Anticancer properties of selenium nanoparticles encapsulated by oncolytic virus capsids

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Introduction: Selenium Nanoparticles (SeNPs) have shown anticancer potential while having high biocompatibility and their functionalization using specific ligands demonstrated to have additional therapeutic effect.[1]. Viral membranes has been used to deliver anticancer cargoes [2]. Oncolytic virus (OVs), such as the chimeric adenovirus 5/3 (Ad5/3), have been studied for cancer therapy, not only by their ability to specifically target, infect and kill cancer cells while unaffecting healthy cells, but also by activating immune cells, such as Natural Killer (NK) and T cells towards the tumour itself [3,4]

Methods: SeNPs were produced using sodium selenite, ascorbic acid as reducing agent and bovine serum albumin as stabilizing agent, adjusting the pH reaction environment to 1. Ad5/3 virus were obtained by infecting A549 cells and further purification of the virus capsid was performed by CsCl density-gradient ultracentrifugation, after separating and lysing the cells by freeze-thaw. The SeNPs encapsulation by the virus capsids (Ad-SeNPs) was performed by both extrusion and pH-dependent encapsulation. The stability of Ad-SeNPs was performed in human plasma, cell medium, pH 7.4 and 5.5. Also, the antitumor properties were evaluated *in vitro*, including the antiproliferative potential, the internalization efficiency, the intracellular oxidative stress, and the caspase activation, using breast (4T1) and lung (A549) cancer cell lines, and a human fibroblast cell line to evaluate the systemic toxicity. The potential of Ad-SeNPs for T and NK cells polarization was also evaluated

Results: After the SeNPs encapsulation by viral membranes, Ad-SeNPs demonstrated a size around 100 nm, moderate polydispersity, and a negative surface charge. The nanosystem produced was stable at cell medium, human plasma, physiologic pH, although degraded at acidic pH. Ad-SeNPs presented higher anticancer properties when compared to the non-encapsulated SeNPs, increasing the SeNPs internalization into cancer cells, and therefore inducing oxidative stress, caspase-3/9 activation, and consequent cellular apoptosis. Ad-SeNPs was also able to polarize NK and T cells, proving its immunotherapeutic potential.

Conclusion: Our study led to the production of a nanosystem with high antitumour potential, by directly causing cancer cells apoptosis and by inducing an antitumor immunological reaction.

References

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Figures

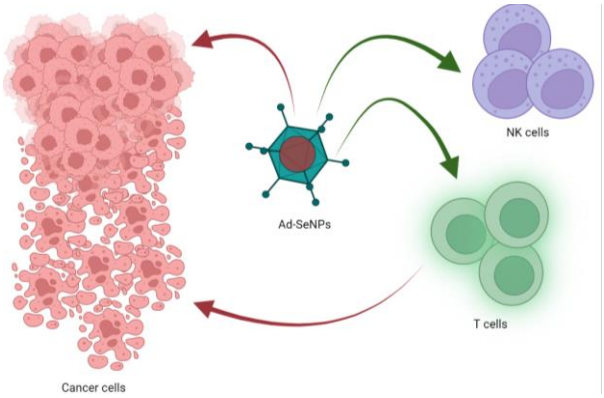

Figure 1. Ad-SeNPs antitumor properties are based in a 2-way mechanism, in which they induce apoptosis in cancer cells while polarizing NK and T cells