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Synthesis of Highly Stable Multi-Functional Iron Oxide Nanoparticles for Active Mitochondrial Targeting in Immunotherapy

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Abstract : Mitochondria- targeting immunogenic cell death inducers (MT-ICD) have been designed to trigger intrinsic apoptosis signalling pathway in malignant cells and revive the antitumour immune system. MT-ICD inducers have considered to be non-specific, which can deteriorate the ability to initiate mitochondria-selective oxidative stress, causing high toxicity. Iron oxide nanoparticles (IONPs) can be an ideal candidate as vehicles for utilizing in immunotherapy due to their biocompatibility, modifiable surface chemistry, magnetic characteristics and multi-functional applications in single platform. These types of NPs can facilitate a real time imaging which can provide an effective strategy to analyse pharmacokinetic parameters of nano-formula, including blood circulation time, targeted and controlled release at tumour microenvironment. To our knowledge, the conjugation of IONPs with MT-ICD and oxaliplatin (a chemotherapeutic agent used for the treatment of colorectal cancer) for immunotherapy have not been investigated. Herein, IONPs were generated via co-precipitation reaction at high temperatures, followed by coating the colloidal suspension with tetraethyl orthosilicate and 3-aminopropyltriethoxysilane to optimize their bio-compatibility, preventing aggregation and maintaining stability at physiological pH, then functionalized with (3-carboxypropyl) triphenyl phosphonium bromide for mitochondrial delivery. Analytical results demonstrated the successful process of IONPs functionalization. In particular, the colloidal particles of doped IONPs exhibited an excellent stability and dispersibility. The resultant particles were also successfully loaded with the oxaliplatin for an active mitochondrial targeting in immunotherapy, resulting in well-maintained super-paramagnetic characteristics and stable structure of the functionalized IONPs with nanoscale particle sizes.

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