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Design of Responsive Peptide-based Hydrogels as Therapeutics

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Hydrogels composed of self-assembled peptides have been designed to allow minimally invasive delivery of cells in-vivo. These peptides undergo sol-gel phase transitions in response to biological media enabling the three-dimensional encapsulation of cells. Peptides are designed such that when dissolved in aqueous solution, exist in an ensemble of random coil conformations rendering them fully soluble. The addition of an exogenous stimulus results in peptide folding into beta-hairpin conformation. This folded structure undergoes rapid self-assembly into a highly crosslinked hydrogel network whose nanostructure is defined and controllable. This mechanism, which links intramolecular peptide folding to self-assembly, allows temporally resolved material formation. In general, peptides can be designed to fold and assemble affording hydrogel in response to changes in pH or ionic strength, the addition of heat or even light. In addition to these stimuli, DMEM cell culture media is able to initiate folding and consequent self-assembly. DMEM-induced gels are cytocompatible towards NIH 3T3 murine fibroblasts, mesenchymal stem cells, hepatocytes, osteoblasts and chondrocytes. As an added bonus, many of these hydrogels possess broad spectrum antibacterial activity suggesting that adventitious bacterial infections that may occur during surgical manipulations and after implantation can be greatly reduced. Lastly, when hydrogelation is triggered in the presence of cells, gels become impregnated and can serve as a delivery vehicle. A unique characteristic of these gels is that when an appropriate shear stress is applied, the gel will shear-thin, becoming an injectable low viscosity gel. However, after the application of shear has stopped, the material quickly self-heals producing a gel with mechanical rigidity nearly identical to the original hydrogel. This attribute allows cell-impregnated gels to be delivered to target tissues via syringe where they quickly recover complementing the shape of the tissue defect. This shear-thin delivery method is a convenient way to introduce cells to wound sites.