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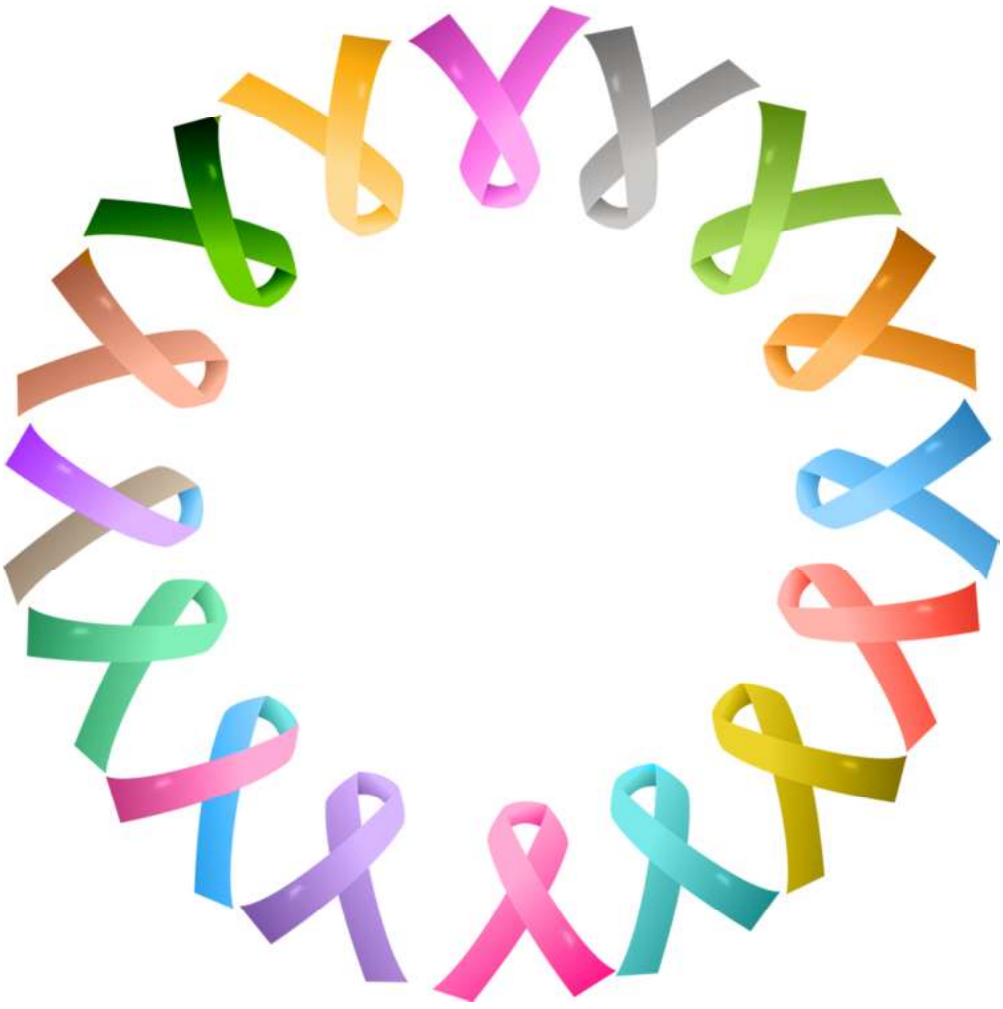

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CONTENTS

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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P51

Cytotoxic activity of extract of *Helichrysum plicatum* DC. on human cancer cells *in vitro*

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Background: Everlasting flowers (*Helichrysum plicatum*) represent a significant source of pharmacologically active secondary metabolites (flavonoids naringenin, kaempferol, apigenin) related to proven spasmolytic, antioxidant, antimicrobial and cytotoxic activity. A critical point in development of polyphenol rich extracts of *H. plicatum* is their limited stability, which can be solved using microencapsulation technique spray drying. The aim of this study was to determine the cytotoxic potential of *H. plicatum* extract *in vitro* on human cervical carcinoma cell line – HeLa, colon cancer cell line – LS-174, prostate cancer cell line PC-3 and normal lung fibroblast cells MRC-5. **Material and methods:** The dried flowers of H. *plicatum* were purchased from the Institute for Medicinal Plant Research "Dr Josif Pančić" (Belgrade, Serbia). The plant material was subjected to a percolation process with an ethanol-water mixture (50:50) for 12 hours, the ratio of solid to solvent being 1:5. After the percolation process, the ethanol was removed using a rotary evaporator (Buchi rotavapor R-114). Then, the obtained extract from the *helichrysum* flowers was spray dried in a Labtex ESDTi spray dryer, and the dried extract was stored in amber glass tubes. The extract of *H. plicatum* was measured and then dilutions were prepared in RPMI-1640 medium. Cytotoxic activity was determined by the colorimetric MTT assay. **Results:** The results of cytotoxic activity of extract of *H. plicatum* against tumor and normal cells are expresed as IC_{50} (half-maximal inhibitory concentration – average ± standard deviation from three independent experiments).

IC_{50} [µg/mL] Av±SD*			
HeLa	LS-174	PC-3	MRC-5
196±16	273±48	297±5	502±44

In all cancer cell lines the extract of *H. plicatum* showed significant cytotoxic activity, with the highest activity in the cervical cancer cell line – HeLa, with good selectivity in activity against all cancer cell lines in comparision to normal MRC-5 cells. **Conclusions:** This study demonstrated the potent anticancer activity of the extract of *H. plicatum*. Future research could show the activity of the extract in other cancers, and identify the main compound that gives it its anticancer activity.
Keywords: cancer cell line, cytotoxicity, extract, *H. plicatum*,

P52

The role of ROS in MAPK-dependent autophagy involved in phorbol myristate acetate-induced macrophage differentiation of HL-60 leukemia cells

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Background: Reactive oxygen species (ROS) have been implicated in autophagy induction and mitogen activated protein kinases (MAPK) activation which both participate in the differentiation of hematopoietic and leukemic cells. We assessed the role of ROS in MAPK activation and autophagy induction in phorbol myristate acetate-(PMA) induced macrophage differentiation of HL-60 leukemia cells. **Material and methods:** The macrophage markers CD11b, EGR1, CSF1R, and IL-8 were assessed by RT-qPCR and flow cytometry. The activation of MAPK was assessed by ERK and JNK immunoblotting, while autophagy was monitored by LC3-II and p62 immunoblotting. Pharmacological inhibition was used to determine the role of MAPK and autophagy in HL60 cell differentiation. Intracellular ROS production was determined by flow cytometric analysis of the green fluorescence emitted by non-selective redox-sensitive dye 2',7'-dichlorodihydrofluorescein diacetate. Antioxidant N-acetylcysteine (NAC) was used to determine the role of ROS in MAPK activation, induction of autophagy and HL-60 macrophage differentiation. **Results:** PMA-triggered

differentiation of HL-60 cells into macrophage-like cells was confirmed by elevated expression of macrophage markers CD11b, EGR1, CSF1R, and IL-8. The induction of autophagy was demonstrated by the increase of autophagic flux. Pharmacological inhibition of ERK or JNK suppressed PMA-triggered autophagy induction and differentiation of HL-60 cells into macrophage-like cells. PMA increased the intracellular ROS generation and the antioxidant NAC reduced the expression of macrophage markers EGR-1, CSF1R, IL-8 and CD11b in PMA-treated HL-60 cells. NAC also blocked PMA-induced LC3-II and ERK phosphorylation, but only slightly reduced the phosphorylation of JNK and did not affect the levels of p62. **Conclusion:** Our study revealed the partial involvement of ROS in MAPK-dependent autophagy in the differentiation of HL60 cells, indicating ROS/MAPK-mediated autophagy for further investigation in differentiation therapy of AML.

Keywords: ROS, leukemia, differentiation, autophagy, ERK, JNK

P53

Monitoring of the presence of EGFR-mutated DNA during EGFR-targeted therapy may assist in the prediction of treatment outcome

Moiseenko F.V.[1,2,4], Volkov N.M.1, Zhabina A.S.[1,2], Stepanova M.L.[1], Rysev N.A.[1], Klimenko V.V.[1], Myslik A.V.[1], Artemieva E.V.[1], Egorenkov V.V.[1], Abduloeva N.H.[1], Ivantsov A.O.[2,3], Kuligina E.S.[2,3],Imyanitov E.N.[2,3,4], Moiseyenko V.M.[1]

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Background: The aim of our trial was to evaluate the prognostic significance of qualitative ctDNA analysis on different stages of EGFR mutated non-small cell lung cancer (NSCLC) treatment. **Materials and Methods:** We included 99 patients amendable for the first line treatment with either gefitinib/erlotinib (n = 87), afatinib (n = 10) or osimertinib (n = 2). Sequential qualitative analysis of ctDNA with cobas® EGFR Mutation Test v2 were performed before first dose, after 2 and 4 months of treatment, and on progression. **Results:** Our analysis showed clinically significant heterogeneity of EGFR-mutated NSCLC treated with 1st line tyrosine kinase inhibitors (TKIs) in terms of progression-free and overall survival. When treated with conventional approach, i.e. monotherapy with TKIs, the patients falls into three subgroups based on ctDNA analysis before and after 2 months of treatment. Patients without detectable ctDNA at baseline (N = 32) possess the best prognosis on duration of treatment (PFS: 24.07 [16.8-31.3] and OS: 56.2 [21.8-90.7] months). Those who achieve clearance after two months of TKI (N = 42) have indistinguishably good PFS (19.0 [13.7 – 24.2]). Individuals who retain ctDNA after 2 months (N = 25) have the worst prognosis (PFS: 10.3 [7.0 – 13.5], p = 0.000). 9/25 patients did not develop ctDNA clearance at 4 months with no statistical difference in PFS from those without clearance at 2 months. **Conclusion:**Prognostic heterogeneity of EGFR-mutated NSCLC should be taken into consideration in planning further clinical trials and optimizing the outcome of patients.

Keywords: EGFR, lung cancer, tyrosine kinase inhibitors.