Research in Pharmaceutical Sciences, 2012;7(5)
School of Pharmacy and Pharmaceutical Sciences
Isfahan University of Medical Sciences

Translational Nanomedicine

S.M. Moghimi

Nanomedicine Laboratory, Centre for Pharmaceutical Nanotechnology and Nanotoxicology, and NanoScience Centre, University of Copenhagen, DK-2100 Copenhagen Ø, Denmark

Advances in design and engineering of nanoscale delivery systems with distinct physical and biochemical properties are beginning to positively impact clinical practice at many levels. These include disease diagnosis and imaging, detection of molecular changes responsible for disease pathogenesis and site-specific targeting of therapeutic agents with triggered-release mechanisms. Indeed, research into targeting of pharmaceutical, therapeutic, and diagnostic agents via intravenous and interstitial routes of administration with multifunctional nanoparticulate entities and nanoconstructs is at the forefront of projects in nanomedicine, but the biological performance of such nanosystems still requires optimization as well as reducing their toxicity at and off target sites. The underlying processes of toxicity are also complex, multifaceted and have had limited investigations at intracellular environments.

We are engaged in tailor-made engineering of nanopharmaceuticals and advanced nucleic acid-based constructs. Here, we design and fully characterize a wide range of lipid, peptidic, polymeric and inorganic nanomaterial libraries and apply a multidisciplinary approach to unravel the molecular basis of nanocarrier/nanomaterial performance and toxicity on the basis of ”structure-activity” assessments at cellular and subcellular (single-cell, single-organelle and real-time microscopy) as well as biological fluid levels in combination with and by improving/optimizing the performance of the state-of-the-art bio-nanotechnology techniques. Through such approaches, we have made significant advances in understanding of key mechanistic processes that regulate lipid fusion processes as well as interactive forces between macromolecular cargo and the nanocarrier in terms of stability optimization and developing new extra- and intra-cellular release mechanisms. Furthermore, our integrated and interdisciplinary approaches have allowed for rational design, nanoengineering and tuning of safer advanced functional nanomedicines (e.g., polymersomes, liposomes and polymeric nanoparticles, and peptidic complexes) applicable to parenteral administration and particularly for CNS disorders, cancer, cardiovascular diseases and inflammatory conditions. Some of our recent breakthroughs include design of peptidic-based nanoparticles/therapeutics exhibiting high specificity for the human brain cerebral endothelial cells and applicable to the Alzheimer’s disease, and development of safe polymer-killer gene complexes tagged with camelid antibody fragments (VHH) for selective destruction of colon and breast cancers cells.

Our efforts are further beginning to provide ’bench-mark’ protocols for toxicity evaluation of nanomedicines and polyplexes at different levels, as the sensitivity and precision of standard toxicological procedures are of arguable value in nanomedicine research as it is limited to spotting extreme toxicity. One key finding was realization of the role of polymer conformation in different triggering the first line of the innate immune defence system, also known as the complement system. This observation has important bearings in design of safe stealth nanocarriers and for prevention of nanomedicine-mediated infusion reactions. Accordingly, our findings have raised further challenges for safe engineering of nanoparticle surfaces with polymers that was previously considered to be inert and safe. We are now paying attention to the role of other physical parameters, such as the shape and the extent of nanoparticle deformability to overcome problems with the immune system.