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Activation of cellular behaviors and wound healing effects of an RGD-engineered extracellular matrix analogue

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Elastin-like proteins (ELPs) modeled after tropoelastin are favored in the development of biomimetic matrices due to their biocompatibility and the possibility to precisely control their environmental responsiveness, mechanical properties, and fate within the cells by recombinant DNA technology-mediated design at the gene level. To activate fibronectin-integrin signaling events from a cell-matrix interface and direct cell survival and proliferation, we biosynthesized a modular ELP, represented as TGPG[VGRGD(VGVPG)$_6$]$_{20}$WPC, consisting of alternating elastic (VGVPG)$_6$ structural domains and cell-binding VGRGD motifs that are intended to emulate various aspects of extracellular matrix proteins. The inverse transition curves of [VGRGD(VGVPG)$_6$]$_{20}$ and (VGVPG)$_{140}$ overlapped with each other, indicating that one VGRGD sequence fused with six elastic pentapeptides did not disturb the thermal sensitivity of [VGRGD(VGVPG)$_6$]$_{20}$. The cell adhesion activity of [VGRGD(VGVPG)$_6$]$_{20}$ toward HEK293 fibroblasts and N2a neuroblasts was similar to that of native fibronectin. Upon contact with [VGRGD(VGVPG)$_6$]$_{20}$, the fibroblasts exhibited a flattened polygonal morphology, and the neuroblasts synthesized new DNA and proliferated. To confirm if the in vitro effect of [VGRGD(VGVPG)$_6$]$_{20}$ is reproduced in vivo, we applied it to wound healing animal model using male C57BL/6 mice. Surprisingly, we observed the significantly accelerated wound closure in gross observation and promoted wound repair showing decreased formation of granulation tissue and increased collagen formation in histopathological observation by [VGRGD(VGVPG)$_6$]$_{20}$ treatment. Moreover, [VGRGD(VGVPG)$_6$]$_{20}$ increased the expression of α-smooth muscle actin (α-SMA) in granulation tissue of wounds, which suggests that [VGRGD(VGVPG)$_6$]$_{20}$ promotes wound healing by stimulating wound contraction via up-regulated α-SMA expression and enhancing matrix formation such as collagen. On the basis of these physiological and pathological changes, we concluded that RGD-functionalized ELP triggers the activation of signaling cascades within cells and can be used as an elastin-like matrix for mammalian cell culture and a therapeutic agent for wound healing.

Biography

Dr. Park has completed his Ph.D at the age of 29 years from Kyungpook National University, College of Veterinary Medicine in South Korea. He is also a veterinary pathologist and has a lot of experiences about regenerative medicine and cell therapy studies for chronic disease. He has published more than 32 papers including a paper published in high impact factor journal (more than 10 point). Now, he works at Daegu Gyeongbuk Institute of Science and Technology as a postdoctoral researcher.