Biointerfaces - a nanoscale world with a huge potential

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There are many issues associated with free drug delivery including: adverse side-effects, multi-drug resistance, premature drug degradation, lack of tissue penetration, and non-specific toxicity. Targeted delivery, which utilises nanocarriers as payload delivery vesicles, has the potential to address and alleviate these prominent issues. Specifically, it involves nanomaterials functionalised with targeting agents, allowing for the selective uptake of these nanocarriers by cells overexpressing specific receptors. This approach explicitly increases the drug concentration in the target cell of interest whilst minimising the exposure of healthy cells to the therapeutic agent.

In this presentation, carbon nano-onions (CNOs) will be discussed as a potential vesicle for nanocarrier-type drug delivery systems.[1] CNOs, or multi-layer fullerenes, consist of multiple concentric layers of sp^2 hybridised carbon and are emerging as platforms for biomedical applications because of their ability to be internalized by cells and low toxicity. [2]

In my research group we have developed a synthetic methodology for the synthesis of pure, monodispersed CNOs and various chemical functionalization strategies for the introduction of different functionalities (receptor targeting unit and imaging unit) onto the surface of the CNOs. The modified CNOs display high brightness and photostability in aqueous solutions and are selectively taken up by different cancer cell lines without significant cytotoxicity. [3]

We have also developed supramolecular functionalization with biocompatible polymers as an effective strategy to develop engineered drug carriers for targeted delivery applications. We reported the use of a hyaluronic acid-phospholipid (HA-DMPE) conjugate to target CD44 overexpressing cancer cells, while enhancing solubility of the nanoconstruct. Non-covalently functionalized CNOs with HA-DMPE show excellent *in vitro* cell viability in human breast carcinoma cells overexpressing CD44 and are uptaken to a greater extent compared to human ovarian carcinoma cells with an undetectable amount of CD44. In addition, they possess high *in vivo* biocompatibility in zebrafish during the different stages of development suggesting a high degree of biosafety of this class of nanomaterials. [4]

To probe the possible applications of CNOs as a platform for therapeutic and diagnostic interventions on CNS diseases, we injected fluorescent CNOs *in vivo* in mice hippocampus. We analyzed *ex vivo* their diffusion within brain tissues and their cellular localization by confocal and electron microscopy. The subsequent fluorescent staining of hippocampal cells populations indicates they efficiently internalize the nanoparticles. Furthermore, the inflammatory potential of the CNOs injection was found comparable to sterile vehicle infusion, and it did not result in manifest neurophysiological and behavioral alterations of hippocampal-mediated functions [5].

Our results encourage further development as targeted diagnostics or therapeutics nanocarriers.

References:

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