Nanoparticle-Mediated Gene Delivery via Balloon Angioplasty to Suppress Intimal Hyperplasia

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In the US alone, 200,000 surgical vascular procedures fail annually, primarily due to restenosis caused by a healing response known as intimal hyperplasia (IH). IH can be attributed to endothelial cell proliferation, narrowing vessel walls through VEGF-A, a gene allowing for the growth of the endothelial cell layer called the intima. Pdx1 is a homeobox whose promoter can induce overexpression of VEGF-A. We hypothesized that genes that interfere with IH, encapsulated in nanoparticles, and coated on a surgical balloon could specifically target the region of interest. shRNA-regulated knockdown of Pdx1 delivered to a rat carotid via PLGA nanoparticles, created via double emulsion method, lowers VEGF-A expression, preventing endothelial growth, neo-intima development and ultimately occlusion. We used TEM to analyze size and quality of the nanoparticles. Glycerol is used to suspend the nanoparticles, allowing adherence on a surgical balloon. The nanoparticle coated surgical construct employed was used to test its efficacy compared to an uncoated and glycerol only coated balloon catheter. Two weeks after we performed the left carotid injury model, we harvested the tissue for histological analysis. We used fluorescence microscopy to detect cells that took up the anti-Pdx1 plasmid, tagged with GFP, to confirm the successful delivery of the contents of the nanoparticles. We used rt-PCR to assess extent of IH and levels of VEGF-A. Significant results ($p < 0.05$) indicated that we have a new, effective treatment for inhibiting intimal hyperplasia, a site specific method of gene delivery, and a newly elucidated pathway between Pdx1 and VEGF-A. While intimal hyperplasia is the initial model, further research will apply the delivery method to various venous and arterial conditions.

Awards Won:

Second Award of $2,000