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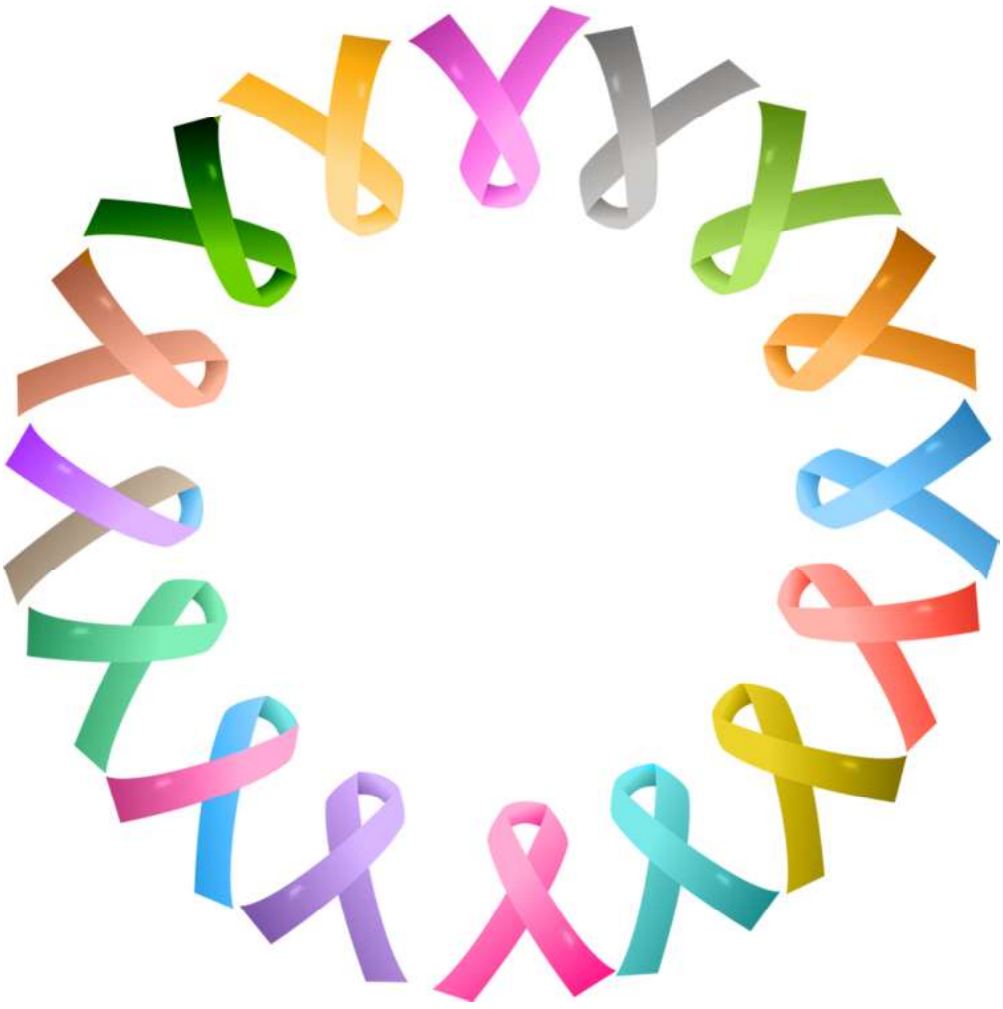
Official Journal of the Serbian Association for Cancer Research



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ONCOLOGY INSIGHTS

Aims and Scope

Oncology Insights is a yearly oncological open-access peer-reviewed journal that publishes new research from different areas of oncology. It strives to provide a platform for the exchange of cutting-edge research and knowledge in the field of oncology. This journal aims to advance the understanding, prevention, diagnosis and treatment through the dissemination of high-quality scientific discoveries.
The journal applies a fair and accurate peer review process, employing double-blind review methodologies. Acceptance of manuscripts is based on their scientific merit, originality, clarity, and contribution to the field.

Topics

Oncology Insights covers a wide spectrum of topics within the field of oncology, including but not limited to:

- Basic and Translational Research
- Clinical Oncology
- Radiation Oncology
- Surgical Oncology
- Pediatric Oncology
- Hematologic Oncology
- Palliative Care
- Epidemiology and Public Health
- Cancer Genetics
- Immunotherapy and Targeted Therapies
- Experimental Therapeutics
- Computational Biology and Artificial Intelligence

About/Information

Oncology Insights welcomes various types of contributions including original research articles, review articles, case reports, case studies, clinical trials, registered reports, comments, brief communications, editorials, letters to the editor, perspectives, and conference papers from a wide range of disciplines related to cancer research.
Through encouraging interdisciplinary collaborations, the journal welcomes contributions that integrate oncology with related fields such as immunology, genetics, biochemistry, radiology, and other relevant disciplines. The journal places a special emphasis on publishing research that highlights emerging trends, novel technologies, and innovative approaches in cancer research and clinical practice.
Oncology Insights is intended for a diverse readership, including oncologists, researchers, clinicians, nurses, allied healthcare professionals, patients, patient advocates, policymakers, and all stakeholders involved in the prevention, diagnosis, and treatment of cancer. It adopts a global perspective, encompassing research from diverse regions addressing oncological challenges that may vary across different populations.
The journal is committed to upholding the highest ethical standards in research and publication provided by established international guidelines.
Periodically, Oncology Insights may publish special issues focusing on specific topics to highlight particular areas of interest or emerging needs.
Authors are provided with clear and comprehensive guidelines for manuscript preparation, including structure, formatting, and other specific requirements.

Esteemed colleagues,

It is a rare honor and privilege in a scientist's career to shape joint efforts and dedication of a group of scientific enthusiasts into a tangible outcome - ***Oncology Insights, the Official Journal of the Serbian Association for Cancer Research*** (srp. Srpsko društvo istraživača raka, SDIR).

The first volume of Oncology Insights has been derived from years of scientific contributions of many individuals and institutions who have selflessly devoted their expertise, ideas and time to establish the SDIR society that today resonates with integrity and charm. In the future, we will strive to maintain those standards, always aiming higher. Thus, we encourage researchers, physicians, nurses, laboratory technicians, as well as patients, survivors, caregivers, and patient advocates to offer their valuable expert insights that will stimulate future progress of oncology in Serbia and worldwide.

Over the last 20 years, we have witnessed remarkable progress in the field of cancer research. Oncology Insights aims to play an integral role in supporting that progress by providing a platform for sharing cutting-edge research, creating a space for new collaborations, partnering established researchers with young investigators, and serving as a home for oncology professionals of various specialties dedicating their careers to this challenging research field.

Oncology Insights pledges to evolve, adapt, reinvent, redefine, and reshape its content to serve its members and inevitable advances in the field. We hope you will be a part of its success story by providing evidence-based, unbiased multidisciplinary content, feeling both an honor and a duty to treat cancer research with the same care, passion, and dedication which individuals with cancer deserve and expect.

Please tune all your senses to enjoy the intellectual feast spread through the pages of this inaugural journal volume. The future of Oncology Insights will be shaped by you.

With kind regards,

Milena Čavić, SDIR President
Editor-in-Chief
Oncology Insights
Official Journal of the Serbian Association for Cancer Research

The first number of Oncology Insights includes
PROCEEDINGS BOOK of
THE SIXTH CONGRESS OF THE SERBIAN ASSOCIATION FOR CANCER RESEARCH
with international participation

From Collaboration to Innovation in Cancer Research

2nd – 4th October 2023
Royal Inn Hotel, Belgrade

SDIR-6 ORGANIZER
Srpsko društvo istraživača raka (SDIR)
Serbian Association for Cancer Research (SACR)
www.sdir.ac.rs

Dear colleagues,

We are very pleased to welcome you to the 6th Congress of the Serbian Association for Cancer Research (SDIR) with international participation "From Collaboration to Innovation in Cancer Research" which will be held on October 2-4 2023, at the Royal Inn Hotel, Kralja Petra 56, Belgrade, Serbia.
During the three-day congress, lectures will be given by distinguished Serbian and international researchers, covering the following topics:

- Tumour metabolism and biology
- Epigenetics and gene regulation in cancer
- Bioinformatics and artificial intelligence in cancer research
- Omics approaches in cancer research
- Therapy response and resistance
- Clinical and translational oncology
- Immunooncology
- New and challenging drug targets
- Pathways to innovation in cancer research

We are pleased to announce that our sixth congress is actively supported by the European Association for Cancer Research (EACR). National and regional cooperation is also important, and so representatives from our friend societies will be attending our congress.
The timing of the organisation of SDIR-6 is important for the establishment of our national society's journal Oncology Insights. The abstracts of the sixth congress will be published in the very first issue of the journal.
Advances and innovations in cancer research are based on growing scientific knowledge and collaboration. We believe you will enjoy the lively atmosphere of the congress and that fruitful scientific discussions will help you build new collaborations and develop new ideas.

We look forward to welcoming you in Belgrade!

Kind regrads,

on behalf of the SDIR-6 Organizing Committee

Prof. dr Katarina Zeljić
Faculty of Biology, University of Belgrade
President of the SDIR-6 Organizing Committee

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P19

The effect of tyrosine kinase inhibitors in high-grade glioma patient-derived cells

Ema Lupšić[1], Jelena Dinić[1], Igor Nikolić[2,3], SofijaJovanović Stojanov[1], Milica Pešić[1] and Ana Podolski-Renić[1]
[1]*Institute for Biological Research "SinišaStanković" – National Institute of the Republic of Serbia, University of Belgrade, DespotaStefana 142, 11060 Belgrade, Serbia*
[2]*Clinic for Neurosurgery, Clinical Center of Serbia, Pasterova 2, 11000 Belgrade, Serbia*
[3]*School of Medicine, University of Belgrade, DoktoraSubotića 8, 11000 Belgrade, Serbia*

Background: High-grade gliomas are the most frequently diagnosed malignant brain tumors in adults, with a very unfavorable prognosis. Although various strategies have been applied in the clinical setting, no significant progress has been made in the treatment of high-grade glioma. Clinical trials continue to expand into new approaches such as targeted agents and immunotherapy. Here, we performed pharmacological screening of tyrosine kinase inhibitors (TKIs) on patient-derived glioma cells *ex vivo* and assessed the expression of multidrug resistance (MDR) marker in glioma and stromal (non-glioma) cells. The effects of TKIs have been compared with chemotherapeutic agents approved for the treatment of high-grade glioma. **Material and Methods:** Primary patient-derived cell cultures were established from resections of high-grade gliomas. After short-term culturing (2-3 weeks), a mixed population of glioma and non-glioma cells was treated with 4 TKIs (alectinib, dabrafenib, trametinib, and nintedanib), as well as temozolomide (TMZ) and carmustine (BCNU). The maximum achieved concentration in human plasma during therapy (Cmax) was set as the upper limit and 4 lower concentrations were also used during the study. An immunofluorescence assay allowing discrimination of glial fibrillary acidic protein antibody-positive glioma cells versus negative non-glioma cells was performed using an ImageXpress Pico high-content imager (Molecular Devices) with CellReporterXpress 2.9 software. The MDR marker (ABCB1) was analyzed with the corresponding antibody in the same immunoassay. **Results:** Among the compounds tested, alectinib and TMZ did not affect cell growth and did not change the number of ABCB1-positive cells. Other compounds significantly inhibited the growth of glioma cells. However, they were not selective towards glioma cells, on the contrary, they showed greater cytotoxicity in non-glioma cells. The number of glioma cells positive for the ABCB1 marker increased significantly after treatment with dabrafenib, nintedanib, and BCNU, while trametinib and did not change ABCB1 expression in glioma cells. Stromal (non-glioma) cells generally followed the pattern of ABCB1 observed in glioma cells. **Conclusions:** Novel functional immunoassay may provide valuable information on the sensitivity of high-grade gliomas to different TKIs and possible treatment outcomes based on the expression of MDR marker.
Keywords: ABCB1, high-grade glioma, immunoassay, patient-derived cell culture, tyrosine kinase inhibitors

P20

The significance of interleukin-8 in hormonally dependent early breast cancer – association with the established parameters ER/PR and HER2

Jelena Milovanović[1], Jelena Hranisavljević[2], Tijana Vujasinović[1], Nataša Todorović-Raković[1]
[1]*Department of Experimental Oncology, Institute for Oncology and Radiology of Serbia, Belgrade, Serbia*
[2]*Laboratory for Radiobiology and Molecular Genetics, Vinča Institute of Nuclear Sciences, Belgrade, Serbia*

Background: Interleukin-8 (IL-8) is a multifunctional cytokine linked to cancer progression. Studies have confirmed high IL-8 levels in HER2-enriched and basal-like (ER–) primary breast tumors. The aim of this study was to evaluate the relationship between intratumoral IL-8 protein levels and clinical outcome in hormone dependent (ER+) primary breast cancer patients. **Patients and methods:** The study included 65 early-stage breast cancer patients with detectable levels of hormone receptors (ER>0, PR>0), all of whom had not received any prior hormonal or chemotherapeutic systemic therapy. The median follow-up was 144 months. Steroid hormone receptor status was determined by ligand-binding assay. HER2 status (absence or presence of gene amplification) was determined by chromogenic in situ hybridization (CISH). IL-8 protein levels were determined in cytosol tumor extracts by quantitative ELISA. ER level of 10 fmol/mg, PR level of 20 fmol/mg and the median IL-8 concentration level of 88.8 pg/mg, were used as cut-off values. **Results:** There was a significant difference in relapse free survival (RFS) between IL8low and IL8high subgroups of patients (Log rank test, p=0.002). Considering subgroups of patients stratified in different phenotypes according to receptor status and the median IL-8 value, if IL-8 is highly expressed, the influence of ER is weaker and there was no significant difference in RFS between subgroups with ERlowIL8high and ERhighIL8high phenotypes. The same is true for PR and HER2 and there was no significant difference in RFS between subgroups with PRlowIL8high and PRhighIL8high phenotypes, neither between subgroups with HER2−IL8high and HER2+IL8high phenotypes. On the other hand, subgroup with ERhighIL8low

phenotype had significantly longer RFS compared to those with ERlowIL8high and ERhighIL8high phenotypes (p=0.02, p=0.04, respectively); subgroup with PRlowIL8low phenotype had significantly longer RFS compared to those with PRlowIL8high and PRhighIL8high phenotypes (p=0.003, p=0.02, respectively); and subgroup with HER2–IL8low phenotype had significantly longer RFS compared to those with HER2–IL8high and HER2+IL8high phenotypes (p=0.01, p=0.02, respectively). **Conclusions:** IL-8 is a potential biomarker of unfavorable prognosis in hormone dependent breast cancer that is associated with the established parameters ER/PR and HER2. Receptor-mediated signaling could act additively with IL-8 signaling in progression of hormone dependent breast cancer.
Keywords: biomarker, breast cancer, HER2, hormone receptor, interleukin-8.

P21

Variant rs745430558 in the *SMAD4* gene promoter as a biomarker for adenocarcinoma of the pancreas

Jelena Ljubičić[1], Aleksandar Bogdanović[2,3], Tamara Babić[1], Jovana Despotović[1], Vladimir Dugalić[2,3], Aleksandra Nikolić[1]
[1] *Institute of Molecular Genetics and Genetic Engineering, University of Belgrade, Serbia*
[2] *Clinic for Digestive Surgery, University Clinical Center of Serbia, Belgrade, Serbia*
[3] *Faculty of Medicine, University of Belgrade, Serbia*

Background: Our previous study has identified variant rs745430558 in the *SMAD4* gene promoter as potential biomarker for adenocarcinoma of the pancreas. The allele delTT (10T instead of 12T) was present in malignant pancreatic tissue with a prevalence of 88%. As analysis of cfDNA in liquid biopsy represents a noninvasive approach for the diagnosis and monitoring of malignancies, the aim of this study was to determine the presence of 12T and 10T alleles in the peripheral blood of patients with suspected pancreatic malignancy. **Material and Methods:** The study was performed using cell-free DNA (cfDNA) isolated from the serum of 15 patients with morphological alterations of the pancreas. The presence of 12T and 10T alleles was assessed by allele specific quantitative real-time PCR. **Results:** Of 15 analyzed samples, 13 were diagnosed with adenocarcinoma of the pancreas (AcP), 1 with neuroendocrine tumor (NET), and 1 with pancreatitis. The 10T allele was present in 84.7% of cases with AcP and also in the sample from the patient with NET. In patient with pancreatitis only the 12T allele was detected. **Conclusion:** Our research has shown that the results of liquid biopsy of patients with AcP are in agreement with tissue specimens analysis. Targeted detection of the rs745430558 10T variant in patients with suspected pancreatic malignancies could be a potential biomarker for diagnosis of AcP inthefuture.
Keywords: cfDNA, liquid biopsy, pancreatic cancer

P22

Effect of BET inhibitors on cancer stem cells sorted from primary oral cancer cell culture

Dijana Mitić, Miloš Lazarević, Milica Jakšić Karišik, Jelena Milašin
Department of Human Genetics, School of Dental Medicine, University of Belgrade

Background: Oral cancer is the most common malignant tumor in the oral and maxillofacial region, and squamous cell carcinoma (OSCC) accounts for 80% of tumors of the oral cavity. Despite improvements in OSCC management, survival rates remain relatively low and the discovery of novel anti-neoplastic agents are urgently needed. The study investigated the cytotoxic effect of three BET inhibitors (JQ1, iBET-151, iBET-762), and one antitumor plant alkaloid (paclitaxel) on cancer stem cells (CSCs), sorted from primary oral cancer cell culture. **Material and methods:** Magnetic sorting was used to gain CD44 and CD133 positive cells. Double negative cells served as a control. Cells were seeded in 96 well plates, and 10 µM dose of drugs were added to the wells. After 24, 72 hours, and 7 days MTT was performed. **Results:** Real-time PCR analysis confirmed adequate sorting of the double positive (CD44+ and CD133+) cells, with negligible to none of the marker's expression in double negative cells. After 24h of treatment no significant cytotoxicity of the drugs was observed, in comparison to untreated cells. On 48h of treatment there was significant reduction of the cells in the presence of the drugs, but no difference was observed between CSCs and control cells. In longer treatment period (7 days), there was significant difference in cell survival between CSCs and control, in presence of the drugs, for JQ1 ($p<0.05$), paclitaxel ($p<0.01$), iBET 151 and iBET 762 ($p<0.001$). **Conclusions:** The investigated drugs were relative efficient in treatment of tumor cells, but CSCs remain more resistant to the therapy in comparison to the control.New investigations should be aimed at the successfulreduction of CSCs.
Keywords: cancer stem cells, iBET, magnetic sorting, oral cancer cell line, qPCR