Title:	Designing Biomulecular Hydrogel Scaffolds for Healthcare Applications
Authors:	Kumar Pal, Vijay
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Abstract:	Abstract Designing Biomolecular Hydrogel Scaffolds for Healthcare Applications Natural biomolecular assemblies commonly involve non-covalent interactions among the specific building blocks, which can also be replicated in an artificial setup to fabricate the next- generation materials. In this direction, self-assembly of short peptides into a well-ordered supramolecular structure has gained immense interest for developing advanced materials at the nano dimension. In particular, differential supramolecular assemblies by modulating the self- assembling pathways can be achieved from a single type of building block, which responds differentially towards different cell types. In this context, we have designed oppositely charged collagen inspired shortest bioactive pentapeptide sequence as a minimalistic building block for development of next-generation biomaterials. Our rational design involves synthesis of two pentapeptides, where the fundamental molecular motif of collagen, that is Gly-X-Y has been mutated at the central position with positively charged, lysine, and negatively charged, aspartate residues, respectively to create ionic complementary peptides. Interestingly, simple mixing of the two peptides was found to induce the co-assembly of these designed peptides, which drives the formation of self-supporting hydrogel at physiological pH and thus enhanced the potential of exploring these peptides for biomedical applications. Furthermore, our approach was focused on mimicking the diverse biomolecular entities present in the native extracellular matrix (ECM) to create a closer mimic of the similar domain. In this direction, we have developed a conjugated hydrogel consisting of nanocellulose and collagen inspired complementary ionic peptides. Further, these biomolecular hydrogel constructs were explored towards cellular studies in order to develop a superior biomaterial, which represents an ideal replica of native ECM. Interestingly, these combined scaffolds supported cellular behaviour of both fibroblast as well as neural cells, highlighting the diversities of these conjugate hydrogels. Furthermore, we have attempted to overcome the limitations of negatively charged collagen inspired peptide to self-assemble at physiological pH along with the decreased cellular viability owing to the surface charge of the peptide by introducing the metal ions in the ensemble state. In this direction, we have explored the cooperative effect of the divalent metal ions to promote hydrogelation in the short collagen inspired peptide for developing advanced biomaterials. The presence of metal ions showed a distinct shift in its equilibrium point of gelation and demonstrated the conversion from sol to gel at physiological pH and thus enabling the scope of fabricating an advanced biomaterial for controlling cellular behaviour. In similar direction, we have demonstrated the process of biomineralization in collagen inspired peptide and growthof Ca/P crystals on the peptide fiber. Furthermore, the peptide hydrogel scaffold exhibited good biocompatibility and supported adhesion of osteoblast cells. To this end, we have also quantified the biochemical marker (ALP) for determining the characteristic features of osteoblast cells. In this context, we have utilized the positively charged collagen inspired peptide to construct the spherical nanoparticles encapsulating an antimicrobial agent, ferulic acid. Interestingly, the nanoparticles demonstrated a dynamic shape transition into nanofibers when exposed to the basic environment of chronic wound, hence releasing the encapsulated ferulic acid. Furthermore, the collagen functionality induced biocompatibility and fast growth of the fibroblast cells on the surface. Thus, the bio-nano construct provided a dual functionality and environmental tunability, and offering advancement in the wound healing applications.
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