Application of a Cryogel-Coated Prosthetic Vascular Graft Material for Delivery of Targeted Gene Therapies in a Rabbit Model

Objectives: The long-term success of prosthetic vascular grafts for revascularization in peripheral arterial disease is limited by the development of anastomotic neointimal hyperplasia (ANIH). We have constructed a bioactive prosthetic graft material (BPGM) by coating polyethylene terephthalate with an antithrombogenic cryogel polymer layer capable of delivering biologic agents in vitro. Our goal is to evaluate our hybrid prosthetic graft material in vivo using a rabbit carotid interposition bypass model.

Methods: Our BPGM was synthesized by cryopolymerization of methacrylated alginate, methacrylated heparin, and ACR-PEG-RGD, circumferentially coating 1.5 cm length by 2 mm diameter electrospun polyethylene terephthalate (ePET) grafts, and dipcoating in fluorescent siRNA complexed with transfection reagent for three hours prior to implantation. A total of six rabbits were divided into two groups, with three rabbits receiving bare ePET dipcoated in fluorescent siRNA and three rabbits receiving cryogel-coated ePET graft material with fluorescent siRNA, for a carotid interposition bypass. After 24 hours, bypass patency was assessed, with samples taken at the proximal anastomosis, mid-graft, and distal anastomosis to examine cell toxicity with hematoxylin and eosin staining. Confocal microscopy was used to visualize fluorescence, correlating with ability to deliver siRNA and transfec in vivo.

Results: All rabbits underwent surgery without complications postoperatively. Graft patency was equal between groups, with no increased cell toxicity in rabbits receiving cryogel-coated ePET. Confocal microscopy demonstrated no difference in retained fluorescence between rabbits receiving cryogel-coated ePET compared to bare ePET graft, and no increased transfection of cells at 24 hours (Figure 1).

Conclusions: Creation of the optimal prosthetic vascular graft remains elusive and demands a material that is biocompatible, responsive, and nonthrombogenic. We have constructed a modified prosthetic graft material capable of in vitro delivery of targeted gene therapies to modulate the inflammatory response leading to the development of ANIH, with comparable patency and biocompatibility in our large animal model. Additional optimization to achieve predictable and sustained release is needed to validate this as an effective and practical method to deliver biologic agents in vivo from a prosthetic graft material.

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