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Tumor necrosis factor related apoptosis inducing ligand-conjugated near IR fluorescent iron oxide/ human serum albumin core-shell nanoparticles of narrow size distribution for cancer targeting and therapy

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The nanoparticles' synthesis and the anti-cancer effect: A unique type of composite multi-functional near IR (NIR) fluorescent iron oxide (IO) nanoparticles (NPs) of narrow size distribution for tumor targeting and therapy have been designed and studied. These NPs were prepared by nucleation followed by controlled growth of thin films of IO onto Cy7-conjugated gelatin nuclei and coated with human serum albumin (HSA) by a thermal precipitation process. The hydrodynamic diameter of these core-shell NPs could be easily controlled by altering the precipitation reaction temperature. For targeting and an anti-cancer effect, we conjugated the Tumor Necrosis Factor Related Apoptosis Inducing Ligand (TRAIL) cytokine to the surface of the NIR fluorescent IO/HSA NPs via a polyethylene glycol (3 kDa) linker. The conjugated TRAIL exhibited enhanced and prolonged anti-cancer activity in both human glioblastoma multiforme and colon cancer cell lines. Further, the combination of these IO/HSA-TRAIL NPs with the commonly used chemotherapeutic drug doxorubicin resulted in a synergistic anti-cancer effect on these cancer cell lines, both *in-vitro* and *in-ovo*.

The NPs' effect on human mesenchymal stem cell growth and differentiation: HSA coating onto the IO NPs enables conjugation of the IO/HSA NPs to various biomolecules including proteins, for example fibroblast growth factor 2 (FGF2), for biomedical applications. We examined the biological activity of the conjugated FGF2 on human bone marrow mesenchymal stem cells (hBM-MSCs). FGF2 enhances the proliferation of hBM-MSCs and stimulates promotes their differentiation toward neuronal, adipogenic and osteogenic lineages *in-vitro*. Covalent conjugation of the FGF2 to the IO/HSA NPs significantly stabilized this growth factor against various enzymes and inhibitors existing in serum and in tissue cultures. Conjugated FGF2 enhanced clonal expansion capacity of hBM-MSCs to a higher extent compared with the free growth factor.

Biography

Itay Levy, male, medicinal chemist, graduated with excellence from chemistry department at Bar Ilan University, B.Sc. on 2011 and M.Sc. on 2013. He started his Ph.D in Bar Ilan University on 2013, researching iron-oxide nanoparticles and its various biomedical effects and applications. Since 2011, he is collaborating with a startup company to develop a medicine for glioblastoma multiform (GBM) brain cancer, which recently has been approved for clinical trials. Now he is writing a new patent of new iron-oxide nanoparticles for biomedical applications.

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