Salinomycin as a Molecular Trojan Horse for Targeting Mn-Induced Malignancy in Aggressive Tumors

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Manganese is a central promoter of malignancy in cancer. In the previous project, it was observed that Mn alters gene expression of metal transporters, favoring the accumulation of this element, while balancing possible toxicity by downregulating the main Mn transporter, DMT1, before Mn accumulation could reach damaging levels. Therefore, the following question arose: Does salinomycin inhibit Mn transport mediated by DMT1, affecting Mn uptake and reducing the malignancy caused by this element? Tumor cells and healthy cells were used to investigate. The cells were incubated with $MnCl_2$ and salinomycin for 24 h, followed by 24 h of recovery in standard medium. To quantify tumor cell death, I used the clonogenic assay. To assess the invasive potential, I performed the cell migration assay. To analyze Mn levels in culture medium and cells, I applied ICP-OES. Finally, to map Mn subcellular distribution, I performed X-ray fluorescence. In addition to the tumor cells treated with salinomycin showing marked cell death, surviving cells have a lower capacity for Mn uptake. This is relevant because, even if salinomycin is not 100% effective, the resistant population is potentially less aggressive, with indications of a lower proliferation rate and possibly less invasive potential. Next steps involve testing different treatments with salinomycin and other tumor and healthy cell lines to define the level of specificity of salinomycin. Heparin will also be tested as an Mn chelator in combination with salinomycin. This innovative project has great potential for the development of new therapeutic targets in cancer.

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