Proteomimetic Polymers for Expanding the Druggable Proteome

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In this presentation, we will describe the organization of functional peptides as densely arrayed sidechains on polymer scaffolds as leading to a new class of proteomimetic material. We call these materials, Protein-Like Polymers (PLPs), wherein peptide-brush polymers are composed from monomers, each containing a peptide side-chain. Peptides organized in this manner imbue polymers with a range of functional qualities inherent to their specific sequence. Therefore, polymers otherwise lacking bioactivity, or responsiveness to stimuli, once linked to a peptide of choice, can now bind proteins, enter cells and tissues, have controlled and switchable biodistribution patterns, and exhibit exceptionally long half lives in circulation (days to weeks). Synergistically with the peptide influencing the polymer, the polymer enforces changes in peptide activity and function by virtue of packing and constraining the peptide. For example, the scaffold can protect the peptide from proteolysis, change the pharmacokinetic profile of an intravenously injected peptide, increase the cellular uptake of an otherwise cell impermeable therapeutic peptide, or change peptide biological activity. Moreover, in addition to the sequence-controlled peptides (generated by solid phase synthesis) the polymer can carry its own sequence-dependent information, especially through living polymerization strategies allowing well-defined blocks and terminal labels (dyes, contrast agents, charged moieties). Hence, the two elements, peptide and polymer, cooperate to yield materials with unique function and properties quite apart from each alone. Herein, we describe the development of synthetic strategies for accessing this class of biomolecule polymer conjugates, discuss their physicochemical and structural properties and will describe their utility in a range of settings, including as a new type of therapeutic modality. We will highlight some examples of biomedical applications including by engaging critical intracellular protein-protein interactions driving neurodegenerative disease and cancer.