A MACROPHAGE-SPECIFIC SYNTHETIC PROMOTER FOR THERAPEUTIC APPLICATION OF ADIPONECTIN

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Background: Foam cell formation is a major cause of atherosclerosis. We aimed to develop a macrophage-specific synthetic promoter for the therapeutic application of adiponectin (APN).

Methods: Synthetic promoter-146 (SP146) was tested in two non-acrophage cell lines (293T and HeLa) and macrophage cell line (RAW264.7). To enforce macrophage specificity, partial elements of p47phox including the PU.1 site with various lengths (-C1, -C2, and -C3) were inserted. Therapeutic effect was confirmed by foam cell formation. We developed an atherosclerosis by sub-total occlusion of carotid artery in atherogenic diet-fed ApoE knockout mice for four weeks. Lenti-SP146-C1-APN was administered to atherogenic artery.

Results: SP146-C1 showed the highest specificity and efficacy in RAW264.7 cells and was selected. GFP- or APN-expressing lentivirus under SP146-C1 (Lenti-SP-GFP or Lenti-SP-APN, respectively) showed the highest expression efficacy in RAW264.7 cells, and SP146-C1-APN inhibited intracellular lipid accumulation. In atherosclerosis model, the administrations of Lenti-SP146-C1-APN reduced lipid deposition significantly.

Conclusions: The synthetic promoter SP146-C1 was successfully developed to target macrophages with high specificity, and the introduction of APN under SP146-C1 ameliorated the atherosclerotic pathology.