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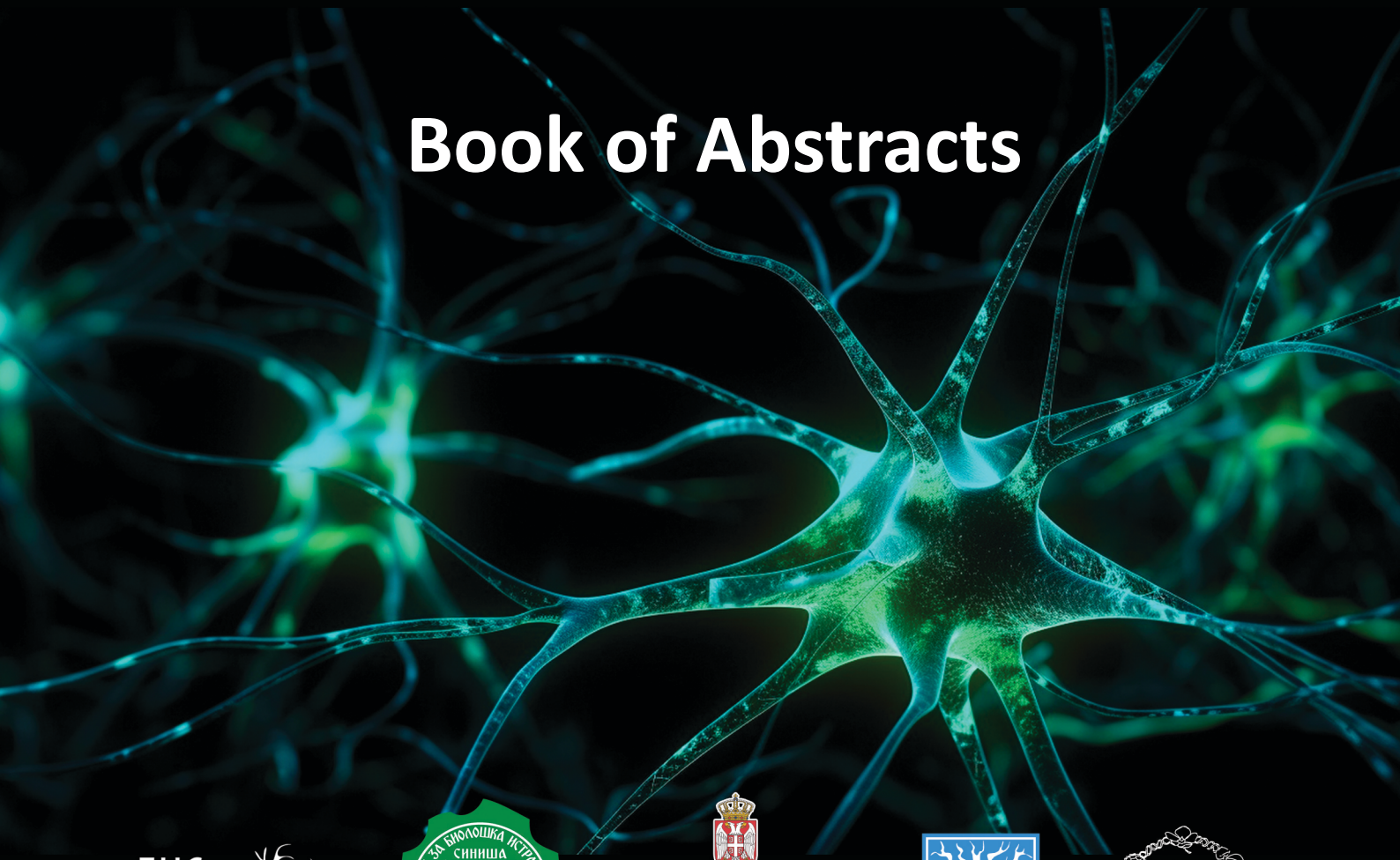

Book of Abstracts

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New anti-glioblastoma strategy with natural compounds sclareol and doxorubicin

Ana Stepanović[1], Ema Lupšić[1], Jelena Dinić[1], Ana Podlski-Renić[1], Milica Pajović[1], Sofija Jovanović Stojanov[1], Miodrag Dragoj[1], Nataša Terzić Jovanović[3], Igor Opsenica[2], Milica Pešić[1]

[1]*Institute for Biological Research "Siniša Stanković" – National Institute of the Republic of Serbia, University of Belgrade, Department of Neurobiology, Belgrade, Serbia*
[2]*University of Belgrade – Faculty of Chemistry, Belgrade, Serbia*
[3] *University of Belgrade - Institute of Chemistry, Technology, and Metallurgy, National Institute of the Republic of Serbia, Belgrade, Serbia*
ana.kostic@ibiss.bg.ac.rs

Background: Doxorubicin (DOX) has been very effective against glioblastoma *in vitro*. Its application *in vivo* is hampered because it cannot pass the blood–brain barrier (BBB). Significant research efforts are invested to overcome this limitation. Sclareol (SC) is an aromatic compound naturally found in clary sage. The combination of SC and DOX showed promising effects in different tumor types *in vitro* and *in vivo*. Therefore, we tested their combination and innovative hybrid molecules (SC:DOX) on glioblastoma cells with the expression of P-glycoprotein, a major component of BBB and cancer multidrug resistance marker. Methods: Cytotoxicity and selectivity towards glioblastoma cells of SC, DOX, their combination, and SC:DOX were examined by MTT assay. The effect of SC on DOX accumulation was determined by flow cytometry. We also studied SC:DOX accumulation, cellular uptake, localization imaging, and DNA damage induction. Results: The effects of simultaneous SC and DOX treatments demonstrated the considerable potential of SC to reverse DOX resistance in glioblastoma cells and increase DOX accumulation. SC:DOX hybrids, named CON1 and CON2 were less cytotoxic than DOX, but with reduced resistance and increased selectivity towards glioblastoma cells. Cellular uptake of CON1 and CON2 was increased in glioblastoma cells compared to DOX. Perinuclear localization of CON1 and CON2 vs. nuclear localization of DOX as well as no DNA damaging effects suggest a different mechanism of action for SC:DOX. Conclusion: The combination of SC and DOX, and their innovative hybrids, could be considered a promising strategy that can overcome the limitations of DOX application in glioblastoma.