor destruction, antigen release, and antitumor immunity. This presentation will include our immunological research results using gold nanoparticles, tungsten disulfide, carbon nanotubes, carbon quantum dots, and nanocellulose. Overall, the immune response to nanomaterials should be viewed as a complex, tunable interaction among diverse immune cell components, involving both direct cell–cell contacts and the influence of soluble mediators. Future development requires careful selection of immune endpoints and rational nanomaterial design to maximize clinical benefit while minimizing unintended immune activation or suppression.

KL-06 Global Nanoplastics Problem

Dušan Materić

Department of Environmental Analytical Chemistry, Helmoltz Centre for Environmental Research – UFZ, Permoserstraße 15, 04318 Leipzig, Germany

Plastic pollution has been recognized as a global environmental issue, with particles of various sizes detected in oceans, surface waters, soils, and the atmosphere, from densely populated urban centers to remote regions. Plastics are among the most widely used materials, with an annual production of approximately 368 million tonnes worldwide, of which 57.9 million tonnes (15.7%) are produced in Europe.

Most research on environmental plastic pollution has focused on plastic litter (macroplastics) and their degradation products, microplastics (particles ranging from 1 μm to 5 mm). In contrast, nanoplastics (particles <1 μm) have, until very recently, remained largely unmeasurable in environmental or biological samples. Recognizing this gap, many groups have developed rapid measurement approaches; however, these often suffer from limited quality control, leading to frequent overestimations or false positives. As a result, high-quality nanoplastic measurements remain scarce, and much of the literature-contentiously-consists of review articles rather than original data.

Here, we present results obtained using a conservative and selective method, Thermal Desorption-Proton Transfer Reaction-Mass Spectrometry (TD-PTR-MS), applied to a diverse set of environmental and biological samples. We report nanoplastic loads from several remote locations across the globe, establishing background levels for some of the cleanest regions in Europe and worldwide, and link these findings to the presence of nanoplastics in human immune tissues, including the tonsils.

KL-07 Closing the Translational Gap: PDTX Models in Cancer Therapy Development

Ivan Ranđelović

Department of Experimental Pharmacology and the National Tumor Biology Laboratory, National Institute of Oncology, Budapest, Hungary

The development of effective anticancer therapies remains challenging, with ~95% of candidates failing in clinical trials, largely due to poor predictive preclinical models. Traditional cell line-derived in vitro models and xenografts (CDX) lack tumor heterogeneity and microenvironmental complexity, limiting their clinical relevance. Patient-Derived Tumor Xenograft (PDTX) models address these limitations by implanting patient tumor tissue into immunodeficient mice, preserving tumor architecture, molecular features, and biological behavior.

PDTX models closely replicate human tumor heterogeneity, metabolism, vascularization, and drug response, making them highly valuable for translational oncology, drug testing, and biomarker discovery. PDTX-derived organoids and cell cultures further enhance preclinical screening efficiency and support personalized medicine approaches. However, limitations include lack of human immune response, stromal replacement over time, engraftment bias, and high operational complexity.

Our laboratory has established a diverse PDTX biobank from multiple cancer types, including rare and metastatic tumors, with detailed molecular and histological characterization. These models are complemented by matched in vitro systems, enabling comparative analysis of tumor behavior and drug response.

We developed a vemurafenib-resistant BRAF V600E melanoma PDTX model, revealing novel resistance mechanisms. Notably, ABCB1 transporter activity was implicated in drug efflux, while additional studies identified metabolic alterations, including cysteine metabolism changes, in resistance to combined dabrafenib-trametinib therapy.

Overall, PDTX platforms enable the identification of resistance pathways and support preclinical evaluation of targeted therapies. Despite limitations, they provide a clinically relevant framework that improves drug development, supports personalized treatment strategies, and accelerates the translation of research findings into effective cancer therapies.

PL-01 Tirzepatide amplifies NK mediated antitumor response and inhibits breast cancer growth

Nevena Gajovic[1], Isidora Stanisavljevic[1], Sladjana Pavlovic[1], Bojana Simovic Markovic[1], Tamara Krajnović[2], Irfan Corovic[1,3], Marija Spasojevic[4], Slobodanka Mitrovic[4], Marina Jovanovic[5], Milan Jovanovic[6], Milena Jurisevic[1,7], Danijela Maksimović-Ivanić[2], Ivan Jovanovic[1]

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Background: Breast cancer is the most frequently diagnosed cancer worldwide, accounting for approximately 2.3 million new cases and 666,000 deaths annually. Since diabetes mellitus and metabolic syndrome share several molecular and immunological mechanisms with cancer, repurposing antidiabetic drugs has emerged as a promising therapeutic strategy against various malignancies. This study aimed to investigate the effects of tirzepatide on breast cancer growth and antitumor immune responses.
Methods: Female BALB/c wild-type mice were inoculated with 4T1 breast cancer cells and subsequently treated intraperitoneally with tirzepatide.
Results: Tirzepatide treatment delayed tumor onset and significantly inhibited tumor growth. Additionally, treatment markedly reduced tumor necrosis. No direct cytotoxic effects of tirzepatide were observed on breast cancer cell lines *in vitro*. Tirzepatide enhanced NK cell-mediated antitumor immune responses by increasing the expression of CD69, FasL, and CD107a. Furthermore, tirzepatide enhanced dendritic cell maturation and infiltration into tumor tissue by upregulating CD86 expression, while simultaneously decreasing the percentage of myeloid-derived suppressor cells, thereby alleviating the immunosuppressive tumor microenvironment.
Conclusion: Tirzepatide modulates multiple components of the antitumor immune response, resulting in effective suppression of breast cancer growth.

PL-02 Myeloid-derived suppressor cells as targets of dysregulated immune response and potential therapeutics

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Myeloid-derived suppressor cells (MDSCs) are a heterogeneous population of immature/pathologically activated myeloid cells emerging during chronic inflammation. Due to their potent immunosuppressive mechanisms, MDSCs are considered a major contributor to the therapeutic failure of standard immune checkpoint inhibitors (ICIs) in cancer immunotherapy, while their roles in autoimmunity and infections remain incompletely understood. In contrast to the traditional view of MDSCs as exclusively immunosuppressive, our research demonstrates that these cells simultaneously acquire complex proinflammatory and suppressive properties. Consequently, MDSCs promote both Th17-mediated inflammation and the expansion of various regulatory T cell (Treg) subsets. This dual functionality has been observed in severe COVID-19, during interactions with tumor cells/tumor microenvironment, and in multiple autoimmune diseases, highlighting their central role in immune dysregulation. Interestingly, we found that the proinflammatory and regulatory arms of MDSCs' function can be selectively targeted using different nanoparticles. The targeted potentiation of MDSCs' suppressive properties via this approach could be exploited for the treatment of autoimmune diseases, as shown in human *in vitro* models and in animal models of experimental autoimmune encephalomyelitis (EAE). Overall, a deeper understanding of the complex mechanisms governing MDSCs activity could enable the development of novel, targeted immunotherapies for diseases characterized by chronic inflammation.

PL-03 Targeting Ferroptosis in Diabetic Liver Injury: The Protective Role of Hydrogen Sulfide and Reactive Sulfur Species

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Diabetes-induced liver damage is a serious condition that can progress to cirrhosis and eventually hepatocellular carcinoma. Recently, we discovered ferroptosis contribution to diabetes-related liver damage suggesting that targeting this pathway represents a potential therapeutic strategy. Disturbances in hydrogen-sulfide (H_2S) metabolism are associated with diabetes, and H_2S/reactive sulfur species (RSS) donors treatment have been implicated in ferroptosis regulation, but their ability in preventing diabetes-induced liver damage via ferroptos inhibition remains unclear. Here, we investigated whether targeting ferroptosis with donors of H_2S (GYY4137), polysulfides (Na_2S_4) and persulfides (cysteine-3-sulfide, Cys-3S) could have antidiabetic effects and alleviate diabetic liver damage.
Diabetes was induced in male C57BL/6 mice using streptozotocin (150 mg/kg, i.p.). Two months later, mice were treated for four weeks with the GYY4137 (0.25 mg/kg), Na_2S_4 (0.5 mg/kg), Cys-3S (1.25 mg/kg), or ferroptosis inhibitor liproxstatin-1 (10 mg/kg). After treatment, blood and liver samples were collected for biochemical, molecular and microscopic analysis.
H_2S/RSS donors, especially Cys-3S, attenuated ferroptotic phenotype in the liver of diabetic rats, reflected through: decreased accumulation of pro-oxidative parameters (ACSL4, labile iron, lipofuscin, and lipid peroxides); normalization of iron metabolism regulators (FTH1 and FPN1); Nrf2 activation followed by increased FSP1 expression and GSH-related antioxidative defense parameters (GPX4, GCLC, GSS). Observed mitigation of ferroptotic events by H_2S/RSS donors culminated in improved liver function, as evidenced by improved biochemical parameters, reduced hepatocyte size and liver fibrosis, with effects comparable to the ferroptosis inhibitor liproxtatin-1. H_2S/RSS donors also restored diabetes-altered expression of endogenous H_2S-producing enzymes, particularly the predominant hepatic form CSE, suggesting involvement of H_2S biosynthetic/signaling pathways in their antiferroptotic/antidiabetic effects.
Study clearly demonstrates the strong antiferroptotic potential of H_2S/RSS donors in diabetic liver complications and suggest a new approach for the prevention/treatment of this pathology.

PL-04 From Research to new Applications on Personalized Medicine: Microbiome Profiling and Fecal Microbiota Transplantation

Nevena Todrović

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Over the past two decades, microbiome research has reshaped our understanding of both human health and disease, highlighting the critical role of microbial communities in inflammation/immune and metabolic homeostasis, and host-environmental interplay. These advances have generated an evolving translational field in which microbiome science is increasingly being explored in personalized and patient-centered medicine.This talk will focus on the two major applications: microbiome profiling and fecal microbiota transplantation (FMT). The first one may provide insight into microbial diversity, taxonomic composition, dysbiosis patterns, and their potential relevance to gastrointestinal, inflammatory, metabolic, infectious, immune-mediated, and nutrition-related contexts. FMT represents one of the most advanced examples of microbiome-based therapeutic interventions, with established clinical relevance in recurrent *Clostridium difficile* infection.
The talk aim is to bridge microbiome research and practical applications, highlighting how microbiome-based approaches are currently being used, and how may further support personalized medicine.

PL-05 Tumor cell modulation by halogenated boroxine

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Halogenated boroxine $K2[B_3O_3F_4OH]$, (HB) a boron-containing inorganic compound, has demonstrated promising anti-proliferative and cytotoxic effects in different human cancer cell lines, including melanoma and bladder carcinoma. This study aimed to investigate the effects of HB on cell growth, bioenergetic metabolism, autophagy, and the expression of apoptosis- and autophagy-related genes in human Caucasian melanoma (GR-M) and bladder carcinoma (5637) cells, as well as in peripheral blood mononuclear (PBM) cells. Cytotoxicity was assessed using the Alamar blue assay, while gene expression of BCL-2, BECN1, DRAM1, and SQSTM1/P62 was analyzed by real-time PCR. In bladder carcinoma cells, autophagy levels were additionally evaluated microscopically, and mitochondrial respiration and glycolysis were measured simultaneously. HB significantly inhibited tumour cell growth, with melanoma cells showing higher sensitivity at lower concentrations (0.2 mg/mL). In 5637 bladder carcinoma cells, HB disrupted cellular bioenergetics by decreasing both glycolysis and oxidative phosphorylation (OXPHOS), indicating reduced intracellular survival potential. Molecular analyses revealed downregulation of the anti-apoptotic gene *BCL-2* and upregulation of autophagy-related genes *BECN1, DRAM1,* and *SQSTM1/P62*, suggesting activation and expansion of autophagic pathways. Microscopic observations confirmed increased autophagy in HB-treated bladder carcinoma cells. In contrast, HB increased *BCL-2* expression in PBM cells, indicating activation of protective mechanisms in normal cells against induced cytotoxicity. Overall, these findings demonstrate that HB selectively affects tumour cells by inhibiting proliferation, altering metabolic activity, and modulating apoptosis- and autophagy-related pathways, highlighting its potential as a promising anti-cancer agent.

PL-06 The IL-33/ST2 axis drives mucosal inflammation and epithelial injury during acute gastric damage

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Acute gastric injury is characterized by a rapidly evolving inflammatory cascade that disrupts mucosal integrity and promotes epithelial cell death, yet the molecular mechanisms orchestrating these processes remain incompletely understood. Therefore, we investigated the contribution of IL-33/ST2 signaling to the pathogenesis of acute sterile gastric injury using an ethanol-induced model in ST2-deficient and wild-type mice.

Deletion of ST2 conferred marked protection against gastric injury, significantly reducing mucosal ulceration while preserving tissue architecture. This protective phenotype was accompanied by suppression of innate and adaptive immune activation, including diminished recruitment and activation of neutrophils, macrophages, dendritic cells, eosinophils, $CD8^+$ T cells, and ILC2s, together with substantially lower production of IL-1β, TNF-α, IL-17, and IFN-γ. Mechanistically, ST2 deficiency attenuated activation of the NF-κB/NLRP3 inflammatory axis, limiting pro-inflammatory cytokine production by gastric myeloid cells and reducing epithelial apoptotic signaling. Moreover, exogenous IL-33 markedly aggravated mucosal injury, implicating that activation of this pathway amplifies inflammatory tissue damage.

These findings identify IL-33/ST2 signaling as an upstream molecular checkpoint integrating inflammatory activation with epithelial cell death during acute gastric injury. Targeting this pathway may represent a promising mechanism-based therapeutic strategy for acute gastric mucosal injury and peptic ulcer disease.

PL-07 Targeting the Inflammatory Tumor Microenvironment in Colorectal Carcinoma Using Advanced 3D Organoid Models

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Colorectal carcinoma progression is strongly associated with extensive cell death and activation of compensatory proliferation pathways within the tumor microenvironment (TME). The presented study focuses on the role of the "Phoenix rising" mechanism and arachidonic acid-derived inflammatory mediators in tumor repopulation, with particular emphasis on prostaglandin E2 (PGE2) signaling and coordinated COX-2/LOX activity. Aligning with 3R principle, in order to reproduce the complexity of aggressive tumors, mouse-derived organoid models generated from tumors induced either by viable tumor cells alone or by a combination of live and dead tumor cells were developed, thereby mimicking inflammatory and repopulation-driven conditions characteristic for high-grade colorectal cancer.

Transcriptomic profiling of tumors and derived organoids identified differential expression patterns of genes involved in inflammation, redox regulation, signaling pathways, stemness, and tumor repopulation. Subsequent RT-qPCR analyses confirmed altered expression profiles between tumors induced by live cells and tumors generated by live/dead cells. Additional immunohistochemical characterization of tumors and corresponding organoid models included analysis of amphiregulin (AREG), epiregulin (EREG), microsomal glutathione S-transferase 2 (MGST2), alanyl aminopeptidase (Anpep), and PGE2 (EP2) receptors. Comparative analyses demonstrated distinct inflammatory and repopulation-associated expression profiles between organoids generated by viable and by live/dead cells, indicating the contribution of dying cell-derived mitogenic signaling to aggressive tumor phenotypes.

The established 3D organoid models were further employed for treatment with experimental therapeutics – platinum(IV)-NSAID hybrid molecules, carborane-based COX-2/LOX inhibitors, and nanostructured drug formulations designed to preserve cytotoxic activity while suppressing inflammatory tumor repopulation, followed by evaluation of treatment-associated changes in inflammatory and repopulation-related markers.

Overall, the study highlights advanced 3D colorectal cancer models as valuable tools for investigating therapy resistance and developing novel strategies targeting the inflammatory TME.

PL-08 Novel models of chronic obstructive pulmonary disease: unraveling immunological mechanisms driven by nitrosative stress

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Long-term exposure to environmental noxious gases or particulate matter coming from cigarette smoke (CS) or air pollution drives the development of chronic obstructive pulmonary disease (COPD). COPD pathology comprises chronic obstructive bronchitis and irreversible destruction of distal lung respiratory surface - pulmonary emphysema (PE). While chronic bronchitis is manageable with available therapies, treating and modeling pulmonary emphysema represents a great challenge. PE is characterized by abnormal, permanent enlargement of airspace distal to the terminal bronchiole, accompanied by the destruction of their walls, loss of respiratory surface without obvious fibrosis. It is linked to the activity of proteases derived from abundantly present immune cells and increased nitrosative and oxidative stress contributing to cellular damage. Elastase-induced pulmonary emphysema (EIPE) is a widely studied model that replicates end-stage COPD observed in humans and it is based on enzymatic degradation of lung structure. This model, while resembling patients with COPD, lacks the complex physiological response observed in CS exposure. However, the model of chronic CS exposure is time consuming, the animals do not develop the severe PE observed in the end-stage COPD, the model stabilizes over time, with no further progression of emphysema or pulmonary vascular alterations after smoke cessation. We are focused on refining the available models of COPD, by combining EIPE model, which mimics disease severity, with strategies that provoke oxidative and nitrosative stress and the infiltration of immune cells seen in CS exposure in order to achieve a more precise representation of COPD pathology observed in human patients and to replicate the relevant cellular pathways.

PL-09 From Hair to Repair: personalized therapeutic potentials of stem cells from hair follicles

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Plucked human hair follicles constitute a minimally invasive, patient-specific reservoir of outer-root-sheath and bulge stem cells that can be efficiently expanded while retaining clonogenicity, migration, and multilineage potential. These cells express neural crest- and mesenchymal-associated markers, including Nestin, CD44, STRO-1, and CD271, and can directly support hair regeneration, diabetic wound repair, vascularization, and osteogenic tissue engineering. Importantly, follicle-derived cells can be reprogrammed into induced pluripotent stem cells, creating an autologous platform for lineage-specific differentiation and disease modeling. Optimized three-dimensional protocols generated spontaneously contracting cardiomyocytes and cardiac organoids, as well as stage-defined pancreatic progenitors and endocrine cells expressing SOX17, HNF4A, PDX1, NKX6.1, and C-peptide. This dual capacity for direct somatic-cell therapy and iPSC-mediated organoid generation positions hair follicle stem cells as a versatile source for personalized treatment of alopecia, chronic wounds, cardiovascular disease, and diabetes, while also enabling drug screening, mechanism discovery, and scalable regenerative manufacturing. Their accessibility facilitates repeated sampling, longitudinal monitoring, genomic correction, biobanking, and standardized quality-controlled clinical translation.

P-001 Galectin-3 Deficiency Attenuates Postoperative Peritoneal Adhesion Formation and Collagen Deposition in Experimental Adhesive Peritonitis

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Background: Postoperative peritoneal adhesions represent a frequent and clinically relevantconsequence of abdominal surgery, driven by local inflammation, impaired fibrin clearance,fibroblast activation, and collagen deposition. Galectin-3 is a multifunctional β-galactoside-binding lectin involved in inflammatory signaling, wound healing, tissue remodeling, andfibrosis. This study aimed to investigate whether Galectin-3 contributes to postoperativeadhesion formation in an experimental model of adhesive peritonitis.
Methods: Adhesive peritonitis was induced in male Galectin-3 knockout mice (Gal-3 -/-) andwild-type C57BL/6 mice by laparotomy, cecal abrasion, and parietal peritoneal abrasion. Sevendays after surgery, postoperative severity was assessed using the Post-surgery SeverityAssessment (PSSA) score. Peritoneal adhesion formation was evaluated macroscopically usingthe gross adhesion score and the Nair macroscopic adhesion score. Collagen deposition inperitoneal/adhesive tissue was quantified histologically as Sirius Red-positive area (%).
Results: Gal-3 -/- mice showed significantly lower postoperative PSSA scores compared withGal3 WT mice after induction of adhesive peritonitis (2.20 ± 1.96 vs. 10.00 ± 0.00; p = 0.016).The macroscopic gross adhesion score was also significantly reduced in Gal-3 -/- mice (1.00 ±0.32 vs. 3.00 ± 0.00; p = 0.030), indicating fewer intra-abdominal adhesions. Similarly, Gal-3 -/-mice had significantly lower Nair adhesion scores than WT animals (1.40 ± 0.51 vs. 3.50 ±0.50; p = 0.045), suggesting less severe and less complex adhesion formation. Histologicalanalysis demonstrated a significantly reduced Sirius Red-positive area in Gal-3 -/- micecompared with WT C57BL/6 mice (21.45 ± 2.73 SEM vs. 37.12 ± 4.34; p = 0.010), indicatingdecreased collagen deposition and attenuated fibrosis.
Conclusion: Galectin-3 deficiency is associated with reduced postoperative severity, lowermacroscopic adhesion formation, and decreased collagen accumulation in experimentaladhesive peritonitis. These findings suggest that Galectin-3 may play an important role inpostoperative inflammation, fibrotic tissue organization, and peritoneal adhesion development.

P-002 Green Strategies for Enhancing the Biological Activity of Rh(III), Os(II), and Cu(II) Complexes

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Malignant tumors continue to pose a significant challenge in modern medicine due to high mortality rates and the limitations of conventional therapies, including systemic toxicity and the development of resistance in cancer cells. In the pursuit of more effective and selective treatments, transition metal complexes have emerged as promising candidates owing to their distinct chemical behavior
and versatile biological activity. Among them, Rh(III) and Os(II) complexes have attracted considerable attention due to their structural adaptability, finely tunable reactivity, and strong affinity for biologically relevant targets. Cu(II) complexes also represent a valuable class of antitumor agents, primarily due to their ability to generate reactive oxygen species (ROS), interact with DNA and other biomolecules, and their generally lower toxicity compared to platinum-based drugs. Their structural versatility allows for the design of tailored therapeutic agents through strategic ligand modification. In this study Rh(III), Os(II), and Cu(II) complexes featuring various nitrogen-donor ligand classes were synthesized and comprehensively evaluated. Investigations included substitution reactions with biologically relevant ligands, DNA and serum albumin binding studies, lipophilicity assessments, and in vitro cytotoxicity against selected cancer cell lines. Special emphasis was placed on eco-friendly strategies: the influence of ionic liquids on the reactivity and biological behavior of Rh(III) and Os(II) complexes was systematically examined. Concurrently, Cu(II) complexes were studied in the presence of *Salvia pratensis* and *Lythrum scutellaria* plant extracts to explore potential synergistic effects within a green chemistry framework. The findings highlight the potential of environmentally conscious approaches in enhancing the therapeutic performance of transition metal-based anticancer agents.

P-003 Development of a Oxaliplatin-Based Pt(IV)-Nateglinide Conjugate for Next-Generation Platinum Chemotherapy

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Cancer remains one of the leading causes of death worldwide, highlighting the urgent need for more effective and selective chemotherapeutic strategies. Although platinum-based drugs such as cisplatin and oxaliplatin play a central role in cancer therapy, their clinical application is frequently limited by systemic toxicity, low selectivity and the development of resistance. Consequently, the development of novel platinum-based systems with improved biological and pharmacological properties represents an important research focus.
In this study, we report the synthesis and characterization of a novel Pt(IV)-based hybrid based on oxaliplatin bearing two axial nateglinido moieties (OXNat). The proposed approach combines the cytotoxic activity of oxaliplatin with the metabolic activity of nateglinide, an antidiabetic agent capable of interfering with glucose uptake and metabolic adaptation in cancer cells. By integrating both functionalities into a single Pt(IV) platform, the resulting hybrid OXNat system represents a promising strategy for simultaneous cytotoxic and metabolic targeting of malignant cells. The OXNat was synthesized starting from an oxaliplatin and characterized using ^{1}H, ^{13}C and ^{195}Pt NMR, as well as IR spectroscopy, together with elemental analysis, confirming successful formation of the target complex.
The biological activity of the OXNat hybrid is evaluated in tumor cell lines, with particular focus on its antiproliferative potential compared with conventional platinum therapeutic oxaliplatin. The obtained results will contribute to the development of next-generation multifunctional platinum systems with improved therapeutic potential and metabolic targeting capabilities.

P-004 Biofriendly UV-Reflective Fe_3O_4 and Fe_3O_4@SiO_2 Nanomaterials for Safe Biomedical and Cosmetic Applications

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Titanium dioxide nanoparticles (TiO_2-NPs) are widely used as UV filters due to their effective absorption of UV-A and UV-B radiation. However, recent studies have raised concerns regarding their potential toxicity to human health and the environment. TiO_2-NPs have been associated with oxidative stress, neurotoxicity, and the generation of reactive oxygen species, while their release into ecosystems has been linked to coral bleaching and toxicity toward marine microorganisms. These concerns emphasize the need for safer and more sustainable UV-protective materials. In this study, Fe_3O_4 and Fe_3O_4@SiO_2 nanomaterials were investigated as potential biofriendly alternatives to conventional TiO_2-based UV filters. Magnetite (Fe_3O_4), a naturally occurring ferromagnetic oxide, exhibits promising UV-reflective properties, while silica coating improves particle stability and suitability for biomedical and cosmetic applications.

The present work focuses on the synthesis, characterization, and investigation of the UV–Vis optical properties of Fe_3O_4 nanoparticles and Fe_3O_4@SiO_2 core–shell nanostructures. X-ray diffraction (XRD) confirmed the crystalline structure of magnetite, while the silica coating did not induce detectable structural changes, indicating excellent stability of the Fe_3O_4 core after surface modification. The UV reflectance properties of the synthesized materials showed a strong dependence on particle size and silica shell thickness. Variations in these parameters significantly influenced the optical response, demonstrating the tunable nature of these nanostructures. The obtained results suggest that such biofriendly nanomaterials may represent promising candidates for safe UV-protective systems with potential applications in biomedical, cosmetic, and environmentally sustainable technologies.

P-005 HSA interaction of Nickel(II) complex with pentadentate type of ligand

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Human serum albumin (HSA) is the most abundant protein in plasma, indicating its significant binding capacity and making it the most important drug-carrying protein. Because HSA acts as a carrier for various drugs in plasma, knowledge of the type of interaction between HSA and different complexes is very important and provides appropriate information to determine how drugs can be transported. The interactions of the previously synthesized nickel(II) complex with a pentadentate ligand were investigated with albumin (HSA) using fluorescence spectroscopy. The interaction tests were performed at three temperatures. The obtained values for the binding constants (Kb) and Stern-Volmer quenching constants (K_{SV}) indicate that the complex binds to HSA.

P-006 Adaptive Cellular Immunity Drives Sterile Acute Gastric Injury Through Dendritic Cell–T Cell Interactions

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Background: Acute gastric injury is traditionally attributed to epithelial toxicity and innate immune activation, whereas the contribution of adaptive cellular immunity remains poorly defined. We investigated the role of T helper and cytotoxic T cells in ethanol-induced acute gastric injury.
Methods: Acute gastric injury was induced in BALB/c mice by intragastric administration of 80% ethanol. Gastric tissues were assessed using macroscopic and histological analyses, ELISA, qPCR, and flow cytometry to evaluate cytokine production, immune cell infiltration, and epithelial apoptosis.
Results: Ethanol exposure induced severe gastric mucosal injury characterized by epithelial disruption, inflammatory infiltration, and enhanced apoptosis. Gastric tissues exhibited elevated levels of pro-inflammatory cytokines, including TNF-α, IL-1β, IL-17, and IFN-γ. Ethanol treatment increased the accumulation of activated $CD11c^+$ dendritic cells with enhanced IL-12 production. Furthermore, marked infiltration of $CD4^+$ and $CD8^+$ T lymphocytes producing IFN-γ and IL-17 was observed, while $CD8^+$ T cells demonstrated increased CD107a expression, indicating enhanced cytotoxic activity.
Conclusions: Adaptive cellular immunity is mobilized early during sterile acute gastric injury and may amplify mucosal damage through dendritic cell-T cell interactions. These findings identify T-cell-driven inflammation as a previously underrecognized mechanism in acute gastric injury and suggest potential immunomodulatory targets for gastric mucosal protection.

P-007 Development of novel hybrid antitumour agents based on a cisplatin scaffold with nateglinide immobilized into mesoporous nanostructured silica

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Platinum-based drugs remain among the most important chemotherapeutics in breast cancer treatment; however, their clinical use is limited by systemic toxicity, poor selectivity and therapy resistance. To overcome these limitations, novel multifunctional platinum systems capable of targeting tumor metabolic vulnerabilities are being intensively explored. In this study, we developed and evaluated a novel Pt(IV) complex, nateglinide-cisplatin hybrid system (CPNat), against triple-negative breast cancer (TNBC) cell lines. The proposed strategy combines a cisplatin scaffold with nateglinide, an antidiabetic agent involved in glucose metabolism modulation, aiming to enhance cytotoxic efficacy through simultaneous metabolic and platinum-mediated targeting. The novel CPNat was synthesized and to further improve delivery properties and tumor selectivity, the hybrid system was immobilized into SBA-15 mesoporous silica nanostructures (SBA-15|CPNat). The synthesized compound and nanostructures were characterized using multinuclear (^{1}H, ^{13}C and ^{195}Pt) NMR and IR spectroscopy, SEM, EDX and elemental analysis, confirming successful synthesis and immobilization of the target systems.
Biological evaluation was performed in human and murine triple-negative breast cancer cell lines. The CPNat hybrid demonstrated superior cytotoxic activity compared with cisplatin and nateglinide applied individually or in combination. Furthermore, immobilization within SBA-15 improved selectivity toward the malignant phenotype, supporting the potential of metabolically responsive platinum nanoformulations.
These findings demonstrate that CPNat systems combined with SBA-15 nanostructures represent a promising strategy for the development of next-generation metabolically guided platinum therapeutics for advanced breast cancer treatment.

P-008 Ni-Modified MCM-41 Mesoporous Nanostructures as Potential Bio-Safe Materials

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Mesoporous silica materials of the MCM-41 type have attracted considerable attention due to their high specific surface area, uniform pore distribution, and potential applications in medicine, catalysis, adsorption, and hydrogen storage. In this study, Ni-modified MCM-41 materials were synthesized using an *in situ* modification approach with different nickel precursors.

The synthesis was performed using nickel chloride hexahydrate, nickel nitrate tetrahydrate, and nickel acetate hexahydrate. Nickel was incorporated during synthesis in amounts of 5, 10, 15, and 20 wt%, resulting in mesoporous silica materials with different nickel contents. The influence of precursor type and nickel loading on morphology, particle size, pore structure, and structural order of MCM-41 was investigated. Comprehensive characterization of the synthesized materials was performed using several analytical techniques. XRD was used to evaluate the preservation of the hexagonal mesoporous structure after nickel incorporation. BET analysis provided information about specific surface area, pore volume, and pore size distribution. Morphology and particle size variations were analyzed using SEM and DLS. The chemical composition and successful incorporation of nickel species were confirmed by EDX analysis. The obtained results demonstrated that both the type of nickel precursor and nickel loading significantly influence the structural and textural properties of MCM-41 materials, particularly particle morphology, pore ordering, and pore size distribution. These findings suggest that such bio-safe mesoporous materials could be utilized for efficient H_2 storage and transport, while also offering potential for the development of advanced nanostructured systems relevant to biomedical and nanotechnology-related applications.

P-009 Synthesis and biological profiling of asperilactone B derivatives

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Many natural products are characterized by complex and intriguing molecular architectures, including the furofuranone bicyclo[3.3.0] ring system, which occurs in several bioactive compounds. A representative example is asperilactone B (ASL B), a secondary metabolite isolated from the fungus Aspergillus nidulans.Beyond its unusual structural framework, ASL B and related furofuranone-containing natural products have been investigated for their diverse pharmacological properties, ranging from antimicrobial and anticancer activities to immunomodulatory effects. Our research group accomplished the first total synthesis of asperilactone B, thereby providing access to this rare molecule in sufficient quantities for further study. This achievement opened the door to systematic exploration of its biological properties and the design and synthesis of structural analogues of ASL B. These analogues were developed to investigate the relationship between molecular structure and biological activity, allowing assessment of how subtle modifications of the furofuranone scaffold influence its function. In this context, the immunomodulatory activity of asperilactone B and its analogues is evaluated, and the latest results on their biological potential are presented. By combining synthetic innovation with biological evaluation, this work provides new insights into the role of the furofuranone scaffold in modulating biological activity and its potential applications in drug discovery.

P-010 Cardioprotective effects of *Trapa natans L.* extract in a rat model of cisplatin-induced cardiotoxicity

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Chemical composition of *Trapa natans* L. fruits and leaf extracts have drawn significant attention from scientists and clinicians because of their immunomodulatory, anti-inflammatory, and antioxidant effects. We used rat model of cisplatin-induced cardiotoxicity to explore the potential beneficial effects of *Trapa natans* L. extract (TNE) on the pathogenesis of this serious side effect of the platinum-based antineoplastic drug. TNE treatment markedly attenuated cisplatin-induced myocardial inflammation, necrosis, and fibrotic remodeling. Daily administration of TNE decreased level of proinflammatory cytokines (TNF-α, IFN-γ and IL-6) and prooxidative parameters (NO_2, O_2 and H_2O_2) in the systemic circulation, while increased level of immunosuppressive IL-10 and antioxidative GSH, CAT and SOD. At the molecular level, TNE downregulated the expression of proinflammatory and profibrotic genes, alongside suppression of iNOS expression and reduced macrophage infiltration in cardiac tissue. *In vitro* experiments demonstrated that, TNE promoted macrophage polarization toward an anti-inflammatory and pro-regenerative phenotype, suggesting that immunomodulation contributes substantially to its cardioprotective activity. In conclusion, *Trapa natans L*. extract exerts pronounced cardioprotective effects against cisplatin-induced cardiac injury through coordinated anti-inflammatory, antioxidative, and antifibrotic mechanisms, highlighting its potential as a complementary therapeutic strategy to mitigate chemotherapy-associated cardiotoxicity.

P-011 Metformin licensing enhances cardioprotective potential of mesenchymal stem cells in cisplatin-induced cardiotoxicity

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Mesenchymal stem cells (MSCs) have shown cardioprotective potential, however their efficacy dependents on the inflammatory milieu and microenvironmental conditions to which they are exposed after transplantation. Thus, preconditioning strategies have been increasingly recognized as a critical step in achieving a stable, reliable, and clinically effective immunomodulatory response. *In vitro* studies have shown that metformin, an AMPK activator, has the potential to improve MSCs survival, as well as their regenerative and immunoregulatory capacities, however, its role in enhancing MSC-mediated cardioprotection remains unexplored. Murine bone marrow-derived MSCs were pretreated with metformin (5 mM, 3 days) and administered in a C57BL/6 mouse model of cisplatin-induced cardiotoxicity. Cardiac injury was assessed using serum biomarkers, histopathology, fibrosis analysis, cytokine profiling, qRT-PCR, and flow cytometry. Cisplatin induced marked cardiac injury, inflammation, and fibrosis. MSC treatment attenuated these effects, while metformin-preconditioned MSCs (MSC^{metf}) provided significantly greater protection. MSC^{metf} reduced cardiac enzyme levels, myocardial damage, and fibrosis, suppressed pro-inflammatory cytokines (TNF-α, IL-1β, IFN-γ), increased IL-10 levels, and promoted a shift toward M2 macrophage polarization with reduced immune cell infiltration.
Conclusion. Metformin preconditioning enhances the cardioprotective and immunomodulatory effects of MSCs in cisplatin-induced cardiotoxicity, suggesting a promising strategy for improving MSC-based therapies in onco-cardiology.

P-012 Synthesis and characterization of copper(ii) and palladium(ii) complexes with S,O-tetradentate ligands derived from thiosalicylic and thioglycolic acid

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Although cisplatin remains widely used in antitumor therapy, its severe side effects and acquired resistance make the development of new metal complexes highly desirable. Copper(II) and palladium(II) complexes have demonstrated significant cytotoxic effects against various tumor cell lines. Additionally, thiosalicylic acid derivatives have shown activity in inflammatory, allergic and respiratory conditions, while glycolic acid derivatives are recognized as activators of the innate immune response, providing a strong basis for further research.

The tetradentate S,O-ligands derived from thiosalicylic and thioglycolic acids (Ts-2-TG and Ts-3-TG) were synthesized from thiosalicylic acid and thioglycolic acid in a two-step procedure. In the first step, thiosalicylic acid was alkylated with 1,2-dibromopropane or 1,3-dibromopropane to form the S-ethyl or S-propyl derivative. In the second step, this intermediate was reacted with thioglycolic acid under basic conditions to yield the final tetradentate ligands, Ts-2-TG and Ts-3-TG. The corresponding copper(II) (**C1**) and palladium(II) (**C2**) complexes were prepared by direct reaction of the ligands with $Cu(NO_3)_2 \cdot 3H_2O$ or $K_2[PdCl_4]$ in aqueous solution in a 1:1 metal-to-ligand molar ratio, in the presence of an equimolar amount of LiOH.

The prepared compounds will be characterized by elemental microanalysis, IR and ^{1}H and ^{13}C NMR spectroscopy. Interactions with molecules such as BSA and DNA, will also be investigated in order to evaluate their potential biological relevance.

P-013 Nanoplastic size and exposure complexity reprogram human monocyte states through ER-driven metabolic adaptation under physiological flow

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Nanoplastic materials interact with circulating immune cells, yet how material size and exposure complexity shape transcriptional state organization under physiological flow remains unresolved. For the first time, we combined a microfluidic exposure platform with single-cell RNA sequencing (scRNA-seq) to investigate how polystyrene nanoplastics (PSNPs) modulate transcriptional states in human peripheral blood mononuclear cells (PBMCs). PBMCs were cultured under continuous physiological flow in a microfluidic platform and exposed for 24 h to 40 nm PSNPs, 200 nm PSNPs, or a mixed exposure containing both particles. Following exposure, cells were subjected to droplet-based scRNA-seq. Major immune populations were analyzed for differential gene expression and transcriptional state organization across exposure conditions. PSNP exposure induced size-dependent and lineage-specific transcriptional responses across immune populations without altering overall immune cell composition. Monocytes exhibited the highest transcriptional sensitivity and underwent remodeling of pathways that depended on particle size. Exposure to 40 nm PSNPs preferentially enriched mitochondrial metabolic and bioenergetic pathways, whereas 200 nm PSNPs predominantly engaged immune signaling pathways, including TNF and IL-17 signaling. Mixed exposure generated integrated transcriptional configurations characterized by simultaneous metabolic and regulatory pathway enrichment. In contrast, adaptive immune cells displayed distributed, lineage-preserving transcriptional modulation without dominant pathway-level reorganization. These findings demonstrate that nanoscale material size and exposure complexity shape immune transcriptional state architecture under physiological flow and establish a framework for understanding dynamic material-immune interfaces at single-cell resolution.

P-014 Cytotoxic and genotoxic effects of polystyrene nanoplastics on mesenchymal stem cells

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The widespread environmental presence of polystyrene nanoparticles (PSNPs) has raised increasing concerns regarding their potential biological effects on stem cell populations involved in tissue repair and regeneration. The aim of this study was to investigate the intracellular accumulation and toxicological effects of PSNPs on MSC viability and genomic stability. Human MSCs were exposed for 24 h to 40 nm and 200 nm PSNPs at environmentally relevant concentrations (0.47 and 4.7 μg/ml). Nanoparticle internalization was analyzed using transmission electron microscopy (TEM). Morphological alterations were evaluated by hematoxylin-eosin and Giemsa staining, while apoptosis was quantified using Annexin V-FITC/PI flow cytometry. DNA damage was assessed by Comet assay, and intracellular oxidative stress parameters were analyzed through reactive oxygen and nitrogen species measurements. TEM analysis demonstrated efficient uptake and intracellular retention of PSNPs within endocytic vesicles of MSCs. Exposure to PSNPs induced pronounced apoptotic morphology, including cell shrinkage, chromatin condensation, and apoptotic body formation. Flow cytometric analysis revealed a significant increase in early apoptotic MSCs following treatment with both nanoparticle sizes, particularly at higher concentrations. PSNP exposure also resulted in dose-dependent DNA damage, confirmed by increased genetic damage index values in treated cells. Notably, PSNP-treated MSCs exhibited markedly elevated intracellular nitric oxide levels, while reactive oxygen species production showed only minor alterations, suggesting that nitrosative stress may play a central role in PSNP-mediated genotoxicity.
Conclusion. PSNPs induce significant cytotoxic and genotoxic effects in MSCs through mechanisms associated with intracellular accumulation and nitrosative stress.

P-015 Diagnostic Importance of RNA Sequencing in Myxoid Lipoblastoma with CHCHD7::PLAG1 Fusion

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Lipoblastoma is a rare benign adipocytic tumor of infancy and early childhood arising from embryonal white fat. Due to significant histopathological overlap with other pediatric myxoid soft tissue tumors, accurate diagnosis may be difficult and often requires molecular confirmation. We report the case of an 18-month-old girl presenting with a painless soft tissue mass in the middle third of the right leg. Imaging studies demonstrated a well-circumscribed hyperechoic lesion without bone involvement. Histopathological examination revealed a lobulated and pseudo-encapsulated neoplasm composed of spindle- and stellate-shaped prelipoblasts and lipoblasts in different stages of maturation, separated by fibrovascular septa and embedded in abundant myxoid stroma with focal chondroid-like appearance. Immunohistochemical analysis showed diffuse positivity for S100, CD34, CD56, and NSE, while Ki67 expression was detected in less than 1% of tumor cells. Myogenin, MyoD1, SOX10, alpha-SMA, caldesmon, Rb, and LCA were negative. Due to the unusual morphology and broad differential diagnosis including myxoid liposarcoma and primitive myxoid mesenchymal tumor of infancy, additional molecular analyses were performed. Targeted RNA sequencing identified a rare CHCHD7::PLAG1 fusion generated by intrachromosomal rearrangement at 8q12. The fusion involved CHCHD7 exon 1 and PLAG1 exon 2 or 3, preserving the complete PLAG1 coding region and supporting a promoter-swap mechanism responsible for PLAG1 overexpression. This case highlights the importance of integrating histopathological, immunohistochemical, and molecular findings in the diagnosis of pediatric adipocytic tumors with myxoid features. Identification of the rare CHCHD7::PLAG1 fusion was crucial for confirming lipoblastoma and excluding malignant entities, thereby preventing unnecessary aggressive treatment.

P-016 A Multitargeted Strategy for Colorectal Cancer: Platinum(IV)–Ibuprofen Conjugate in Free and SBA-15 Immobilized Forms

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The clinical use of cisplatin in oncology is limited by severe side effects and drug resistance, prompting the development of platinum(IV) prodrugs and novel delivery systems to improve efficacy and reduce toxicity. In colorectal cancer (CRC), the COX-2/PGE2 pathway is frequently overexpressed and associated with tumor progression and compensatory proliferation, a process in which dying cells stimulate the proliferation of nearby surviving tumor cells. In this study, a platinum(IV)–ibuprofen conjugate with anticancer and anti-inflammatory properties was developed and immobilized within the mesoporous silica carrier SBA-15 to enhance tumor targeting, delivery efficiency, and antitumor activity. The cytotoxic effects of free and immobilized cisplatin–ibuprofen conjugate were evaluated in murine (MC38) and human (HCT116, HT29, and SW480) colorectal cancer cells, as well as in two types of mouse-derived organoids generated from MC38-induced tumors in C57BL/6 mice: the "classical" model established with viable MC38 cells and the "alternative" model generated using a mixture of viable and dead cells. Cell viability was assessed by MTT and crystal violet assays in 2D cultures and by CellTiter-Glo® in organoids, while the mechanism of action in MC38 cells was analyzed by flow cytometry. *In vivo* antitumor activity was further investigated using both tumor models. After 72 h of treatment, both compounds induced a dose-dependent reduction in viability in all tested tumor cell lines, confirming strong cytotoxic activity. A significant decrease in viability was also observed in both types of colon cancer organoids after 6 days of treatment. Flow cytometry analysis showed that their anticancer effect was mainly associated with inhibition of cell division, particularly in the case of the cisplatin–ibuprofen conjugate. *In vivo* studies in C57BL/6 mice demonstrated that the free conjugate did not significantly reduce tumor growth in the classical model, whereas the SBA-15–immobilized formulation notably reduced tumor volume in both the "classical" and "alternative" tumor models, indicating enhanced antitumor efficacy. The results demonstrated pronounced antitumor activity of the cisplatin–ibuprofen conjugate in a murine colon cancer model *in vitro* and *in vivo*, particularly after immobilization into SBA-15. The SBA-15-loaded formulation showed enhanced *in vivo* efficacy, supporting this multitargeted approach as a promising strategy for colorectal cancer treatment and a basis for further investigation.

P-017 Pancreatic Cancer Mortality in Serbia

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Background: Pancreatic cancer is a significant public health problem worldwide. This study aimed to investigate sex-specific and age-specific pancreatic cancer mortality trends and disparities in the Serbia from 2000 to 2021.
Methods: A descriptive epidemiological population-based study analyzing pancreatic cancer mortality was conducted. Age-standardized mortality rates (ASMRs) were calculated using the Segi's world standard population. Temporal trends for pancreatic cancer mortality were assessed using the joinpoint regression analysis.
Results: Age-standardized rate of pancreatic cancer in Serbia was 6.4/100,000 (7.9/100,000 in men, 5.1/100,000 in women). The rates were found to be 1.6 times higher in men than women. Pancreatic cancer mortality trend significantly increased from 2000 to 2010 in men (APC=+2.4%, 95%CI: 0.3–1.4), after 2010 rates nonsignificantly decline (APC=-0.4%; (95%CI: -2.5–0.5). In women, mortality trend significantly increased by +1.8% at an annual level (95%CI: 0.7–2.7). The mortality of pancreatic cancer increased by age. The joinpoint analysis showed a significant rising trend of mortality rates in all age groups 60+, with the highest average annual percent change being reported in the age groups 85+ (AAPC=+3.1 (95%CI: 1.6–4.5)).
Conclusions: The provision of updated statistics on the occurrence and outcomes of pancreatic cancer, time trends among various population groups, along with a better understanding of its etiology and identification of causal changeable risk factors – are essential when it comes to the primary prevention of this particular disease.

P-018 Anticancer potential of Amino Chalcones as Potential COX-2 Inhibitors in Colorectal Cancer Models

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Colorectal cancer represents a significant global health challenge, characterized by high incidence rates and the need for therapies that combine efficacy with low systemic toxicity. Contemporary research focuses on multi-target therapeutic approaches that simultaneously affect inflammation and the proliferation of malignant cells. Particular importance is attributed to the enzyme COX-2, whose overexpression is associated with tumor progression. Chalcones (1,3-diaryl-2-propen-1-ones) represent an important chemical class due to their broad spectrum of biological activities, including anticancer and anti-inflammatory effects. Their ability to inhibit COX-2 suggests a potential dual mode of action: suppression of inflammation and direct cytotoxic effects on tumor cells. In this study, the antiproliferative activity of eight synthesized amino chalcones (chalcones 21–27 and 29) with different substituents on the second aromatic ring of the propiophenone structure was investigated. The evaluation was conducted on four colorectal cancer cell lines (HCT 116, HT29, SW480, MC38) and one healthycell line (MRC-5). Cells were treated for 72 h, and viability was assessed using MTT and CV assays. IC_{50} values were calculated as a measure of cytotoxicity. The results showed a dose-dependent decrease in tumor cell viability. The SW480 cell line exhibited the highest sensitivity. The most effective compounds were chalcone 23 with a -F substituent, while chalcone 29 with a –CH3 group showed the lowest activity. All compounds demonstrated higher IC_{50} values in healthy MRC-5 cells, indicating selectivity towards malignant phenotype. Chalcone 23 emerged as the most promising candidate due to the greatest differential effect between tumor and healthy cells. These preliminary results suggest that amino chalcones are promising candidates for further investigation of their mechanisms of action and the development of new potential chemotherapeutic agents for colorectal cancer treatment.

P-019 Association of extracellular matrix gene polymorphisms (*COL5A1*, *COL1A1* and *TNC*) with biochemical parameters in hemodialysis patients

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Patients with end-stage renal disease undergoing maintenance hemodialysis (HD) frequently develop complications associated with extracellular matrix remodeling and connective tissue alterations. Functional polymorphisms in extracellular matrix genes may contribute to inter-individual variability in disease characteristics. This study aimed to investigate the distribution of polymorphisms in extracellular matrix genes (*COL5A1* rs12722, *COL1A1* rs1800012, and *TNC* rs2104772) and evaluate their association with biochemical parameters in patients undergoing hemodialysis. A total of 106 participants were enrolled, including HD patients and healthy controls. Genomic DNA was isolated from peripheral blood samples, and genotyping of the *COL5A1* rs12722, *COL1A1* rs1800012 and *TNC* rs2104772 polymorphisms was performed. Genotype and allele frequencies were compared between groups, and associations with biochemical parameters were analyzed. A significant difference in genotype and allele distribution was observed for both *COL5A1* rs12722 and *TNC* rs2104772 polymorphisms between HD patients and healthy controls ($p < 0.05$), with the TT genotype being more frequent in the HD group for both polymorphisms. No significant differences were observed for *COL1A1* rs1800012 ($p > 0.05$). Among HD patients, *COL5A1* rs12722 polymorphism was significantly associated with baseline serum creatinine levels ($p < 0.05$), with the TT genotype occurring more frequently in patients with higher creatinine concentrations. In HD patients, the TT genotype was additionally associated with lower hemoglobin levels ($p < 0.05$). *Conclusion:* The present findings demonstrate significant differences in the distribution of *COL5A1* rs12722 and *TNC* rs2104772 polymorphisms between HD patients and healthy controls. In addition, the association of the *COL5A1* rs12722 variant with biochemical parameters suggests a potential role of extracellular matrix genetic variability in the clinical phenotype of end-stage renal disease.

P-020 Dual immune checkpoint modulation via PD-1 and IL-33/ST2 inhibition reshapes adaptive anti-tumor response in mammary carcinoma

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Introduction: Breast cancer continues to represent a formidable therapeutic challenge despite the expanding arsenal of immunotherapeutic strategies. Building on earlier findings demonstrating that simultaneous disruption of the IL-33/ST2 and PD-1/PD-L signaling axes potently restrains tumor growth through augmented natural killer cell activity, the present study sought to characterize how this combined intervention specifically shapes T lymphocyte and macrophage responses within the tumor immune landscape.
Aims: The main aim of this study was to elucidate the precise contribution of dual IL-33/ST2 and PD-1/PD-L co-blockade to the activation and functional reprogramming of T lymphocytes and macrophages in a murine model of breast carcinoma.
Materials and Methods: Mammary carcinoma was established via orthotopic inoculation of 4T1 cells into female BALB/C and ST2-deficient BALB/C (BALB/C $ST2^{-/-}$) mice, with anti-PD-1 antibody administered at defined time points throughout the experimental protocol. Immune profiling of harvested tissues was performed by flow cytometry.
Results: Dual pathway inhibition markedly shifted macrophage polarization toward the M1 phenotype in the tumor microenvironment, accompanied by elevated expression of CD86 and TNFα. Concurrently, T cell infiltration into both splenic and intratumoral compartments was substantially augmented, with upregulation of the activation-associated markers IL-17, CD69, NKG2D, and FasL, alongside downregulation of the immunosuppressive IL-10 and FoxP3. Conclusion: Dual blockade of the PD-1/PD-L and IL-33/ST2 axes can reconfigure the immunosuppressive tumor milieu, lending support to this dual-targeting strategy as a rational framework for advancing immunotherapy in breast cancer.

P-021 Differential modulation of IL-41 by biological therapies in rheumatoid arthritis

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Introduction and Aim: Although biological therapies have transformed the treatment of rheumatoid arthritis (RA), reliable biomarkers for treatment monitoring and response prediction remain limited. Interleukin-41 (IL-41; Meteorin-like/Subfatin) is a novel immunomodulatory cytokine whose elevated serum levels have been associated with RA disease activity. We hypothesized that different therapeutic modalities exert distinct effects on IL-41 secretion and that its serum concentration may serve as a clinically relevant biomarker of treatment response.
Methods: A total of 189 patients fulfilling the ACR/EULAR 2010 classification criteria for RA were enrolled in this observational study and stratified by treatment: methotrexate (MTX) monotherapy (n=31), MTX combined with TNF-α inhibitors (n=70), tocilizumab monotherapy (TCZ; n=43), and a DMARD-naive control group (n=45). Serum concentrations of IL-41, IL-17, and IL-23 were measured using ELISA, and disease activity was assessed using composite indices (DAS28-ESR, CDAI, and SDAI). Independent predictors of serum IL-41 levels were identified using multivariate linear regression analysis.
Results: All treatment groups demonstrated significantly lower disease activity parameters compared with the DMARD-naive control group ($p<0.001$). TCZ treatment was associated with the greatest reduction in serum IL-41 levels (302.6±87.3 vs. 348.3±72.8 ng/mL in controls; $p=0.042$), followed by MTX+TNFi therapy (304.1±81.4 ng/mL; $p=0.024$), whereas MTX monotherapy showed no significant reduction. Smoking independently predicted higher IL-41 levels ($B=33.635$; $p=0.009$).
Conclusion: Our findings suggest differential effects of biological therapies on serum IL-41 levels in RA. Greater reductions in IL-41 with TCZ and MTX+TNFi support its potential as a biomarker of treatment response, while the association with smoking suggests possible involvement of the IL-41/TNF-α/IL-17 axis in RA pathogenesis.

P-022 A Distinct Immunometabolic Signature in Ulcerative Colitis with Metabolic Syndrome: Insights from Fecal Galectin-1, sST2, and CXCL8

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Background: Metabolic syndrome (MetS) is traditionally considered a pro-inflammatory comorbidity; however, emerging evidence suggests a paradoxical attenuation of ulcerative colitis (UC) severity in patients with MetS. We investigated whether this phenomenon is associated with compartmentalized intestinal immune modulation involving galectin-1 (Gal-1), soluble ST2 (sST2), and CXCL8.
Methods: Two cross-sectional cohorts of newly diagnosed UC patients were analyzed and stratified according to the presence of MetS using ATP III criteria. Clinical, endoscopic, and histological disease activity was assessed using validated scoring systems. Serum and fecal concentrations of Gal-1, sST2, CXCL8, and pro-inflammatory cytokines were quantified by ELISA and compared between UC patients with and without MetS.
Results: Across both studies, UC patients with MetS demonstrated a distinct metabolic profile, including higher lipid, hepatic, and renal biochemical parameters, but lower systemic leukocyte counts. Despite metabolic dysregulation, these patients exhibited milder UC activity, reflected by lower Mayo clinical and endoscopic scores and reduced chronic inflammatory and eosinophilic infiltration. Serum levels of Gal-1, sST2, and CXCL8 did not differ significantly between groups. In contrast, fecal Gal-1, sST2, and CXCL8 were significantly elevated in UC patients with MetS. Moreover, Gal-1 showed predominance over pro-inflammatory mediators, with increased Gal-1/TNF-α, Gal-1/IL-6, and Gal-1/IL-17 ratios, particularly in fecal samples.
Conclusions: MetS is associated with a paradoxically milder UC phenotype and a compartmentalized immune signature characterized by attenuated systemic inflammation but enhanced local intestinal immunoregulation. Increased fecal Gal-1 and sST2 may reflect counter-regulatory mucosal responses, while elevated CXCL8 suggests preserved local immune recruitment. These findings identify a distinct immunometabolic phenotype of UC with MetS and support fecal Gal-1, sST2, and CXCL8 as candidate biomarkers of gut-specific immune modulation.

P-023 Impact of Nano/Microplastics on the Development of Polycystic Ovary Syndrome (PCOS)

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Introduction: Microplastics represent a ubiquitous environmental pollutant with potential adverse effects on human health. As endocrine disruptors, they are increasingly associated with reproductive system disorders, including polycystic ovary syndrome (PCOS). Recent studies have, for the first time, confirmed the presence of microplastics in human follicular fluid, suggesting a potential impact on ovarian function and fertility.
Aim: The aim of this review was to investigate the potential association between microplastic exposure and female reproductive health disorders, with a particular focus on PCOS, through an analysis of current literature and preliminary findings from our own research.
Materials and Methods: A review of recent scientific literature available in PubMed and ScienceDirect databases was conducted, focusing on experimental and epidemiological studies examining the effects of microplastics and their additives on the endocrine system, ovarian function, and hormonal regulation. Molecular mechanisms analyzed included oxidative stress, inflammation, disruption of steroidogenesis, and changes in gene expression related to reproductive function. Additionally, preliminary results from a cross-sectional study conducted via an online survey on a sample of 59 participants were included.
Results: Recent evidence indicates that microplastics are biologically active particles detected in various human tissues and biological fluids, including follicular fluid, where they may directly affect the oocyte microenvironment and ovarian function. Microplastics have been shown to impair oocyte quality, likely through mechanisms involving increased oxidative stress, inflammation, and altered gene expression related to steroidogenesis and cellular homeostasis. At the molecular level, changes have been observed in the expression of genes involved in steroidogenesis (CYP19A1, STAR), as well as genes associated with inflammatory response and antioxidant defense (TNF-α, IL-6, SOD). Furthermore, disruptions in signaling pathways related to insulin resistance—one of the key pathophysiological mechanisms of PCOS—have been reported. Survey results showed that 10.2% of participants had a diagnosed PCOS, while 30.5% reported symptoms suggestive of the disorder, potentially indicating underrecognition of the condition in the population. Hormonal imbalance was reported by 22% of participants, while 20.3% were uncertain about their status. A high level of exposure to microplastics was indicated by the fact that 84.8% of participants regularly used plastic bottles, while despite relatively good awareness, most rarely paid attention to the composition of cosmetic products.
Conclusion: The integration of findings from recent literature and preliminary data suggests a potential biologically plausible association between microplastic exposure and female reproductive health disorders. Of particular concern is their ability to accumulate in reproductive tissues and their potential impact on ovarian function. These findings highlight the need for further research, as well as the importance of assessing microplastic exposure as a potential emerging risk factor in clinical practice. As the study is ongoing, additional research is required to confirm causal relationships.

P-024 Repurposing Metformin for Pancreatic Cancer: Molecular Docking Insights into Comparison with Olomorasib and Gemcitabine

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Pancreatic cancer is one of the most serious oncological diseases with high mortality and extremely low five-year survival rates. Standard treatment protocols, including chemotherapy, surgical removal of the tumor, and radiation therapy, have limited efficacy, especially when the disease is detected at a late stage. Due to these challenges, new experimental therapies for pancreatic cancer are fundamentally changing the treatment approach, ranging from molecular inhibition to advanced targeted drug delivery. In this paper, the effects of repurposing metformin, in addition to the two already known drugs olomorasib and gemcitabine, are examined using molecular docking. The results showed that the binding affinity order is olomorasib > gemcitabine > metformin for all three proteins. The strongest olomorasib score (–9.6 kcal/mol in 6TVG) drops markedly to –5.6 kcal/mol in 7XKJ, suggesting that the conformation or residue composition in 7XKJ is less accommodating for the inhibitor. Gemcitabine shows its best score in 7XKJ (–7.7 kcal/mol), possibly reflecting favorable hydrogen-bonding interactions with polar residues that are absent or differently oriented in 6TVG and 1I09. Metformin exhibits nearly uniform scores (–5.0 to –5.2 kcal/mol), indicating limited sensitivity to protein identity. This finding supports the hypothesis that its anticancer effects are mediated by off-target or indirect mechanisms—such as inhibition of mitochondrial complex I and subsequent AMPK activation—rather than by direct, high-affinity binding to a single protein. In contrast, the pronounced affinity and selectivity of olomorasib, particularly in 6TVG and 1I09, are consistent with its design as a targeted inhibitor. We can conclude that metformin potentially inhibits pancreatic cancer growth through multiple mechanisms: AMPK activation and mTOR pathway inhibition; reductions in insulin and IGF-1 levels; direct antiproliferative effect, including apoptosis of cells resistant to gemcitabine; disturbances in glucose metabolism (Warburg effect); and targeting tumor stem cells responsible for relapse and resistance.

P-025 Modified bile acids and androstanes–Novel promising inhibitors of human cytochrome P450 17A1

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Cytochromes P450 are key enzymes for steroid hormone biosynthesis in human body. They are considered as targets for the screening of novel high efficient drugs. We present the results of screening of bile acids and androstane derivatives toward human recombinant steroid 17α-hydroxylase/17,20-lyase (CYP17A1). A group of steroids, binding with micromolar or submicromolar affinity (in a range from 9 μM – less than 0.1 μM), was identified. Results presented here showed that these steroidal compounds are able to decrease rate of hydroxylation of essential CYP17A1 substrate – progesterone, while some compounds completely inhibited enzyme activity. Structure-activity relationship (SAR) analysis based on in vitro and in silico studies showed that high affinity of the enzyme to bile acids derivatives is correlated with side chain hydrophobicity and presence of hydroxyl or keto group at C3 position. From the other side, bile acid-derived compounds with more polar side chain or substituents at C7 and C12 positions possess higher Kd values. Among androstane-derived steroids couple of Δ5-steroids with hydroxyl group at C3 position, as well as 16,17-secosteroids, were found to be high affinity ligands of this enzyme. The data obtained could be useful for the design of novel highly efficient inhibitors of CYP17A1, since the bile acids-derived compounds are for first time recognized as very effective CYP17A1 inhibitors.

P-026 Green synthesis of metal nanoparticles using plant extracts: comparison of Ag, ZnO and CuO systems and their potential biomedical applications

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Green synthesis of metal nanoparticles using plant extracts represents a significant experimental challenge, as it requires careful optimization of reaction conditions such as pH, temperature, and the ratio of plant extract to metal precursors. Nevertheless, this approach offers an environmentally friendly and sustainable route for the production of nanomaterials with considerable application potential, particularly in the field of medicine. This paper presents a comparative analysis of the green synthesis of silver, zinc, and copper nanoparticles, with emphasis on differences in formation mechanisms, particle characteristics, stability, and potential applications. Special attention is given to their biomedical potential, which was systematically evaluated. The study is primarily based on the authors' experimental results, including both published and unpublished data, supported by relevant literature. Nanoparticle formation was monitored by UV–Vis spectroscopy, while interactions between plant biomolecules and nanoparticle surfaces were examined using FTIR analysis. Particle morphology and size were determined by SEM and TEM techniques. The results indicate that silver nanoparticles are predominantly obtained in elemental form, whereas zinc and copper tend to form oxide nanoparticles (ZnO and CuO) due to their higher susceptibility to oxidation. Compared to ZnO and CuO, silver nanoparticles exhibit faster formation kinetics, narrower size distribution, and improved colloidal stability. Overall, all investigated nanoparticles demonstrate significant potential for biomedical applications.

P-027 Time-Resolved Singlet Oxygen Detection in 5-ALA–Sensitized Glioma Cells

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Photodynamic therapy (PDT) is a light assisted cancer treatment in which the therapeutic outcome is determined by the spatiotemporal generation of reactive oxygen species and singlet oxygen ($^1O_2$). For PDT to progress toward more reliable, personalized clinical use, quantitative insight into $^1O_2$ kinetics and oxygen availability is essential for treatment planning, light dosimetry, and response prediction. This study establishes a translational framework that links $^1O_2$ measurements to mechanistic modeling in glioma cells. Glioma cells were treated with 5 ALA, resulting in intracellular accumulation of protoporphyrin IX (PpIX). Upon excitation with a 635 nm pulsed laser, PpIX generates $^1O_2$ via energy transfer to molecular oxygen. Time-resolved detection of $^1O_2$ phosphorescence at 1270 nm was performed using time-correlated multiple-photon counting in the near-infrared, providing direct access to relevant photochemical dynamics. The measured luminescence decay profiles reflect the coupled effects of photosensitizer triplet state kinetics, local oxygen concentration and microenvironmental conditions. Biexponential analysis of time-resolved singlet-oxygen luminescence yields effective kinetic parameters related to the PpIX triplet state and $^1O_2$ lifetime. These parameters indicate photodynamic efficiency and oxygen availability and may help constrain oxygen diffusion and consumption models in spherical geometry. This supports the extension from monolayers to tumor spheroids, where oxygen gradients and hypoxic regions are more realistically represented, thereby better capturing clinically relevant hypoxia. By integrating direct $^1O_2$ detection with physiologically motivated modeling, this work highlights the importance of singlet oxygen kinetics as a decision relevant metric in PDT. The presented approach supports rational optimization of light delivery and dosimetry and contributes to the scientific foundation for model informed, light assisted cancer therapy.

P-028 New bis-pyrazolate zinc(II) complexes as potential anticancer drugs: from structure to anticancer activity

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Three novel Zn(II) complexes, [$ZnCl_2(H_2LtBu)$], [$ZnCl_2(Me_2LtBu)$] and [$Zn_2Cl_4(H_2LCatBiPyPh)_2$], based on pyrazole-derived ligands, were synthesized and comprehensively characterized by UV–Vis, IR, ^1H and ^{13}C NMR. The molecular structures of [$ZnCl_2(H_2LtBu)$] and [$Zn_2Cl_4(H_2LCatBiPyPh)_2$] were further confirmed by X-ray crystallography. The interactions of the complexes with calf thymus DNA (CTDNA) and human serum albumin (HSA) were investigated using UV–Vis and fluorescence spectroscopy. All complexes exhibited quenching constants (Ksv) of the order of 10^4 with CT-DNA. Similarly, moderate interactions with HSA were observed. Biological evaluation revealed significant cytotoxic effects against colon (HCT-116) and pancreatic (MIA PaCa-2) cancer cell lines, with particularly pronounced activity toward pancreatic cells after 72 h of treatment. Apoptosis was identified as the dominant mechanism of cell death, especially for [$ZnCl_2(H_2LtBu)$], while necrosis was present at lower levels across all treatments. Gene expression analysis showed consistent downregulation of the tumor suppressor gene TP53. Notably, treatment with [$ZnCl_2(H_2LtBu)$] also led to downregulation of CASP3 and IGF1R, suggesting a complex influence on apoptotic signaling pathways and cell proliferation. These findings highlight the potential of Zn(II) complexes as promising candidates for further anticancer investigation.

P-029 Immobilization of Triphenyl(2-tolyl)tin(IV) into SBA-15 Mesoporous Silica Nanostructures for Biomedical Applications

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Over the past decades, organotin(IV) compounds have attracted considerable attention as potential non-platinum anticancer agents due to their pronounced biological activity and promising results obtained in both *in vitro* and *in vivo* studies. Previous research has demonstrated that organotin(IV) compounds can be successfully immobilized within mesoporous silica nanostructures, yielding systems capable of suppressing tumor growth. Importantly, available data indicate that the combined action of organotin(IV) compounds and nanostructures does not induce toxicity toward normal tissues, while preliminary studies suggest significantly enhanced efficacy compared to the free compounds.

In this study, a novel organotin(IV) compound, triphenyl(2-tolyl)tin(IV), was synthesized via a Grignard reaction between triphenyltin(IV) chloride and 2-bromotoluene under an inert nitrogen atmosphere. The obtained compound was characterized by multinuclear NMR spectroscopy (^{1}H, ^{13}C and ^{119}Sn), IR spectroscopy, and elemental analysis, confirming the successful synthesis and
high purity of the desired product. To improve its potential biological activity, the synthesized compound was successfully incorporated into SBA-15 mesoporous silica nanostructures. The obtained hybrid system was characterized by SEM, EDX and BET analyses, confirming successful immobilization within the mesoporous carrier. These findings provide a basis for further investigations involving interactions with biomolecules, as well as future *in vitro* biological evaluations.

P-030 Development of Plant-Based Functional Smoothies with Enhanced Iron Bioavailability for Dietary Support of Iron Deficiency Anemia

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Iron deficiency anemia (IDA) is a widespread condition caused by insufficient iron availability, leading to reduced hemoglobin synthesis and impaired oxygen transport. Symptoms include fatigue, weakness, dyspnea and decreased cognitive and physical performance. According to the WHO, IDA affects around 30% of non-pregnant women, 37% of pregnant women and 40% of preschool children globally. Although oral iron supplementation is effective, it often causes gastrointestinal side effects, resulting in poor adherence. Dietary strategies offer an alternative; however, many plant-based iron sources have low bioavailability due to inhibitors such as polyphenols and phytic acid. To evaluate which combinations of fruits and vegetables can secure high iron bioavailability, we conducted a comprehensive study combining detailed chemical characterization of selected plant species with *in vivo* assessments of iron absorption efficacy. Initially, we performed an extensive analysis of phytochemical composition, identifying species with high iron content and low levels of absorption inhibitors. These were then combined in defined ratios to develop functional food products in the form of smoothies. The formulated smoothies were subsequently produced and evaluated for their efficacy. Their impact on iron absorption was assessed both *in vivo* using an IDA rat model and in a human interventional nutritional study. In the animal study, 28 days of oral administration resulted in significant improvements in hematological parameters associated with IDA. Importantly, in the human study, anemic women consumed the formulated smoothies daily for 60 days. Hematological parameters were monitored and compared with an untreated control group. The intervention group demonstrated a significant improvement in key anemia-related blood parameters. These findings indicate that the selected plant combinations provide a source of bioavailable iron and support their potential application in the development of functional foods. Notably, the positive outcomes observed in the human study highlight their relevance for dietary prevention and supportive management of IDA.

P-031 Tumor repopulation template and differential response of colorectal cancer organoids to Platinum IV-NSAID hybrids

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Therapeutic failure in high-grade tumors is often associated with resistance to cell death. However, dying cells can promote tumor regrowth through the PGE2-mediated Phoenix rising pathway. To simultaneously induce cancer cell death and inhibit pro-regenerative signaling, platinum(IV) hybrid molecules based on cisplatin and anti-inflammatory agents (naproxen, flurbiprofen, or diacetyl caffeate) were developed. Enhanced passive tumor targeting was achieved by immobilizing these hybrids within SBA-15 mesoporous silica. To simulate crosstalk between dying and surviving cells in the tumor microenvironment organoids were derived from tumors induced by live MC38 cells (MLO) and mixtures of live and dead MC38 cells (MLDO) and treated with experimental therapeutics. CellTiter-Glo® assay was used to determine drug effects on organoid viability. Treatment induced a decrease in viability in both organoid types. Following three days of treatment with the previously determined IC50 concentrations, organoids were analyzed for COX-2, 5-LOX, EP4, caspase 3, and HMGB1 expression using a semi-quantitative scoring system. Baseline analyses revealed differences between untreated organoids derived from live tumor cells (MLO) and mixed live/dead tumor cells (MLDO). COX-2 and HMGB1 were strongly expressed in both groups, indicating a persistent inflammatory microenvironment. EP4 and caspase 3 expression were lower in MLDO, whereas 5-LOX expression was approximately two-fold higher in MLDO than in MLO, suggesting its involvement in the metabolic and inflammatory profile of MLDO. Treatment responses differed markedly between organoid types. Caspase 3 and EP4 expression increased significantly in MLDO following treatment, while opposite trends were observed in MLO. The enhanced caspase 3 activity in MLDO suggests apoptosis as the predominant mode of cell death. In addition, all treatments substantially modulated 5-LOX expression, with effects depending on both organoid origin and hybrid molecule formulation. These differences in protein expression and treatment responses underscore the need for tailored therapeutic strategies targeting both tumor cells and the tumor microenvironment in aggressive tumors.

P-032 Metal-dependent antifungal activity of iminodiacetato-dithiocarbamato based complexes against *Botryosphaeria dothidea*

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Dithiocarbamates are well-known sulfur-donor ligands with broad biological relevance, including applications in agriculture as fungicidal agents. Their coordination to transition metal ions may significantly modify the biological response of the parent ligand, depending on the nature of the metal center, coordination geometry and physicochemical properties of the resulting complexes. In this contribution, the antifungal activity of ligand precursor, ammonium-iminodiacetato-dithiocarbamate, $(NH_4)_3$idadtc, and its mixed-ligand Zn(II) complexes, NH_4[Zn(idadtc)(en)] and NH_4[Zn(idadtc)$(en)_2$], was evaluated against the phytopathogenic fungus *Botryosphaeria dothidea*.

The inhibitory effect was assessed under laboratory conditions by monitoring fungal mycelial growth on potato dextrose agar medium containing different concentrations of the investigated compounds. The obtained results were compared with the commercial dithiocarbamato-based fungicide Ziram. Under the applied experimental conditions, the free ligand did not show significant inhibition of *B. dothidea* growth. In contrast, both Zn(II) complexes exhibited weak but measurable antifungal activity, with NH_4[Zn(idadtc)$(en)_2$] showing the highest inhibitory effect among the tested Zn(II)-based systems. However, the activity of both complexes remained considerably lower than that of Ziram.

To place these findings in a broader context, the results are discussed in relation to previously reported Co(II), Co(III), Mo(VI) and Pt(II) complexes with $(NH_4)_3$idadtc, which showed that complexation may enhance antifungal activity, but not uniformly for all metal centers. Comparison with these literature data suggests that the dithiocarbamate ligand framework contributes to biological activity, while the final antifungal response is governed by the combined influence of ligand coordination, metal identity and complex geometry.

P-033 Antimicrobial activity of the Au(III) complex containing ammonium iminodiacetatodithiocarbamate

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The development of microbial resistance to existing antibiotics represents one of the greatest challenges of modern medicine, highlighting the urgent need for the discovery of new antimicrobial agents. In this context, transition metal complexes containing dithiocarbamate ligands have attracted significant attention due to their pronounced biological and pharmacological properties. Numerous studies have shown that dithiocarbamate complexes exhibit significant antibacterial activity against Gram-positive and Gram-negative bacteria. To direct research efforts toward combating drug-resistant pathogens, the World Health Organization (WHO) published a list of priority pathogens in 2017, including critical species such as *Acinetobacter baumannii, Pseudomonas aeruginosa, Staphylococcus aureus* and *Salmonella spp*. (Tacconelli et al., 2018). In the present study, the antimicrobial activity of the Au(III) dithiocarbamate complex was evaluated at eight different concentrations on two Gram-positive (*Bacillus subtilis* ATCC 6633, *Staphylococcus aureus* ATCC 25922) and three Gram-negative bacteria (*Escherichia coli* ATCC 8739, *Pseudomonas aeruginosa* ATCC 9027, *Salmonella enteritidis* ATCC 13076) as well as three fungi strains (*Candida albicans* ATCC 10231, *Penicillium sp.* and *Aspergillus niger* ATCC 16404). The test was performed using the microdilution method. The results showed that the synthesized Au(III) dithiocarbamate complex exhibited varying levels of activity depending on the tested microorganisms. The strongest effect was observed against *B. subtilis* ATCC 6633 (bactericidal) and against *C. albicans* ATCC10231 (fungicidal), while it showed an inhibitory effect against other microorganisms. These results provide a basis for further research of the synthesized Au(III) dithiocarbamate complex and its potential biological significance.

P-034 Montelukast Promotes Apoptosis, Cell Cycle Arrest and Autophagy in Breast Cancer Cells while Modulating Immune Responses

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Background: Montelukast, used in the treatment of asthma and allergic rhinitis, acts as a selective antagonist of CysLTR1. Expression of these receptors has also been demonstrated in tumor cells, suggesting that montelukast may be a candidate for drug repurposing in breast cancer treatment.
Methodology: The effect of montelukast on the viability of murine and human breast cancer cell lines was assessed by MTT assay. Molecular mechanisms of cell death and cell cycle regulation in montelukast treated 4T1 cells were analyzed using flow cytometry. The immunomodulatory effects of montelukast were evaluated *in vitro* by ELISA in splenocytes isolated from BALB/c mouse.
Results: Montelukast exhibited cytotoxic effects on murine and human breast cancer cell lines (4T1, E0771 and MDA MB 231). In 4T1 cells, montelukast induced apoptosis and cell cycle arrest in the G0/G1 phase, shown by an increased percentage of caspase-3^+, Bax^+, and Annexin V^+PI^- cells, a reduced Bcl2/Bax ratio, alongside increased p21 and p16 expression, and decreased Ki67 and cyclin D expression, compared to untreated cells. Montelukast increased ROS production, induced mitochondrial membrane depolarization and cytosolic cytochrome c release. Autophagy modulation was also observed, with an increased AO red/green ratio and decreased LC3B-II expression. Montelukast increased IFN-γ, IL-10, IL-1β, IL-4 and IL-17 and decreased TNF-α compared to medium, attenuated most pro-inflammatory cytokines under ConA stimulation, and under LPS stimulation reduced IL-4 and IL-1β while increasing IFN-γ, indicating predominant anti-inflammatory effects under strong immune activation.
Conclusion: Montelukast showed antitumor effects on breast cancer cells through induction of apoptosis, cell cycle arrest and autophagy modulation, while also demonstrating immunomodulatory effects, supporting its potential repurposing as an adjuvant agent in breast cancer therapy.

P-035 Silver(I) Complex with S-Propyl Derivative of Thiosalicylic Acid Suppresses Murine Breast Tumor Growth through Apoptosis Induction and Cell Cycle Arrest

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Background: Antibacterial, antifungal, and antitumor activities of silver complexes have been confirmed. However, antitumor activity of silver(I) complexes with S-alkyl thiosalicylic acid derivatives remains unexplored.
Methodology: The cytotoxic potential of the newly synthesized Silver(I) complexes with S-alkyl derivatives of thiosalicylic acid (C1-C5) was determined by MTT assay. Colony formation and scratch assays, analyses of cell death and cell cycle distribution after C3 treatment were performed. After the orthotopic application of 4T1 cells (3×10^4) and the appearance of a palpable tumors, female BALB/c mice were randomly assigned to four groups. Mice were treated with C3 (3 mg/kg), C3 (6 mg/kg), CDDP (6 mg/kg), or vehicle (untreated group). On the day 30 of the experiment, the animals were sacrificed, Blood samples were collected and tissue sections (liver and kidney) were stained with H&E.
Results: Complexes C1-C5 exhibited strong cytotoxicity against murine and human cancer cell lines (4T1, CT26, LLC1, A549, HCT116, MDA-MB-468). Complex C3 triggered apoptosis in 4T1 cells. The expression of pro-apoptotic Bax cells was increased in 4T1, while the percentages of Bcl-2^+, Bcl-XL^+, and MCL-1^+ 4T1 cells were significantly decreased after C3 treatment compared to untreated 4T1 cells. Treatment with C3 was associated with increased ROS production and reduced mitochondrial membrane depolarization. The C3 induced 4T1 cell cycle arrest in G0/G1 phase, by decreasing the expression of cyclin D3 and increasing theexpression of p16, p21, and p27. C3 treatment markedly reduced the proliferation capacity of 4T1 cells. The C3 complex significantly diminished tumor growth in an orthotopic mammary carcinoma model while demonstrating good systemic tolerance.
Conclusions: Based on antitumor capacities of silver(I) complex with S-propyl derivative of thiosalicylic acid, this compound may represent a promising candidate for the development of new anticancer drug.

P-036 Development of new generation quinone-based synthetic agents with potential anticancer activity

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According to GLOBOCAN 2022 data, breast cancer is the most frequently diagnosed cancer type in women (15.4%), while lung cancer remains the deadliest cancer type globally with a rate of 18.7%. The inadequacy of current treatments necessitates the development of next-generation strategies targeting signallingpathways. Recent study has demonstrated that anilino-1,4-naphthoquinone derivatives exhibit potent EGFR inhibitory activity at the nanomolar level (IC_{50}: 3.96-18.64 nM), with certain compounds reported to be up to four times more active than erlotinib. Structurally, the 1,4-quinone core is capable of acting as a bioisosteric analogue of the quinazoline scaffold present in erlotinib, suggesting its potential as a promising pharmacophore for kinase inhibition. Based on this rationale, the present study is designed around a dual inhibition strategy targeting both EGFR and HER2 receptors, aiming to overcome drug resistance and reduce adverse effects. In this study, a new series of aminoquinones was synthesized by the reaction of nucleophiles containing different substituents at different positions with 1,4-benzoquinone, and their structures were characterized by spectroscopic methods (^{13}C NMR, ^{1}H NMR, High-Resolution Mass Spectrometry and FTIR). Subsequently, the biological activities of these compounds were evaluated.

P-037 Ensuring reliability in laboratory diagnostics: comparative study of estradiol results across analytical and middleware systems

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Introduction: Accurate determination of estradiol is important in laboratory diagnostics, particularly in clinical and endocrine assessments. Reliable results depend not only on the performance of analytical systems but also on the effectiveness of post-analytical data management tools.
Aim of the Study: The aim of this study was to perform a comparative analysis of estradiol results obtained from two laboratory systems, an analytical platform (Atellica) and a middleware system (Remisol), using 15 patient samples.
Results: The comparative evaluation demonstrated a strong correlation between the two systems. Statistical analysis indicated predominantly low to moderate percentage differences (bias) among the examined samples. The observed variability remained within acceptable analytical limits, suggesting good agreement between the systems in routine laboratory practice.
Conclusion: The findings highlight the necessity of continuous verification and quality assessment of both analytical and post-analytical processes. Combined evaluation of analytical performance and data management is essential for ensuring accuracy, consistency, and reliability of laboratory diagnostic results.

P-038 A Novel Pd(II)-Pincer Complex Stimulates Pro-Inflammatory Splenocyte Responses and Exhibits Selective Antimicrobial Activity *In Vitro*

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Background: The clinical exploration of palladium(II) complexes has gained traction due to their structural similarities to platinum-based drugs, with pincer-type ligands effectively optimizing their kinetic stability. Building upon its previously established in vitro antitumor efficacy, this study aimd to evaluete the immunomodulatory potential and antimicrobial profile of a newly sintethesized mononuclear Pd(II)-pincer complex, [Pd(N^2,N^6-bis(5-methylthiazol-2-yl)pyridine-2,6-dicarboxamide)Cl]Cl.
Methods: Primary mouse splenocytes were treated with the Pd(II) complex either alone or alongside lipopolysaccharide (LPS) or Concanavalin A (ConA) to stimulate innate and adaptive immune pathways, respectively. The concentrations of key cytokines (IFN-γ, IL-17, IL-4, TNF-α, IL-1β, and IL-10) were quantified using commercial ELISA kits. Additionally, the antimicrobial profile was evaluated against reference Gram-positive and Gram-negative bacterial strains, as well as yeasts, by determining Minimal Inhibitory Concentration (MIS) and Minimal Bactericidal/Fungicidal Concentrations (MBC/MFC) via the broth microdilution method.
Results: The Pd(II) complex independently stimulated an increase in all evaluated cytokines compared to untreated controls. In co-treatment with LPS, it significantly enhanced the secretion of IFN-γ, IL-1β, and IL-17. When combined with ConA, the complex significantly elevated TNF- α and IL-17 levels, while concurrently suppressing the anti-inflammatory cytokines IL-10 and IL-4, as well as IFN-γ. Antimicrobial screening revealed week to moderated activity, with Gram-positive bacteria demonstrating superior susceptibility over Gram-negative strains. Staphylococcus epidermidis exhibited the highest sensitivity (MIC/MBC of 15.63μg/mL), whereas Escherichia coli and Proteus mirabilis showed poor susceptibility. Weak antifungal effects were recorded against Saccharomyces cerevisiae and Candida albicans.
Conclusion: The novel Pd(II)-pincer complex demonstrates a robust immunomodulatory capacity by shifting the cytokine production profile toward a pro-inflammatory phenotype, complemented by selective antimicrobial action. These dual characteristics suggest its potential as a multifunctional candidate for further preclinical development in antitumor and antimicrobial therapies.

P-039 H_2S Donors Attenuate Renal Injury in NOD Mice by Inhibiting Ferroptosis

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The role of ferroptosis, an iron-dependent form of regulated cell death, is increasingly recognized in the pathogenesis of diabetic nephropathy (DN). This study evaluates the antiferroptotic efficacy of hydrogen sulfide (H_2S) donors, specifically the synthetic cysteine-3S (Cys-3S) and the natural sulforaphane (Sfn), in a diabetic model. Upon confirmation of persistent hyperglycemia in female NOD mice, treatment was maintained for three weeks. To confirm that the observed renal protections were specifically due to the inhibition of ferroptosis, the specific inhibitor liproxstatin-1 (Lip-1) was utilized as a positive control and mechanistic benchmark. Diabetic conditions typically induce glomerular hypertrophy and significant iron overload within the renal cortex. Treatment with Sfn successfully reduced renal corpuscle dimensions, effectively returning them to the morphometric profile of nondiabetic controls. Both H2S donors mitigated iron accumulation, with Cys-3S demonstrating high efficacy in restoring iron scores to levels observed in young healthy mice. These results mirrored the effects of Lip-1, the findings suggesting that the reduction in iron-mediated damage is a direct consequence of ferroptosis inhibition. Molecular analysis further supported the protective role of H2S donors against oxidative damage. Immunostaining for 4-hydroxynonenal (4-HNE), a biomarker of lipid peroxidation, was markedly attenuated by Cys-3S. Furthermore, Cys-3S selectively decreased the expression of the autophagy marker LC3B, while Sfn robustly increased ferritin heavy chain 1 (FTH1) levels to improve iron sequestration. Crucially, glutathione peroxidase 4 (GPX4), the primary enzymatic defense against ferroptosis, was restored to control levels by both H2S donors, a result validated by the similar restorative action of Lip-1. These findings demonstrate that H2S donors exert protective effects against DN by suppressing iron accumulation, reducing lipid peroxidation, and upregulating antioxidant defenses. The consistent performance of Cys-3S and Sfn relative to the specific inhibitor Lip-1 confirms their status as potent antiferroptotic agents. The targeted restoration of GPX4 and the modulation of FTH1 suggest that these compounds represent viable therapeutic strategies for inhibiting ferroptosis in chronic hyperglycemic states.

P-040 Burnout Syndrome Is Associated with Shift-Dependent Alterations in Serum Cytokine Profile among Emergency Medical Workers

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Background: Burnout syndrome is a major occupational and health problem among emergency medical workers and may be associated with immune dysregulation and chronic low-grade inflammation. This study aimed to examine whether burnout is related to serum cytokine changes after day and night shifts in employees of the Institute for Emergency Medicine Belgrade.
Methods: This observational, comparative, non-interventional study included physicians and medical technicians stratified according to burnout status using the Maslach Burnout Inventory. Burnout was defined by at least two criteria: high emotional exhaustion, high depersonalization, and low personal accomplishment. Psychological distress and sleep quality were assessed using the Hospital Anxiety and Depression Scale and Jenkins Sleep Questionnaire. Venous blood was collected after 12-hour day and night shifts. Serum TNF-α, IL-17, IL-33, IL-4, IL-12, IL-10, and IFN-γ were measured by commercial human ELISA assays. Cytokine/IL-10 ratios, lipid parameters, and the LDL/HDL atherosclerosis index were additionally analyzed.
Results: Participants with burnout had significantly higher TNF-α after the night shift than those without burnout (24.89 ± 1.00 vs. 21.75 ± 0.66 pg/mL; p = 0.009). IL-17 was also increased after the night shift (165.99 ± 19.39 vs. 126.71 ± 12.82 pg/mL; p = 0.003), as was IL-4 (4.22 ± 0.21 vs. 3.74 ± 0.18 pg/mL; p = 0.045). After the day shift, burnout was associated with higher IFN-γ (18.74 ± 0.65 vs. 17.03 ± 0.28 pg/mL; p = 0.011) and IL-10 (22.38 ± 2.64 vs. 17.92 ± 1.76 pg/mL; p = 0.042). IL-10 was also higher after the night shift in the burnout group (26.44 ± 13.75 SEM vs. 9.66 ± 0.75 pg/mL; p = 0.045).
Conclusion: Burnout syndrome in emergency medical workers is associated with shift-dependent cytokine alterations, including enhanced pro-inflammatory activity and a compensatory anti-inflammatory response, particularly after night work

P-041 Influence of pH on the Inhibitory Potential of Icaritin toward Myeloperoxidase

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Myeloperoxidase (MPO), a heme-containing enzyme responsible for the generation of reactive oxidizing species during inflammatory and oxidative stress-related processes, represents an important therapeutic target in numerous pathological conditions. In search of potential MPO inhibitors, naturally occurring antioxidants have attracted considerable attention due to their favorable biological activities. Icaritin (ICT), a flavonoid with pronounced antioxidant potential, exists in several protonation states depending on pH because of its acid–base properties (pKa1 = 7.02, pKa2 = 8.62, pKa3 = 9.09), which may significantly influence its interactions with biological targets. The binding interactions of neutral (ICT), monoanionic (ICT-), dianionic (ICT2-), and trianionic (ICT3-) forms of ICT toward MPO were investigated using molecular docking simulations. All protonation states exhibited favorable binding within the MPO active site, with binding free energies (ΔGbind) ranging from −6.25 to −6.66 kcal mol^{-1}, while ICT3- showed the highest affinity. A similar trend was observed for inhibition constants (Ki), decreasing from 26.22 to 13.22 μM with increasing deprotonation. Effective binding affinities were further evaluated under acidic (pH = 5.5), physiological (pH = 7.4), and slightly basic (pH = 8.5) conditions. The effective affinity increased with increasing pH, from −6.25 kcal mol^{-1} at pH = 5.5 to −6.36 kcal mol^{-1} at pH = 7.4 and −6.47 kcal mol^{-1} at pH = 8.5. A similar pH-dependent trend was observed for the effective inhibition constants, which decreased from 26.03 to 21.90 and 18.15 μM with increasing pH. The enhanced binding observed at higher pH values is associated with the increased prevalence of deprotonated ICT species, which exhibit more favorable interactions within the MPO active site. Overall, these findings highlight the important role of protonation equilibria in ICT–MPO interactions.

P-042 Influence of pH on the Inhibitory Potential of Icaritin toward Xanthine Oxidase

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Icaritin (ICT), a natural flavonoid with antioxidant activity, has attracted attention due to its biological potential. Owing to its acid–base properties (pKa1 = 7.02, pKa2 = 8.62, pKa3 = 9.09), ICT exists in several protonation states depending on pH, which may influence its interactions with biological targets. Xanthine oxidase (XOD), a key enzyme in purine metabolism and a major source of reactive oxygen species, is an important therapeutic target in oxidative stress-related disorders. The interactions of the neutral (ICT), monoanionic (ICT-), dianionic (ICT2-), and trianionic (ICT3-) forms of ICT with XOD were investigated using molecular docking. All forms exhibited favorable binding within the active site, with binding free energies ranging from −7.60 to −8.24 kcal mol-^{1}, while ICT3- showed the highest affinity. To obtain a more realistic description of ICT–XOD interactions, effective binding affinities were evaluated under acidic (pH = 5.5), physiological (pH = 7.4), and slightly basic (pH = 8.5) conditions. ICT predominates under acidic conditions, ICT- at physiological pH, whereas deprotonated species (ICT- and ICT2-) become dominant under slightly basic conditions. The effective binding affinity becomes more favorable with increasing pH, as reflected in the decrease in binding free energy from –7.61 kcal mol^{-1} under acidic conditions to –7.90 kcal mol^{-1} under physiological conditions and –7.97 kcal mol^{-1} under slightly basic conditions. A similar trend was observed for effective inhibition constants, decreasing from 2.63 to 1.62 and 1.44 μM. These findings indicate that ICT–XOD interactions involve multiple protonation states, with deprotonated forms prevailing at higher pH and showing slightly enhanced binding affinity. Although the differences are modest, a consistent trend was observed, highlighting the importance of including acid–base equilibria in docking studies and supporting ICT as a potential XOD inhibitor.

P-043 Indoor pollution from fragranced products and lung cancer

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Despite the fact that up to 25% of lung cancer cases occur in non-smokers, the prevailing misconception that the disease is primarily linked to tobacco use often leads to the neglect of other risk factors. Perfumes and scented products are widespread in daily life. The long-term exposure to various ingredients used in these products has been associated with endocrine disruption, respiratory and reproductive issues. Considering that the majority of non-smokers (up to 80%) are diagnosed with lung adenocarcinoma, the overall aim of this study was to evaluate the exposure of lung cancer patients to fragrances and scented products. Differences in exposure to these risk factors among adenocarcinoma (LUAD) and squamous cell carcinoma (SQCC) were assessed as well. In this study 66 patients with LUAD (59% male) and 62 patients with SQLC (51.6% male) with inoperable stage IIIB and IV of lung cancer, diagnosed in the Institute for Pulmonary Diseases of Vojvodina, Serbia, were enrolled. The exposure habits were assessed through multiple questions. Based on the obtained results, scented laundry detergents were used by the majority of the included patients (95.3%), followed by scented household cleaning products (94.5%) and fabric softeners (93.0%). Almost half of the patients (46%) of both genders used deodorant from every day to a couple of times per week, while only 21.9% of individuals of both genders applied frequently perfumes and colognes. Only 7.8% of total respondents used organic, fragrance-free cleaning products in everyday life. The gender differences were observed regarding the deodorant use. Women with LUAD and SQLC more frequently applied deodorant than men ($p=0.003$ and $p=0.005$, respectively). These differences are probably the result of women's hygiene habits. Although no gender differences were observed in the usage of other scented products, men with LUAD and SQLC were more exposed to cleaning products in comparison to women. Having in mind that scented products are source of volatile organic compounds as well as endocrine disruptors, their role in the development of hormone-dependent cancers requires further attention.

P-044 Household combustion of fossil fuels as risk factor for lung cancer in Serbia

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The increasing levels of airborne particulate matter with aerodynamic diameter of 2.5 microns (PM2.5) have been associated with an increased incidence of non-small lung cancer which accounts for more than 250 000 deaths globally per year. These particles are commonly found in fossil fuels smoke. According to the Material flow indicators in 2024, made by Statistical Office of the Republic of Serbia, the greatest consumption was related to fossil energy material (40 952 thousand tons). Bearing in mind the high lung cancer incidence and mortality, the aim of this study was to examine the exposure of lung cancer patients in the North Serbian Region to household combustion of fossil fuels and to evaluate the gender differences in the exposure source. A total of 128 patients (55.5% males) with non-small lung cancer (stage IIIB and IV), diagnosed in the Institute for Pulmonary Diseases of Vojvodina, Serbia, were included. Adenocarcinoma (LUAD) and squamous cell carcinoma (SQLC) were distributed almost equally among the studied population (51.6% vs. 48.4%). The exposure to household combustion of fossil fuels was evaluated via the questionnaire. The majority of respondents of both genders used individual heating or cooking combustion systems (58.6%), followed by wood (50.8%). Natural gas was reported by 24.2% of patients, while only 6.3% of them used coal. Patients diagnosed with LUAD or SQLC did not used oil as an energy source for cooking and/or heating. Males with SQLC reported statistically significantly higher exposure to wood ($p<0.01$) whereas natural gas combustion was more frequently identified by female respondents ($p<0.05$). The obtained results indicate that individual fossil fuel combustion systems and wood-burning systems are mostly used for heating and cooking by the studied population. A larger cohort is needed to better elucidate how fossil fuel usage and PM2.5 levels in air in Serbia are associated with the lung cancer incidence.

P-045 First-Line Pembrolizumab in Metastatic Non-Small Cell Lung Cancer: A Single-Centre Real-World Analysis of Treatment Response, Survival and Toxicity

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Background: Pembrolizumab has become an important first-line treatment option for patients with metastatic non-small cell lung cancer (NSCLC) and high PD-L1 expression. Real-world data are valuable for assessing treatment outcomes and toxicity outside controlled clinical trials.
Aim: This study aimed to analyze the epidemiological and clinical characteristics of patients with metastatic NSCLC treated with first-line pembrolizumab, with special focus on treatment response, progression-free survival (PFS), overall survival (OS), and treatment-related toxicity.
Methods: A retrospective observational study was conducted at the Centre for Medical Oncology, University Clinical Centre Kragujevac. The study included 52 patients with stage IV NSCLC treated with pembrolizumab between 2019 and 2021. Data were obtained from medical records and included demographic characteristics, histopathological type, PD-L1 expression, metastatic sites, number of treatment cycles, response to therapy, survival outcomes, and adverse events graded according to CTCAE criteria.
Results: The mean age of patients was 63.10 ± 9.41 years, and most were male. Squamous cell carcinoma was the most common histological subtype. Stable disease was observed in 46.2% of patients, disease progression in 44.2%, and partial response in 9.6%. The mean PFS was 7.25 ± 0.56 months, with a median PFS of 6 months, while the three-year OS rate was 59.4%. Treatment-related adverse events were recorded in 23.1% of patients, most commonly thyroid toxicity, hepatitis, and skin reactions. Longer PFS was significantly associated with a higher number of pembrolizumab cycles, favorable treatment response, and the occurrence of adverse events.
Conclusion: In this single-centre real-world cohort, first-line pembrolizumab demonstrated clinically relevant disease control and an acceptable toxicity profile in patients with metastatic NSCLC and positive PD-L1 expression. The findings support the importance of real-world monitoring of treatment outcomes, toxicity, and potential predictive factors in immunotherapy-treated patients.

P-046 Loss of ST2 Signaling Enhances Adhesion Formation and Fibrotic Remodeling in Experimental Adhesive Peritonitis

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Background: Postoperative peritoneal adhesions are clinically relevant complications of abdominal surgery and are driven by local inflammation, impaired tissue repair, fibroblast activation, and collagen-rich fibrosis. The IL-33/ST2 axis is involved in immune regulation, tissue remodeling, and repair responses, but its role in postoperative adhesive peritonitis remains insufficiently defined. This study aimed to evaluate whether disruption of IL-33/ST2 signaling affects postoperative severity, adhesion formation, and collagen deposition in an experimental model of adhesive peritonitis.

Methods: Adhesive peritonitis was induced in male ST2 knockout mice (ST2-/-) and wild-type BALB/c mice by laparotomy, cecal abrasion, and parietal peritoneal abrasion. Seven days after surgery, postoperative severity was assessed using the Post-surgery Severity Assessment (PSSA) score. Peritoneal adhesion formation was evaluated macroscopically using the gross adhesion score and the Nair macroscopic adhesion score. Collagen deposition in peritoneal/adhesive tissue was quantified histologically as Sirius Red-positive area.

Results: ST2-/- mice showed significantly higher PSSA scores compared with WT BALB/c mice after induction of adhesive peritonitis (5.17 ± 1.17 vs. 1.17 ± 0.79; $p = 0.018$). The macroscopic gross adhesion score was also increased in ST2-/- mice (1.83 ± 0.40 vs. 0.83 ± 0.31; $p = 0.048$), indicating a greater quantity of intra-abdominal adhesions. Similarly, ST2-/- mice had significantly higher Nair adhesion scores than WT animals (2.50 ± 0.67 vs. 0.83 ± 0.31; $p = 0.037$), suggesting more severe postoperative adhesion formation. Histological analysis demonstrated a significantly increased Sirius Red-positive area in ST2-/- mice compared with WT BALB/c mice (35.37 ± 2.05 vs. 26.24 ± 1.86; $p = 0.003$), indicating enhanced collagen deposition and fibrosis.

Conclusion: Disruption of the IL-33/ST2 axis is associated with increased postoperative severity, more pronounced peritoneal adhesion formation, and enhanced collagen accumulation in experimental adhesive peritonitis. These findings suggest a potential protective role of IL-33/ST2 signaling in the regulation of postoperative inflammation, fibrotic remodeling, and adhesive tissue organization.

P-047 Pembrolizumab monotherapy in PD-L1-High Metastatic NSCLC Real-World 4-Year Outcomes

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Background: Lung cancer represented the most prevalent malignancy diagnosed in 2022 (12.4% of all cancers worldwide), followed by breast cancer (11.6%) and colorectum (9.6%), accounting for 1.8 million deaths, with non-small cell lung carcinoma (NSCLC) comprising 80-90% of all lung cancers. The KEYNOTE-024 randomized controlled trial demonstrated the first-line efficacy of immune checkpoint inhibitor (ICI), such as pembrolizumab monotherapy in adults with metastatic NSCLC with PD-L1 tumor proportion score (TPS) ≥50% and wild-type EGFR/ALK, yielding superior median progression-free survival (PFS, 10.3 vs. 6.0 months) and overall survival (OS), with a more favorable toxicity profile than platinum-based chemotherapy, albeit a higher incidence of immune-related adverse events (irAEs, 29.2%). However, real-world evidence (RWE) on its effectiveness remains scarce, specially within Eastern European patients.
Methods: We performed a retrospective single-center analyis of 52 patients with metastatic NSCLC and high PD-L1 expression (TPS≥50%) treated with first-line pembrolizumab monotherapy from 2021 to 2022. Information regarding patient demographics, clinical features of disease, and treatment outcomes, including treatment efficacy and safety was retrospectively obtained and analyzed. Survival outcomes, including PFS and OS, was calculated using Kaplan – Meiers curves. Results: A total of 52 patients were included. The median patient age at the time of diagnosis was 62 years, with 75% of the population having non-squamous histology. The majority of the population had a smoking history, with 55% of patients being current smokers. CNS metastases were known at baseline in 30% of the population. The median PFS in the real world (rwPFS) was 5.33 months (95% Cl 2.74-7.92), and the median OS was 9.93 months (95% Cl 7.61-12.25). irAEs occurred in 29% of patients.
Conclusions: Our findings align with randomized controlled trial data, providing RWE that corroborates the therapeutic benefit and safety profile of first-line pembrolizumab monotherapy in Serbian metastatic NSCLC patients with high PD-L1 expression (TPS ≥50%). Moreover, these results validate high PD-L1 expression and irAE occurrence as reliable predictive biomarkers associated with improved clinical outcomes.

P-048 Approaches to Identifying Clinically Significant SNPs in Cancer Research

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Single nucleotide polymorphisms (SNPs) are single-base alterations (purine or pyrimidine) at specific DNA nucleotide. Unlike mutations, SNPs are generally defined as common germline variants present in at least 1% of the population. They are important targets in numerous clinical applications, including the assessment of disease susceptibility, the diagnostic and prognostic biomarkers, and the prediction of therapeutic response. Clinically significant SNPs located within coding regions may alter protein structure or function, whereas those in promoter regions can influence gene expression. The identification of clinically relevant SNPs in cancer involves a range of bioinformatic approaches, including database mining, literature review, and, where appropriate, experimental validation. Depending on the research objective, several public databases provide information on SNP location and functional annotation. For example, dbSNP, maintained by the National Center for Biotechnology Information (NCBI), is a widely used repository of genetic variation. ClinVar is an archive of genomic variants and their relationships to disease, including evidence regarding drug response; however, its data are intended for research rather than diagnostic use. The GWAS Catalog contains thousands of publications and tens of thousands of SNP–trait associations. OMIM (Online Mendelian Inheritance in Man) catalogs variants associated with Mendelian disorders across more than 16,000 genes and is a valuable resource for genotype–phenotype correlations. The 1000 Genomes Project provides comprehensive data on SNPs and structural variants across diverse populations, generated with high-throughput sequencing technologies. Bioinformatic tools such as SIFT, PolyPhen-2, GTEx, and FASTSNP are commonly used to predict the functional impact of novel SNPs. Confirmation of clinical significance typically requires experimental validation, including PCR-based genotyping methods (e.g., TaqMan assays or high-resolution melting analysis), next-generation sequencing, and functional assays to assess effects on protein activity. All in all, these resources and approaches form a robust framework for identifying clinically significant SNPs in cancer research.

P-049 Biological Activity Assessment of Cinnamon Bark Essential Oil (*Cinnamomum zeylanicum* L.): Cytotoxic and Immunomodulatory effects

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Cinnamon bark essential oil (*Cinnamomum zeylanicum* L.) has attracted considerable scientific interest due to its diverse biological activities and therapeutic potential. The aim of this study was to investigate cytotoxic and immunomodulatory properties of commercially available cinnamon bark essential oil (CEO). The cytotoxic potential of CEO was evaluated against human and murine breast and colorectal cancer cell lines, as well as non-cancerous human fibroblasts (MRC-5). CEO exhibited selective antitumor activity, with the strongest effect observed in HCT116 human colorectal cancer cells (IC_{50} = 1.18 μg/mL), while showing lower toxicity toward non-cancerous cells (IC_{50} = 7.21 μg/mL). The selectivity index was highest for HCT116 cells (SI = 6.1), indicating pronounced tumor selectivity. Further analysis revealed that CEO induced both early and late apoptosis in HCT116 cells, accompanied by increased expression of the pro-apoptotic proteins Bax and caspase-3 and decreased expression of the anti-apoptotic protein Bcl-2. Furthermore, CEO significantly reduced Ki67 and Cyclin D expression, increased p21 and p27 levels, and downregulated phosphorylated AKT, indicating inhibition of cell proliferation and G1-phase cell-cycle arrest. The immunomodulatory activity of CEO was investigated using murine splenocytes. In activated immune cells stimulated with concanavalin A (ConA), CEO significantly reduced the production of IL-1β, TNF-α, IFN-γ, IL-17 and IL-10, demonstrating an immunosuppressive effect on ongoing inflammatory responses. In contrast, CEO alone increased cytokine production in naive splenocytes and promoted a predominance of pro-inflammatory cytokines over IL-10, suggesting activation of innate immune mechanisms. These findings indicate a dual immunomodulatory profile of CEO, characterized by suppression of excessive immune activation while simultaneously stimulating immune responses in resting cells. The results highlight the potential of cinnamon bark essential oil as a selective anticancer and immunomodulatory agent with potential in the development of new therapeutic agents.

P-050 Targeting Ferroptosis in Diabetic Liver Injury: The Protective Role of Hydrogen Sulfide and Reactive Sulfur Species

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Diabetes-induced liver damage is a serious condition that can progress to cirrhosis and eventually hepatocellular carcinoma. Recently, we discovered ferroptosis contribution to diabetes-related liver damage suggesting that targeting this pathway represents a potential therapeutic strategy. Disturbances in hydrogen-sulfide (H2S) metabolism are associated with diabetes, and H2S/reactive sulfur species (RSS) donors treatment have been implicated in ferroptosis regulation, but their ability in preventing diabetes-induced liver damage via ferroptos inhibition remains unclear. Here, we investigated whether targeting ferroptosis with donors of H2S (GYY4137), polysulfides (Na2S4) and persulfides (cysteine-3-sulfide, Cys-3S) could have antidiabetic effects and alleviate diabetic liver damage. Diabetes was induced in male C57BL/6 mice using streptozotocin (150 mg/kg, i.p.). Two months later, mice were treated for four weeks with the GYY4137 (0.25 mg/kg), Na_2S_4 (0.5 mg/kg), Cys-3S (1.25 mg/kg), or ferroptosis inhibitor liproxstatin-1 (10 mg/kg). After treatment, blood and liver samples were collected for biochemical, molecular and microscopic analysis.H2S/RSS donors, especially Cys-3S, attenuated ferroptotic phenotype in the liver of diabetic rats, reflected through: decreased accumulation of pro-oxidative parameters (ACSL4, labile iron, lipofuscin, and lipid peroxides); normalization of iron metabolism regulators (FTH1 and FPN1); Nrf2 activation followed by increased FSP1 expression and GSH-related antioxidative defense parameters (GPX4, GCLC, GSS). Observed mitigation of ferroptotic events by H_2S/RSS donors culminated in improved liver function, as evidenced by improved biochemical parameters, reduced hepatocyte size and liver fibrosis, with effects comparable to the ferroptosis inhibitor liproxtatin-1. H_2S/RSS donors also restored diabetes-altered expression of endogenous H_2S-producing enzymes, particularly the predominant hepatic form CSE, suggesting involvement of H_2S biosynthetic/signaling pathways in their antiferroptotic/antidiabetic effects. Study clearly demonstrates the strong antiferroptotic potential of H2S/RSS donors in diabetic liver complications and suggest a new approach for the prevention/treatment of this pathology.

P-051 Synthesis, HSA/DNA binding, molecular docking and cytotoxicity study of new palladium(II) complexes with derivatives of leucine

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A series of novel propylenediamine-derived of leucine ligands (R2-S,S-pddmp·2HCl; L1-L4, where pddmp = (S,S)-1,3-propylenediamine-N,N'-di-2-(4-methyl)pentanoate and R = ethyl, propyl, butyl, and pentyl) and their palladium(II) complexes (C1-C4) were synthesized and characterized using elemental analysis, infrared spectroscopy, and 1H/13C NMR spectroscopy. The interactions of the complexes with biologically relevant molecules, such as human serum albumin (HSA) and calf thymus DNA (CT-DNA), were investigated using UV-Vis absorption and fluorescence spectroscopy. Binding constant (Kb) and Stern-Volmer quenching constant (Ksv) values indicated strong affinities for both HSA and CT-DNA. Molecular docking simulations were used to further elucidate the binding interactions, showing good agreement with experimental data. In vitro cytotoxicity activities were investigated on four tumor cell lines: mouse breast cancer (4T1), mouse colorectal cancer (CT26), human breast cancer (MDA-MB 468), and human colorectal cancer (HCT116), and nontumor control cells: mesenchymal stem cell (mMSC), and human fibroblast (MRC-5) cell lines. Analyses of cytotoxic activity of tested complexes and ligands revealed that C2 demonstrates the most prominent dose-dependent antitumor activity, primarily against colorectal cancer cells, and with least harmful effect on healthy nontumor cells. C2 complex induces apoptosis of colorectal cancer cells by decreasing antiapoptotic Bcl-XL expression together with increasing caspase-3 expression. C2 inhibits proliferation of mouse colorectal cancer cells proliferation *in vitro*, via reduced expression of proliferation marker Ki-67 and panAKT, involved in regulation of proliferation and cell survival, together with upregulation of Cdk inhibitors p16 and p27, important regulators of cell cycle. These results highlight C2's potential as a promising candidate for targeted colorectal cancer therapy.

P-052 Colorectal cancer mortality trend in Serbıa from 2000 to 2021

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Background: Colorectal cancer is the second leading cause of cancer-related death worldwide, with over 900,000 deaths annually. This study aimed to assess the mortality trends of colorectal cancer in Serbia between 2000 and 2021.
Methods: Age-specific and age-standardized mortality rates were used in the data analysis, standardized using the direct method, with the SEGI world standard population as the reference (ASR–World). Joinpoint regression analysis was used to estimate annual percent change (APC) and average annual percent change (AAPC) with the corresponding 95% confidence interval (CI).
Results: Joinpoint regression analysis demonstrated a significantly increased trend in colorectal cancer mortality in men (AAPC = 0.51%, 95% CI: 0.11%–0.94%, p=0.028, $P < 0.05$). The overall rate increase, with an average annual percent change of 0.20% AAPC (95% CI: -0.03 – 0.46), was not statistically significant (p=0.080). The analysis showed a decrease in the mortality rates among women, with an average annual percent change of -0.09% AAPC (95% CI: -0.40 – 0.34), which was also not statistically significant. The highest mortality rates were reported among men older than 65 years, with a statistically significant increase in the 65–69, 75–79, 80–84, and 85+ age groups.
Conclusions: Mortality rates were reported to have increased particularly among men, but the trends differed according to age group. The impact of colorectal cancer can be significantly reduced by adopting a healthy lifestyle, avoiding risk factors, and monitoring symptoms to enable timely diagnosis and treatment.

P-053 Association between inflammatory markers and lipid profile disorders in patients with chronic kidney disease

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Chronic kidney disease (CKD) is associated with systemic disturbances, including inflammation and dyslipidemia, which contribute to increased cardiovascular risk. The aim of this study was to evaluate differences in inflammatory markers and lipid profile between CKD patients and healthy controls. The study included 70 patients with CKD and a control group of healthy subjects. The following parameters were analyzed: C-reactive protein (CRP), fibrinogen, total cholesterol, LDL, HDL, triglycerides, and creatinine. Statistical analysis was performed using Student's t-test, with significance set at $p < 0.05$. Patients with CKD showed significantly higher levels of CRP (11.9 vs 1.05 mg/L), fibrinogen (3.65 vs 2.74 g/L), LDL cholesterol (3.51 vs 2.62 mmol/L), and triglycerides (1.81 vs 1.04 mmol/L), along with lower HDL cholesterol levels (1.22 vs 1.46 mmol/L) compared to controls. Creatinine levels were significantly higher in CKD patients. CKD is associated with increased inflammation and an atherogenic lipid profile, indicating elevated cardiovascular risk and the importance of integrated monitoring in clinical practice.

P-054 Differential Therapeutic Modulations of Adiponectin: Beneficial, Adverse, and Context-Dependent Effects in Chronic Coronary Syndromes

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Chronic metabolic inflammation and adiponectin resistance are pivotal in the pathogenesis of cardiovascular diseases and metabolic syndrome. Adiponectin, a pleiotropic adipokine, exerts anti-inflammatory, anti-atherogenic, and anti-diabetic effects. In early metabolic dysfunction, adiponectin levels rise as a compensatory response, whereas advanced coronary disease is characterized by hypoadiponectinemia due to adiponectin resistance. This review highlights how contemporary cardiovascular therapies modulate adiponectin levels to reduce low-grade systemic and vascular inflammation in chronic coronary syndromes. Evidence suggests that Peroxisome proliferator-activated receptor (PPAR) agonists, Sodium-glucose cotransporter 2 (SGLT2) inhibitors, Glucagon-like peptide-1 receptor agonists (GLP-1RA), Renin-angiotensin-aldosterone system (RAAS) blockers, metformin, statins, and fibrates may increase adiponectin levels, though effects vary by drug type and disease stage. Cardioprotective effects of angiotensin-converting enzyme (ACE) inhibitors resemble those of adiponectin, as both promote vasodilation and autophagy. Furthermore, Angiotensin II receptor blockers (ARBs) stimulate adiponectin secretion via partial PPAR-γ activation. SGLT2 inhibitors increase adiponectin synthesis, enhance insulin sensitivity, and reduce leptin levels in type 2 diabetes mellitus (T2DM). GLP-1RA mechanisms are multifaceted. These agents increase adiponectin levels by stimulating the protein kinase A (PKA) signaling pathway and upregulating adiponectin messenger RNA (mRNA) in adipocytes. Emerging data suggest GLP-1RA ameliorate endothelial dysfunction, oxidative stress, intravascular inflammation, and smooth muscle cell proliferation. Mineralocorticoid receptor antagonists (MRAs) reduce pro-inflammatory cytokines and profibrotic processes while increasing cardiac adiponectin expression. Conversely, intensive statin therapy may reduce Adiponectin receptor (AdipoR) expression in human monocyte-macrophage cell lines. High-dose atorvastatin can inhibit adiponectin levels while reducing oxidized Low-density lipoprotein (oxLDL) particles. Fenofibrate anti-inflammatory effects occur via PPAR-α activation, Inducible nitric oxide synthase (iNOS) and Cyclooxygenase 2 (COX2) inhibition, and release of adiponectin and Inhibitory kappa B (IκB). Adiponectin inhibits Tumor necrosis factor-alpha (TNF-α)-induced nuclear factor-kappa B (NF-κB) activation. TNF-α inhibitors increase circulating adiponectin and reduce myocardial infarction risk in autoimmune diseases; however, their direct effect on serum adiponectin in coronary patients remains insufficiently clarified. Lifestyle interventions, including physical activity and diet, are strongly associated with increased adiponectin. Physical activity activates Adenosine monophosphate-activated protein kinase (AMPK) and PPAR-α, enhancing fatty acid oxidation and glucose uptake. Omega-3 fatty acids, low-calorie, Mediterranean, Dietary Approaches to Stop Hypertension (DASH), and high-fiber diets also increase adiponectin gene expression. Finally, small-molecule AdipoR agonists like AdipoRon, which directly activate AdipoR1 and AdipoR2, represent a promising future strategy. Further research is necessary to fully establish drugs based on this pathway.

P-055 Dinuclear Platinum(II) Complexes: Electrostatic Interactions with DNA and Human Serum Albumin

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Two novel dinuclear platinum(II) complexes, [{Pt(1,3-pnd)Cl}$_2$(μ-4,4′-bipy)]Cl$_2$ (Pt1) and [{Pt(1,3-pnd)Cl}$_2$(μ-4,4′-SS-bipy)]Cl$_2$ (Pt2), containing 1,3-pentanediamine (1,3-pnd) as a bidentate chelating ligand and 4,4′-bipyridine or 4,4′-dithiodipyridine as bridging ligands, were synthesized and characterized by elemental analysis, UV–Vis spectroscopy, and 1H/13C NMR spectroscopy. The structural variation introduced by the bridging ligands enabled evaluation of structure–interaction relationships toward biologically relevant targets. The interactions of Pt1 and Pt2 with calf thymus DNA (CT-DNA) were investigated using UV–Vis and fluorescence spectroscopy, and cyclic voltammetry. Absorption, fluorescence, and electrochemical studies indicated that Pt1 and Pt2 interact with DNA predominantly through electrostatic, non-intercalative binding to the phosphate backbone. Similar DNA-binding parameters for both complexes suggest that replacing bipyridine with its disulfide analogue does not significantly influence the interaction mechanism. Interactions with human serum albumin (HSA), an essential transport protein in the bloodstream, were evaluated by fluorescence quenching experiments. Both complexes efficiently quenched the intrinsic fluorescence of HSA through a static quenching mechanism and displayed moderate binding affinities, indicating their potential for reversible transport under physiological conditions. Competitive binding studies using ibuprofen as a site marker demonstrated that neither Pt1 nor Pt2 binds to Sudlow's site II, suggesting alternative binding regions and reducing the possibility of competition with commonly administered site-II-binding drugs. The synthesized dinuclear Pt(II) complexes showed stable interactions with key biological targets through predominantly electrostatic mechanisms and favorable albumin-binding properties. The obtained results provide valuable insight into the biological behavior of these complexes and support their further investigation as promising candidates for the development of platinum-based therapeutic agents.

P-056 Coumarin N-Acylhydrazones as Potential Antioxidant Agents

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Oxidative stress is caused by the excessive generation of reactive oxygen and nitrogen species (ROS/RNS) and plays a key role in the development of numerous pathological conditions, including neurodegenerative, cardiovascular, metabolic, and inflammatory diseases. Although natural antioxidants have been widely studied, their practical application is often limited by poor stability, low bioavailability, and insufficient selectivity. Therefore, the development of new synthetic antioxidants remains an important research goal. Among heterocyclic compounds, coumarins have attracted considerable attention due to their broad spectrum of biological activities and relatively low toxicity. Various coumarin derivatives show significant pharmacological potential, including antioxidant, anticancer, antimicrobial, antiviral, antitubercular, antifungal, and anticoagulant activities. A series of coumarin N-acylhydrazone derivatives were synthesized by the reaction of 3-acetylcoumarin with various benzohydrazides using molecular iodine as a catalyst under mild reaction conditions. The synthetic protocol used allowed for rapid conversion of the reactants and gave the desired products in good to excellent yields. The antioxidant potential of the obtained compounds was assessed in vitro using DPPH, ABTS, and FRAP assays. The results showed that derivatives containing the catechol moiety exhibited the strongest antioxidant activity, highlighting the importance of hydroxyl substitution patterns for radical scavenging efficiency. These findings indicate that coumarin-based N-acylhydrazones represent promising candidates for the development of novel synthetic antioxidants with potential biomedical applications.

P-057 Five-year survival in ultra-low-risk endometrial cancer in resource-limited settings: Is it safe to avoid adjuvant therapy without molecular classification?

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Introduction: Molecular classification of endometrial cancer has further emphasized the heterogeneity of this disease and refined risk stratification for adjuvant treatment. However, in many resource-limited settings, implementation of molecular classification and its integration into the FIGO 2023 staging system remain challenging, limiting accurate patient stratification. This study aimed to evaluate five-year overall survival (OS) and disease-free survival (DFS) in ultra-low-risk endometrial cancer patients treated without adjuvant therapy and without molecular stratification.

Materials and Methods: This retrospective study included patients with ultra-low-risk endometrial cancer (FIGO IA, endometrioid type, no lymphovascular space invasion, low-grade tumors) who underwent surgery alone without molecular testing or adjuvant therapy. Patients were managed at the University Clinical Center Kragujevac between January 2016 and January 2022, following radical hysterectomy with bilateral adnexectomy, with or without pelvic lymphadenectomy. All patients were followed for five years. Survival outcomes were analyzed using the Kaplan–Meier method and log-rank test.

Results: Among 49 patients, five-year OS was 91.8% and DFS 89.8%. Age, residence, lifestyle factors, menopausal status, comorbidities, lymphadenectomy, myometrial invasion, and tumor grade did not significantly affect DFS. In contrast, parity, preoperative magnetic resonance imaging (MRI), surgery in a tertiary center, and distal uterine tumor location were significantly associated with DFS ($p<0.05$).

Conclusions: Approximately 10% of patients experienced disease progression without adjuvant therapy, suggesting potential underestimation of risk in the absence of molecular classification. Improved outcomes were associated with treatment in tertiary centers and adequate preoperative MRI, highlighting the importance of specialized care in resource-limited settings.

P-058 Association of Leptin, Galectin-1 and Galectin-3 with Tumor Lymphangiogenesis

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Background and study aims: Leptin, Galectin-1 and Galectin-3 play a significant and versatile role in tumor biology, including tumorigenesis, angiogenesis, invasion and metastasis. However, their contribution to lymphangiogenesis remains insufficiently clarified. The objective of study is to evaluate the association of leptin, Galectin-1 and Galectin-3 with markers of tumor lymphangiogenesis.
Patients and methods: The study included 120 patients diagnosed with sporadic CRC. Tissue expression levels of leptin, Galectin-1, Galectin-3 and vascular endothelial growth factor-C (VEGF-C) were assessed and correlated with lymphatic vessel density (LVD) stained immunohistochemically. In addition, serum concentrations of Galectin-1 and Galectin-3 were analyzed in a 38 patients with CRC by Enzyme Linked Immunosorbent Assay (ELISA).
Results: A significantly positive correlation was noticed between LVD and intensity of leptin or Galectin-1 expression in tumor tissue. Although Galectin-3 expression in tissue was not significantly associated with LVD, patients with higher LVD exhibited notably reduced serum levels of Galectin-3. A positive relationship was observed between leptin and VEGF-C expression, while no significant association was found between Galectin-1 and VEGF-C. However, Galectin-3 expression in tumor tissue positively correlated with VEGF-C expression.
Conclusions: These findings suggest that leptin and Galectin-1 may play a role in tumor lymphangiogenesis, potentially through both VEGF-C–dependent and independent mechanisms. Further studies are needed to fully elucidate these complex molecular interactions of leptin and Galectin-1 in tumor lymphangiogenesis.

P-059 Real-time detection and monitoring of singlet oxygen production in glioma spheroids using time-correlated multiple photon counting in the near infrared range

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Glioma is a highly lethal brain tumor that is difficult to treat with traditional approaches because of its location and the blood-brain barrier. Light-assisted therapies are a good alternative, as light can penetrate deeper into tissue, and a proper combination of light and photosensitizers can efficiently remove tumor tissue. This approach, known as photodynamic therapy (PDT), has been clinically evaluated for several tumor types. The mechanism of PDT is light-initiated production of reactive oxygen species (ROS), which cause oxidative damage to biomolecules and eventually lead to cancer cell death. Among intracellular ROSs, singlet oxygen (SO) is highly reactive and is strongly associated with cancer cell death. However, its role in glioma elimination remains unclear. The options for SO detection are scarce and hindered by its low concentration and instability in tissues. Recent developments in nearinfrared detection, such as the Time-Correlated Multiple-Photon Counting (TCMPC-NIR) device, have enabled highly sensitive detection of singlet oxygen luminescence. In this work, we investigated the possibility of SO detection by measuring the signal at 1270 nm using a TCMPC-NIR system in 5-aminolevulic acid (5-ALA)-treated murine glioma cells (SMA 560) organized in spheroids. 5-ALA treatment induced intracellular accumulation of protoporphyrin IX (PpIX), enabling SO generation upon excitation with a 635 nm pulsed laser through energy transfer to molecular oxygen. SMA 560 cells were cultured to form spheroids and illuminated from the bottom with a 635 nm pulsed laser, while SO detection was performed from above. By adjusting the laser frequency from 12 kHz to 375 Hz, reliable detection of SO was achieved. These experiments establish a foundation for real-time monitoring of SO production in glioma cells, enabling the application of advanced light-based therapies, including direct light activation of SO generation at 1267 or 1064 nm.

P-060 Anti-ferroptotic effects of hydrogen (per)sulfide donors on β-cells under diabetic conditions

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Background: Hydrogen sulfide (H_2S) is an important gassotransmiter which level is reduced in diabetic state. Although its donors represent innovative approach in treatment of many diabetes-related pathologies, the data on their role in the regulation of function/destiny of β-cells is not elucidated. We examined the effects of slow releasing H_2S donor (GYY4132), polysulfide (Na_2S_4) and persulfide (cysteine 3-sulfide, Cys-3S) donors on β-cells ferroptosis under diabetic conditions *in vitro* and *in vivo*.
Methods: In parallel with diabetes induction (five streptozotocin doses, i.p. 40 mg/kg), C57BL/6 mice were treated with GYY4137, Na_2S_4, or Cys-3S. After 21 days, blood and pancreas were collected for biochemical, microscopical and molecular analyses. Rin-5F pancreatic islet cells were treated with the same donors or ferroptosis inhibitor (ferrostatin-1) under high glucose conditions to assess cell death and lipid peroxidation.
Results: Cys-3S acted beneficially on diabetes-induced proferroptotic events (accumulation of iron and lipid peroxides and failure in antiferroptotic axis, Nrf2/xCT/GPX4/GSH) in pancreatic islets *in vivo*, which reflected on the maintaining of functional population of β-cells, serum glucose level and decrease in diabetes incidence. In parallel, the expression of CSE in pancreatic islets was significantly upregulated by Cys-3S treatment. *In vitro*, Cys-3S prevented high glucose- and RSL-3-induced β-cell death in similar manner as ferrostatin-1. Na_2S_4 also acted beneficially on the ferroptotic parameters and pancreatic CSE level, but failed to maintain β-cell population and stabilize hyperglycemia in diabetic animals. The effects of GYY4137 on diabetes-induced changes in systemic or tissue ferroptotic parameters were less pronounced and complete.
Conclusion: Although both donors of polysulfide and persulfide ameliorated diabetes-induced ferroptotic phenotype of β-cells and disturbances in H_2S biosynthetic pathways, only in the case of Cys-3S antidiabetic effect and better metabolic control was achieved. This qualifies direct donors of persulfides as an effective approach in the prevention of β-cells death and diabetes development.

P-061 Synthesis and biological evaluation of platinum(II)-aminothiazole complexes

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Platinum(II) complexes continue to attract considerable interest due to their potential applications as anticancer agents. In this study, two novel platinum(II) complexes bearing aminothiazole ligands, namely 2-amino-6-methylbenzothiazole and 2-amino-6-chlorobenzothiazole, were synthesized and comprehensively characterized by elemental microanalysis, IR, and NMR spectroscopy. The proposed structures were further supported by Density Functional Theory (DFT) calculations, including conformational analysis and theoretical simulation of spectroscopic parameters, showing good agreement with experimental data. The interactions of the complexes with human serum albumin (HSA) and calf thymus DNA (CT-DNA) were investigated using fluorescence and UV–Vis spectroscopy. The results indicated good binding affinity toward both biomacromolecules. Viscosity measurements suggested that the complexes do not intercalate between DNA base pairs, but likely interact via minor or major groove binding. The *in vitro* biological evaluation was performed against mouse and human breast and colon cancer cell lines, as well as non-tumor mesenchymal stem cells. Among the tested compounds, the platinum(II) complex containing the 2-amino-6-methylbenzothiazole ligand exhibited the highest cytotoxic activity, particularly against colon cancer cells, with improved selectivity compared to cisplatin in certain models. Overall, the obtained results suggest that these platinum(II)-aminothiazole complexes represent promising candidates for further development of biologically active metal-based anticancer agents.

P-062 *In silico* assessment of pharmacokinetic and toxicological properties of novel lactam androstane thiadiazolines

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In this research, a detailed in silico evaluation of three newly formulated steroid derivatives was conducted: [compound 1: (17E)-thiosemicarbazono-4-azaandrost-5-en-3-one, compound 2: 5'- acetamido-3'-acetylspiro(4-azaandrost-5-en-3-on-17,2'-[1',3',4']-thiadiazoline, and compound 3: 5'- propanamido-3'-propionylspiro(4-azaandrost-5-en-3-on-17,2'-[1',3',4']-thiadiazoline]. The aim was to assess their pharmacokinetic profiles and potential as oral drug candidates. The primary analytical methods involved using the SwissADME web tool for predicting physicochemical properties and ADME parameters, alongside the ProTox-II platform for toxicity assessment. Physicochemical profiling results demonstrated that all tested compounds fully comply with Lipinski's Rule of Five (molecular weight < 500, LogP < 5, number of hydrogen bond donors ≤ 5, and acceptors ≤ 10), indicating a high probability of oral bioavailability. Furthermore, the compounds exhibit optimal flexibility (< 10 rotatable bonds) and a topological polar surface area (TPSA) of less than 140 $Å^2$, which are critical factors for good permeability. Analysis via the BOILED-Egg model predicts high human intestinal absorption (HIA) for all three compounds. However, the results indicated that the compounds cannot cross the blood-brain barrier (BBB), nor would they be retained in the central nervous system due to the action of P-glycoprotein, thus excluding their use in brain tumor treatments. The study of interactions with cytochrome P450 (CYP) isoenzymes showed a favorable profile for compounds 1 and 2, which are predicted not to inhibit any of the five leading isoforms, minimizing the risk of drug-drug interactions. Conversely, compound 3 was identified as a potential CYP3A4 inhibitor, suggesting metabolic instability. Toxicological assessment using ProTox-II classified all derivatives into Class IV oral toxicity, with predicted LD_{50} values between 800 and 1273 mg/kg, characterizing them as non-toxic. Nevertheless, the *in silico* models suggest caution due to the predicted potential carcinogenicity (57–58%) and immunotoxicity of compounds 2 and 3. This research establishes a necessary foundation for further *in vitro* biological activity studies of these promising steroid derivatives.

P-063 *In silico* evaluation of anticancer properties and pharmacological profile of a dinuclear copper(II) terpyridine complex

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Copper-based coordination compounds have attracted increasing attention as potential anticancer agents due to their diverse coordination chemistry, redox activity and ability to interact with biomolecular targets. Dinuclear copper(II) terpyridine complexes are particularly promising because of their high reported *in vitro* anticancer activities and enhanced DNA-binding capacity. This study aimed to evaluate the anticancer potential and pharmacological profile of a dinuclear copper(II) terpyridine complex using molecular docking and ADMET (absorption, distribution, metabolism, excretion and toxicity) prediction approaches. The binding affinity and interaction profile of the synthesized dinuclear copper(II) terpyridine complex were investigated through molecular docking studies against DNA and human serum albumin (HSA). Docking simulations were performed to assess the stability of the ligand–target complexes, identify key intermolecular interactions and estimate binding energies. The interaction with DNA was analyzed to evaluate the potential mechanism related to cytotoxic activity, while HSA docking was conducted to predict transport and bioavailability characteristics. In addition, in silico ADMET predictions were performed to assess the pharmacokinetic behavior and drug-likeness of the complex.The dinuclear copper(II) terpyridine complex demonstrated favorable binding affinity toward both DNA and HSA targets. Docking analysis revealed stable interactions mediated through hydrogen bonding, electrostatic interactions and π-related contacts. DNA binding suggested a possible mechanism for anticancer activity through interference with nucleic acid function. The HSA interaction profile indicated acceptable transport capability and potential systemic distribution. ADMET predictions suggested moderate pharmacokinetic properties with acceptable absorption characteristics and a manageable toxicity profile, supporting the compound's potential as a drug candidate.

P-064 Burnout Syndrome Is Associated with Increased Galectin-3 Levels in Healthcare Workers

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Background: Burnout syndrome is increasingly recognized as a condition associated not only with psychological distress but also with measurable biological alterations. Galectin-3, a β-galactoside-binding lectin involved in inflammation, immune regulation, cellular stress, and tissue remodeling, may represent a relevant marker of stress-related immune imbalance. This study aimed to investigate shift-dependent changes in Galectin-3 and Galectin-3/cytokine ratios among emergency medical workers with and without burnout syndrome.
Methods: This observational, comparative, non-interventional study included physicians and medical technicians from the Institute for Emergency Medicine Belgrade. Burnout status was assessed using the Maslach Burnout Inventory, and participants were classified as having burnout when at least two of the following criteria were present: high emotional exhaustion, high depersonalization, and low personal accomplishment. Peripheral venous blood was collected after 12-hour day and night shifts. Serum Galectin-3, IL-10, IL-17, and IL-4 were measured using commercial human ELISA assays. Galectin-3/IL-10, Galectin-3/IL-17, and Galectin-3/IL-4 ratios were calculated and compared between groups.
Results: Participants with burnout had significantly higher Galectin-3 levels after the day shift than those without burnout (1331.30 ± 96.41 vs. 994.32 ± 54.53 pg/mL; $p = 0.005$). Galectin-3 was also increased after the night shift in the burnout group (1075.74 ± 52.12 vs. 908.98 ± 45.55 pg/mL; $p = 0.008$). During the night shift, the Galectin-3/IL-10 ratio was significantly lower in participants with burnout (116.71 ± 14.95 vs. 383.05 ± 138.28; $p = 0.048$). In contrast, the Galectin-3/IL-17 ratio was significantly higher after the day shift in the burnout group (10.46 ± 0.87 vs. 7.90 ± 0.60; $p = 0.011$). Galectin-3/IL-4 ratios were also higher in participants with burnout after both the day shift (323.32 ± 25.00 vs. 219.54 ± 13.70; $p = 0.001$) and night shift (309.77 ± 19.35 vs. 256.14 ± 15.76; $p = 0.045$).
Conclusion: Burnout syndrome in emergency medical workers is associated with increased Galectin-3 levels after both day and night shifts, together with altered Galectin-3/cytokine ratios. These findings suggest a shift-dependent stress-related inflammatory and immunoregulatory imbalance, with Galectin-3 as a potential biomarker of burnout-associated immune dysregulation.

P-065 Design and microwave-assisted synthesis of chalcones containing morpholine moiety with potential efficacy in the treatment of neurodegenerative diseases

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Neurodegenerative diseases, characterized by progressive neuronal loss, represent a major global health challenge due to the currently limited therapeutic options. Consequently, the rational design and development of novel, target-specific small molecules with neuroprotective potential is a critical frontier in medicinal chemistry. Chalcone derivatives, recognized as privileged scaffolds due to their broad biological activity spectrum, have emerged as promising pharmacophore units in this field. In this study, a series of novel chalcone derivatives integrated with a morpholine moiety were rationally designed to enhance physicochemical properties and target-binding affinity. The target compounds were synthesized utilizing a Microwave-Assisted Organic Synthesis (MAOS) protocol consistent with the principles of Green Chemistry. Optimization of reaction conditions led to significantly reduced reaction times and superior yields compared to conventional heating methods. All synthesized derivatives were purified using chromatographic techniques. The chemical structures of the newly synthesized compounds were characterized using spectroscopic methods, including ^{1}H NMR, ^{13}C NMR, IR, and HRMS. Structure-Activity Relationship (SAR) evaluations demonstrated that the substitution pattern of the morpholine ring and the electronic nature of the B-ring exert a decisive influence on the potential pharmacological profile of the molecules. Our findings indicate that these novel morpholine-containing chalcone hybrids serve as potent lead candidates for the development of next-generation therapeutic agents targeting neurodegenerative diseases.

P-066 Synthesis and Characterization of a Potentially Bioactive Triphenyltin(IV) Complex with an Iminodiacetatodithiocarbamato Ligand

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Metal-based compounds play a significant role in modern coordination, bioinorganic, and medicinal chemistry due to their wide range of biological activities and potential applications in the treatment of various diseases. Particular attention has been devoted to organotin(IV) compounds because of their ability to form stable complexes, interact with biomolecules, and exhibit potential antitumor, antimicrobial, and anti-inflammatory properties. Consequently, they are being intensively investigated as possible alternatives to certain conventional chemotherapeutic agents. This study presents the synthesis and characterization of a new triphenyltin(IV) complex with an iminodiacetatodithiocarbamato ligand. Dithiocarbamates represent an important class of sulfur-donor ligands known for their pronounced ability to coordinate with metal ions and form stable complex compounds. The presence of sulfur donor atoms, together with additional coordination centers within the structure of iminodiacetatodithiocarbamate, enables various modes of coordination with the central tin(IV) ion, which may significantly influence the structure, stability, and potential biological properties of the synthesized complex. The synthesized product is characterized using FTIR spectroscopy, CHNS elemental analysis, and multinuclear NMR spectroscopy. In addition to their coordination versatility, iminodiacetatodithiocarbamato ligands have attracted interest because compounds containing this ligand have shown promising biological activity in previous studies. The results of this research contribute to a better understanding of the coordination chemistry of organotin(IV) systems with multifunctional dithiocarbamate ligands and provide a basis for further physicochemical and biological investigations of the synthesized compound.

P-067 Redox regulation patterns during peptide receptor radionuclide therapy in neuroendocrine tumor patients

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Introduction: Oxidative stress may affect tumor progression and therapeutic response in neuroendocrine tumors (NETs). Although peptide receptor radionuclide therapy (PRRT) induces reactive oxygen species (ROS) generation, the relationship between redox status and PRRT outcome remains unclear. Aims: To evaluate oxidative stress and antioxidant defense parameters during PRRT and their relationship with therapeutic response. Materials and Methods: This prospective study included 50 patients with histopathologically confirmed NETs treated with PRRT. Clinical data, biochemical parameters, prooxidative markers (superoxide anion radical, hydrogen peroxide, nitric oxide, TBARS), and antioxidant defense parameters (SOD, CAT, GSH, uric acid) were analyzed before the first, second, and third PRRT cycles. Treatment response was evaluated using RECIST 1.1 criteria. Results: Distinct redox regulation patterns were observed between the groups according to therapeutic response. In responders, hydrogen peroxide positively correlated with catalase activity, while SOD negatively correlated with liver metastases. In patients with disease progression, hydrogen peroxide positively correlated with superoxide anion radical and De Ritis ratio, while TBARS positively correlated with liver metastases and negatively with ferritin levels. Conclusion: Distinct correlation patterns suggest preserved antioxidant regulation in responders, while disrupted redox balance appears associated with disease progression in NET patients during PRRT.

P-068 Plant-derived alkaloids in cancer therapy: mechanisms of action, and therapeutic potential

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Cancer continues to represent a major global health challenge and remains one of the principal causes of illness and death worldwide. Despite substantial progress in treatment modalities such as chemotherapy, radiotherapy, immunotherapy, and targeted therapies, the overall effectiveness of these approaches is frequently compromised by limitations including severe adverse effects, the emergence of drug resistance, and insufficient tumor specificity. Consequently, the search for novel and safer anticancer agents from natural sources has become a major focus of pharmaceutical research. Among natural products, plant-derived alkaloids represent a diverse class of nitrogen-containing secondary metabolites with remarkable structural complexity and broad pharmacological activities. Owing to their unique chemical diversity, alkaloids have emerged as valuable lead compounds for anticancer drug discovery. Numerous in vitro studies, together with an increasing number of *in vivo* investigations, have demonstrated that many alkaloids possess potent cytotoxic, antiproliferative, pro-apoptotic, antimetastatic, and cell cycle-regulating activities against various cancer types. This review summarizes recent advances in the anticancer potential of plant-derived alkaloids belonging to different structural classes, highlighting their mechanisms of action and therapeutic significance. Despite challenges such as poor aqueous solubility, limited bioavailability, and unfavorable pharmacokinetic properties, these compounds remain promising candidates for the development of next-generation anticancer therapeutics. Future research should focus on improving their pharmacological performance through structural modification, advanced drug delivery systems, and targeted formulations to maximize therapeutic efficacy while minimizing toxicity to healthy tissues.

P-069 Tanshinone IIA-Induced Cytotoxicity in Cancer Cells: Mechanistic Insights and Therapeutic Perspectives

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Tanshinone IIA (Tan IIA), a bioactive diterpene quinone isolated from the roots of Salvia miltiorrhiza, has emerged as a promising natural anticancer compound due to its potent cytotoxic activity against a wide range of human cancer cell lines. Evidence summarized in recent studies demonstrates that Tan IIA inhibits cancer cell proliferation through induction of apoptosis and cell cycle arrest while simultaneously modulating multiple oncogenic signaling pathways, including PI3K/Akt/mT0R, JAK/STAT, MAPK, NF-KB, VEGF, and IGF-1R. In addition to triggering mitochondrial-mediated apoptosis and autophagy, Tan IIA suppresses angiogenesis, invasion, and metastasis, highlighting its multi-target therapeutic potential. Collectively, these findings suggest that Tanshinone IIA represents a promising phytochemical candidate for cancer therapy and warrants further preclinical and clinical investigations to validate its efficacy and therapeutic applicability.

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