The Michigan Nanotechnology Institute for Medicine and Biological Sciences invites you to its Herbert D. Doan Lecture by:

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Protein-Polymer Nanoparticles for Delivery of Therapeutics

He will describe a class of protein-polymers –artificial recombinant polypeptides– that spontaneously undergo self-assembly upon conjugation to the cancer chemotherapeutic Doxorubicin (Dox) and other small hydrophobic molecules. These chimeric polypeptides (CPs) consist of a hydrophilic, biodegradable polypeptide segment that is attached to a short Cys-rich segment. Covalent modification of the Cys residues with a structurally diverse set of hydrophobic small molecules, including Dox, leads to the spontaneous formation of nanoparticles for a range of CP compositions and molecular weights. The CP-Dox nanoparticles are ~40 nm in diameter, release drug at pH 5.0 (relevant to endo-lysosomal release), are taken up by cells, show subsequent localization of the drug to the nucleus, and are cytotoxic. Notably the CP-Dox nanoparticles have a four-fold higher maximum tolerated dose than free drug and induce near complete tumor regression in a murine model following a single dose.

He will also discuss a new protein-polymer conjugate with interesting pharmacological properties: he will describe two new and general routes to grow a PEG-like polymer, poly(oligo(ethylene glycol) methyl ether methacrylate) (poly(OEGMA)), with low polydispersity and high yield solely from the N-terminus or C-terminus of a protein by in situ atom-transfer radical polymerization (ATRP) under aqueous conditions, to yield site-specific (N- or C-terminal) and stoichiometric conjugates (1:1). Notably, both the myoglobin-poly(OEGMA) conjugate (N-terminal conjugate) and green fluorescent protein conjugate (C-terminal conjugate) showed a 40-50 fold increase in their blood exposure compared to the unmodified protein after intravenous administration to mice, thereby demonstrating that comb polymers that present short oligo(ethylene glycol) side-chains are a new class of PEG-like polymers that can significantly improve the pharmacological properties of proteins. We believe that this new approach to the synthesis of N/C-terminal protein conjugates of poly(OEGMA) may be applicable to a large subset of protein and peptide drugs, and thereby provide a general methodology for improvement of their pharmacological profiles.

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LOCATION: Biomedical Sciences Research Building Kahn Auditorium

This lecture is free; no registration required; see www.nano.med.umich.edu