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Inhibition of VEGF mediated corneal neovascularization by anti-angiogenic peptide nanofibers

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Abstract

Atypical angiogenesis is one of the major symptoms of severe eye diseases, including corneal neovascularization, and the complex nature of abnormal vascularization requires targeted methods with high biocompatibility. The targeting of VEGF is the most common approach for preventing angiogenesis, and the LPPR peptide sequence is known to strongly inhibit VEGF activity by binding to the VEGF receptor neuropilin-1. Here, the LPPR epitope is presented on a peptide amphiphile nanofiber system to benefit from multivalency and increase the anti-angiogenic function of the epitope. Peptide amphiphile nanofibers are especially useful for ocular delivery applications due to their ability to remain on the site of interest for extended periods of time, facilitating the long-term presentation of bioactive sequences. Consequently, the LPPR sequence was integrated into a self-assembled peptide amphiphile network to increase its efficiency in the prevention of neovascularization. Anti-angiogenic effects of the peptide nanofibers were investigated by using both *in vitro* and *in vivo* models. LPPR-PA nanofibers inhibited endothelial cell proliferation, tube formation, and migration to a greater extent than the soluble LPPR peptide *in vitro*. In addition, the LPPR-PA nanofiber system led to the prevention of vascular maturation and the regression of angiogenesis in a suture-induced corneal angiogenesis model. These results show that the anti-angiogenic activity exhibited by LPPR peptide nanofibers may be utilized as a promising approach for the treatment of corneal angiogenesis.