Beta-Hairpin Peptide Self-assembly: Construction of Advanced Materials from Injectable Gels to Nanoparticle Arrays

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Self-assembly of molecules is an attractive materials construction strategy due to its simplicity in application. By considering peptidic, charged synthetic molecules in the bottom-up materials self-assembly design process, one can take advantage of inherently biomolecular attributes; intramolecular folding events, secondary structure, and electrostatic interactions; in addition to more traditional self-assembling molecular attributes such as amphiphilicty, to define hierarchical material structure and consequent properties. Design strategies for materials self-assembly based on small (less than 24 amino acids) beta-hairpin peptides as well as longer polypeptides will be discussed. In the case of what is possible with small peptides, the local nano- and overall network structure, and resultant viscoelastic and cell-level biological properties, of hydrogels that are formed via β-hairpin self-assembly will be presented. β-hairpins are excellent examples of the bio-inspiration of materials in that one can design β-hairpins to assemble into soft materials only after undergoing a desired, protein-like folding event. These peptide hydrogels are potentially excellet scaffolds for tissue repair and regeneration due to inherent cytocompatibility, porous morphology, and shear-thinning but instant recovery viscoelastic properties. The 20 amino acid parent peptide MAX1 (H_2N-VKVKVKVKV^{D}PPTKVKVKVKV-$CONH_2$), has been shown to fold and self-assemble into a rigid hydrogel based on environmental cues such as pH, salt, and temperature including physiological conditions. The hydrogel is composed of a network of fibrils that are 3 nm wide and heavily branched and entangled with no covalent crosslinking required for gel stiffness. In addition, slight design variations of the MAX1 sequence allow for tunability of the self-assembly/hydrogelation kinetics. In turn, by controlling hydrogel self-assembly kinetics, one dictates the ultimate stiffness of the resultant network and the kinetics through which gelation occurs.

Importantly, once formed into a solid, self-supporting gel the network can be disrupted by the introduction of a shear stress. The system can shear thin but immediately reheal to preshear stiffness on the cessation of the shear stress. This shear thinning behavior of these physical networks makes them interesting candidates for injectable delivery in vivo where no post injection chemistry is required to set up the network. Thus, biological payloads (e.g. cells, proteins) can be encapsulated during self-assembly and subsuently shear thin injected within a solid scaffold. Peptide design for folding and self-assembly, self-assembly characterization, gel material properties, and cell-level biological properties of these peptide hydrogels will be discussed. In addition, the fibrils can be used to template the growth of inorganic materials as well as the assembly of inorganic nanoparticles. The study of the hybrid assembly process, as well as the shear thinning process will be presented.

Self-assembly need not be limited to small peptides. Larger, polypeptides, when designed correctly and intermolecularly assembled with desired kinetics, can produce desired nanostructures and materials. Examples will be given of polypeptides that can produce 1-d fibrillar nanostructures with desired display of chemistry for inorganic nanoparticle adsorption and display. In summary, the potential of producing advanced materials with defined nanostructure and material properties through peptide/polypeptide self-assembly will be

discussed in the context of the Pochan group and collaborators' research efforts as well as the greater literature.