Targeting DAMPs by Aspirin inhibits Head and Neck Cancer Stem Cells and stimulates Radio-sensitization to Proton Therapy

Matijevic Glavan Tanja[1]

[1]*Rudjer Boskovic Institute, Zagreb, Croatia*

Cancer stem cells (CSCs) are a specific subpopulation of cancer cells that drive tumorigenesis, self-renewal, and treatment resistance. Here we have explored the role of Toll-like receptor 3 (TLR3) in cancer, specifically its pro-tumorigenic effects on head and neck cancer CSCs. Our findings show that TLR3 activation promotes stemness via increased tumor sphere formation, epithelial-to-mesenchymal transition (EMT), upregulation of stemness genes, and elevated ALDH activity. Furthermore, TLR3 activation triggers damage-associated molecular pattern (DAMP) secretion into the microenvironment, enhancing cancer cell migration, which could be inhibited by DAMP inhibitors. Patient tissue samples confirmed TLR3 co-localization with stemness markers CD133 and ALDH1, along with the DAMPs HSP70 and RAGE. To explore CSC-targeted therapies, we combined apoptosis inducer poly(I:C) with DAMP inhibitors and γ-irradiation, which was effective in adherent cancer cells but failed on CSCs. However, proton radiotherapy combined with aspirin (a common drug and a DAMP inhibitor) and poly(I:C) successfully eliminated CSCs. This novel therapy combination highlights promising strategies for treating head and neck cancers.

Short bio:

Dr. Matijević Glavan Tanja is a molecular biologist working in the field of molecular oncology at the Ruđer Bošković Institute (RBI) in Zagreb, Croatia. She is currently a Scientific advisor. Her research focuses on cancer stem cells and targeted therapies with special focus on particle therapy. She has authored 35 papers, co-authored book chapters, and holds an h-index of 16. She has led national and bilateral projects, mentored graduate students, and received three RBI yearly awards. Active in science promotion and journal peer review, she has organized conferences and delivered invited lectures internationally.