

Enzyme-Assisted Assembly of Peptide-Based Gels for Regenerative Medicine

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Spontaneous formation of macroscopic hydrogels from small molecule building blocks via self-assembly provides a route toward designed functional biomaterials. We will show that a number of small peptide amphiphiles, consisting of (mixtures of) dipeptides linked to fluorenylmethoxycarbonyl (Fmoc) form fibrous hydrogels in physiological conditions. The self-assembly process is driven by π -stacking of the conjugated fluorenyl moieties and formation of β -sheet structures as is demonstrated by circular dichroism, FT-IR and fluorescence spectroscopy.

The amino acid sequence within the peptide-based building blocks controls the nano-fibrous architecture and the physical properties of the assembled structures. Combinations of Fmoc-dipeptides were identified that formed fibrous hydrogels that were i) stable under cell culture conditions, ii) of similar dimensions to the fibrous components of the extracellular matrix and iii) capable of supporting cell culture of chondrocytes in 3D.¹ We also demonstrate that these peptide gels can be formed under thermodynamic control by exploiting the selective catalytic action of proteolytic enzymes.^{2,3}

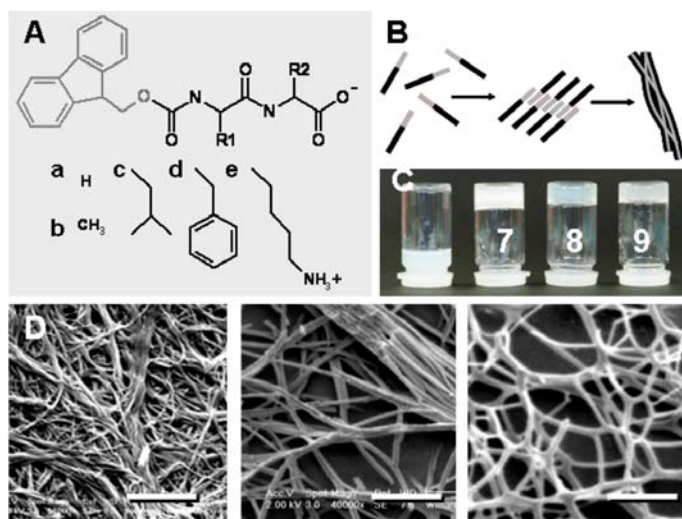


Figure 1: A: Molecular structure of Fmoc-dipeptides. The R groups are for amino acids Gly (a), Ala (b), Leu (c), Phe (d) or Lys (e). B: Proposed self-assembly mechanism. D: Cryo-SEM micrographs of nanofibrous materials.

Conclusions - We demonstrate that enzymes can be used to trigger the assembly of short peptide amphiphiles to form nanofibrous hydrogels that mimic the extracellular matrix. These gels can be used for 3D cell culture of a number of cell-types.

References – 1. V. Jayawarna, M. Ali, A.F. Miller, A. Saiani, J. E. Gough, R. V. Ulijn *Adv. Mater.*, 2006, 18, 611-615. 2. S. Toledano, R.J. Williams, V. Jayawarna, R.V. Ulijn, *J. Am. Chem. Soc.*, 2006, 128(4), 1070-1071. 3. R.V. Ulijn, *J. Mater. Chem.* 2006, 16, 2217-2225.