Title:	Development of multi-component bioactive Scaffolds for tissue regeneration
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Abstract:	Abstract Development of Multi-component Bioactive Scaffolds for Tissue Regeneration Peptide self-assembly is emerging as an interesting approach to develop advanced biomaterials with superior physicochemical as well as biological properties. In this direction, controlling the self-assembly pathways to achieve diverse supramolecular structures from single type of building blocks is particularly interesting as it drastically reduces the existing synthetic as well as purification challenges. Moreover, it is well established that the final functional properties of the nanomaterials are largely dominated by the structural organisation of the building blocks at the nanoscopic level. Thus, controlling the supramolecular organisation of building blocks by tuning the self-assembly pathways could be an advanced approach for fabrication of next- generation biomaterials. In this work, we explored the bioinspired self-assembly approach to fabricate diverse supramolecular hydrogels with potential applications in tissue engineering. In this context, we particularly exploited peptides owing to their well-known chemical diversity and bioactivity in the biological system. First of all, we designed short histidine-based peptide amphiphiles to explore histidine-metal interactions as an alternate pathway to form diverse supramolecular structures from a single type of amphiphile. The amphiphiles showed significant variation in their gelation behavior in the presence of metal salts as reflected in their variable gel stiffness, supramolecular chirality and morphology. Further, owing to the inherent biocompatibility exhibited by peptides, a neuroactive matrix was developed by utilizing minimalistic peptide derived from Tenascin-C protein. Neural tissue is a complex structure having restricted ability to regenerate after injury. Hence, fabrication of neuro-inductive biomaterials for successful delivery and retention of neural stem cells at the site of injury is of utmost importance. Tenascin-C derived shortest peptide showed high propensity to self- assemble into β-sheet like structures at physiological pH. Furthermore, the peptide hydrogel scaffold exhibited good biocompatibility and supported the adhesion, proliferation and migration of various cell lines derived from neural tissue. In similar direction, we have also designed short peptide amphiphiles derived from the bioactive region of the elastin protein present in native extracellular matrix (ECM). The amphiphiles demonstrated hydrogelation ability at physiological pH and showed biocompatibility towards fibroblast cell line. Furthermore, as a step forward in mimicking the diverse biomolecular entities present in native ECM, we have also explored the non-covalent conjugation of various plant and animal derived biopolymers with peptides as an emergent strategy to fabricate advanced bioactive scaffolds. In this direction, we have explored the potential of heparin, which is also a close mimic ofheparan sulfate ubiquitously present in the ECM. However, owing to its high-water solubility, the bioactivity of heparin is mostly utilized after chemically conjugating it with large polymers. Incorporation of the heparin into the peptide hydrogel led to formation of diverse hydrogels of variable gel strength and morphology. Additionally, the heparin-Tc scaffold showed superior cellular viability as compared to only peptide and supported cellular adhesion and proliferation without eliciting any significant immune response. Furthermore, the composite hydrogels were also developed by utilizing the simple non-covalent interactions between the nanofibrous cellulose (NFC) and Nap-FEFK peptide. Interestingly, the composite hydrogels demonstrated superior hydrogel stability, cellular viability as well as proliferation in 3-D culture conditions as compared to the only peptide hydrogel. This approach is expected to be helpful in overcoming the challenges associated with development of single component-based hydrogels and could present the beneficial features of ECM derived sugars and peptide to the cells for successful tissue engineering.
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