Amphiphilic and Acidic β-Sheet Peptide scaffolds; from Design to Bone-Tissue Engineering

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Introduction
Designed biomaterials that accelerate mineralization under physiological conditions may provide new multifunctional biomimetic scaffolds amenable for bone tissue regeneration. Extracellular proteins rich in acidic amino acids have been shown to affect nucleation, and growth of bone carbonated apatite. Various studies have linked biomineralization to acidic rich proteins in β-sheet conformation. Designed peptides that assume β-sheet structures have been shown to form assemblies with unique structural characteristics at the nanometer scale. Here we aimed at developing designed amphiphilic β-sheet peptides composed primarily of acidic amino acids to form multifunctional mineralized hydrogel scaffolds and to demonstrate their suitability to bone tissue regeneration.

Materials and Methods
Peptides were designed based on de-novo physicochemical principles. Self-supporting peptide-hydrogels were generated by dissolving the peptide in NaOH, or in sodium bicarbonate/DMEM solutions. Hydrogels formed in various procedures were characterized by electron microscopy, rheology and IR-spectroscopy. In-vitro cell culture studies were performed with SaOS2 on 2D and 3D hydrogels.

Results
A new family of self-assembled matrices composed of amphiphilic and acidic β-sheet forming peptides were shown to induce in-vitro hydroxyapatite formation. (1) These peptides may intrinsically assemble into hydrogel structures at physiological pHs, several units above the pKa values of their acidic amino acids. (2) Calcium ions were shown to induce hydrogel formation at lower peptide concentrations and to strongly affect the hydrogels rheological properties. Calcified hydrogels were shown to provide a favorable environment to bone forming cells. This new class of designed multifunctional peptide-hydrogels is currently being developed to provide versatile biomimetic scaffolds for engineering and regeneration of bone-tissue.

Discussion and Conclusions
This study demonstrates the bottom-to-top design and synthesis of new mineralized-peptide composite biomaterials. These multifunctional hydrogels are currently being developed to synergistically act with bone forming cells to induce the physicochemical mineralization of hydroxyapatite along with tissue regeneration by bone forming cells.

Fig. 1. Amphiphilic and acidic peptide hydrogels as multifunctional mineralized scaffolds. (a) TEM image of amorphous calcium phosphate particulates adhered to peptide hydrogel fibril. (b) Molecular model showing in details the regular arrangement of hydrogen bonded peptides decorated by calcium phosphate particulates.

References

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