Abstract

Mimicking the functional cues of native extracellular matrix (ECM) is elementary to understand and control the processes that regulate cell physiology and cell fate. Extensive groundwork on the structural and biological complexity of ECM has revealed the critical paramaters for the design of synthetic ECM that can control cellular behavior. These parameters include tuning of biophysical properties (stiffness, elasticity), biochemical properties (bioactive peptide epitopes), and nano-architecture (nanofibrillar structure, porosity) of the designer scaffold. Recent advances in the construction of ECM mimetic materials have directed the efforts towards tissue specific scaffold design and are primarily based on exploration of bioactive peptides. The concept of molecular self-assembly coupled with rich peptide chemistry holds great potential to fabricate diverse functional materials. Inspired by the design of mother nature, we have developed a series of bioactive functional scaffolds, using minimalist design approach to fabricate the synthetic mimics of ECM, which can have potential implications in tissue engineering. To this direction, we initially explored the short functional motifs i.e. IKVAV and YIGSR, of basement membrane protein of natural ECM, i.e. Laminin, which has critical role in cell adhesion, migration and proliferation. Our study emphasizes on the role of differential environmental conditions i.e. solvent switch in tailoring the self-assembling properties of these designed peptides. We tuned the physiochemical and structural properties of these novel peptide based scaffolds to effectively modulate the differential interactions with different cell types. Apart from individual peptides, we explored the self-assembling properties of IKVAV and YIGSR peptides in combination. Interestingly, these short laminin peptides were highly biocompatible and able to mimic biological properties of native protein, including proliferation, adhesion, neurite extension, neuronal marker expression and cell cycle regulation, indicating their role in controlling neuronal cell behavior. The next step was intended to achieve the complex multi-functional hierarchical composition and structure by simply mixing the two functional peptides derived from collagen and laminin proteins. Gelation was induced in short collagen mimetic peptide by the addition of laminin mimetic peptides, thus creating multifunctional scaffolds for regulating the growth of both fibroblast as well as neuronal cells. Our studies revealed that maintenance of hydrophilic-lipophilic balance (HLB) within the molecule is crucial for designing an ideal hydrogelator. In order to achieve detailed understanding on rationale behind the gelator design, our attempt was directed to establish a sequence-structure relationship with respect to systematic variations in hydrophobic-hydrophilic balance within designer peptides. For the first time, differential role of aliphatic vs aromatic hydroxyl group has been established towards shape controlled synthesis of gold nanoparticles. Furthermore, non-conventional approach for modulation of physical parameter of the self- assembly in a single molecular domain was explored, without changing chemistry of the gelator. Highly tuneable gels were created by the interaction of non-gelator peptides and specific proteins which represents the ‘out of equilibrium’ structures. The present work underpins the development of tunable functional materials, mainly inspired from biological origin, which could essentially create the ideal microenvironment to provide essential biochemical and biophysical cues to the relevant cell types. These biomimetic materials hold great potential to be developed as next-generation biomaterials for biomedical applications.