

Enhanced angiogenic effects of RGD, GHK peptides and copper (II) compositions in synthetic cryogel ECM model

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Abstract

Synthetic oligopeptides are a promising alternative to natural full-length growth factors and extracellular matrix (ECM) proteins in tissue regeneration and therapeutic angiogenesis applications. In this work, angiogenic properties of dual and triple compositions containing RGD, GHK peptides and copper (II) ions (Cu^{2+}) were for the first time studied. To reveal specific in vitro effects of these compositions in three-dimensional scaffold, adamantyl group bearing peptides, namely Ada-Ahx-GGRGD (1) and Ada-Ahx-GGGHK (2), were effectively immobilized in bioinert PHEMA macroporous cryogel via host-guest β -cyclodextrin-adamantane interaction. The cryogels were additionally functionalized with Cu^{2+} via the formation of GHK-Cu complex. Angiogenic responses of HUVECs grown within the cryogel ECM model were analyzed. The results demonstrate that the combination of RGD with GHK and further with Cu^{2+} dramatically increases cell proliferation, differentiation, and production of a series of angiogenesis related cytokines and growth factors. Furthermore, the level of glutathione, a key cellular antioxidant and redox regulator, was altered in relation to the angiogenic effects. These results are of particular interest for establishing the role of multiple peptide signals on regeneration related processes and for developing improved tissue engineering materials.