Cornell Dots: Multifunctional Nanomaterials for Theranostic Applications in Oncology

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ABSTRACT

This presentation will describe studies of a particular class of nanotheranostics, i.e. ultrasmall fluorescent core-shell silica nanoparticles referred to as Cornell dots (C dots). C dots, synthesized via sol-gel chemistry in alcohol (C dots) or water (C' dots), have been successfully translated into multiple diagnostic as well as therapeutic clinical trials in oncology. Their ultrasmall size below the cut-off for renal clearance (particle diameters < 7-8 nm) leads to favorable biodistribution (BD) and pharmacokinetics (PK) profiles with high accumulation at the target site, low off-target accumulation, effective solid-tumor penetration, as well as efficient renal clearance ("*target-or-clear*"). The use of targeting moieties, including cyclic peptides as well as antibody fragments, increases targeting efficiencies over non-targeted analogues. Finally, surface modifications of the poly(ethylene glycol) (PEG) surface layer with therapeutic payloads that can be enzymatically cleaved when entering the target site, including small molecule inhibitors as well as chemotherapeutics, leads to unusually high drug loading capacities (>40 drug molecules per particle) without substantially effecting BD and PK profiles. This is enabled by the insertion of these typically more hydrophobic payloads in-between the hydrophilic PEG chains, keeping the overall particle surface characteristics PEG-like. As a result of very careful nanomaterials structure/composition versus biological response studies, including detailed gel permeation chromatography (GPC) and high-performance liquid chromatography (HPLC) particle characterizations enabled by the ultrasmall particle size, durable structure-biological property correlations are emerging providing blueprints for future nanomaterials applications in medicine. Furthermore, the recent discovery of "*self-therapeutic*" properties of such ultrasmall silica-based nanomaterials, i.e. anti-tumoral activities of the particles in the absence of cytotoxic payloads, opens exciting new opportunities for combinatorial treatment regiments. Results suggest that such molecularly engineered ultrasmall multifunctional nanomaterials platforms may overcome limitations, e.g. of biological carrier systems including antibody drug conjugates (ADCs), ultimately improving personalized patient care.

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