See Article page 148.

Commentary: Still searching for the Holy Grail 70 years later: I can see some light

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CENTRAL MESSAGE

There is smooth muscle cell proliferation and rapid growth of extracellular matrix, in line with experiments showing the ability of silk-based small-caliber scaffolds to induce angiogenesis.

The search for the Holy Grail in vascular reconstructive surgery is epitomized by 70 years of efforts to find the ideal graft for small arteries, from the coronaries and intracranial to the below-the-knee or pedal. It is an old story and the subject of research by Sauvage 5 decades ago,[1] who implanted short (4 cm), small (3.5 inner diameter) Dacron vascular grafts between the ascending aorta and right coronary artery with a successful 15-month follow-up. He stated that success with small arterial grafting depends on low graft implant thrombogenicity and rapid, complete healing of implanted prostheses.[1] Materials and coatings, such as umbilical cord vessels,[2] polytetrafluoroethylene,[3,4] polyethylene,[5] tanned ovine grafts,[6] and others, have been tested in animal and humans, with frequently disappointing degrees of success. Small-caliber grafts are <6 mm; although we have grafts like the internal mammary artery for the myocardium,[7] we are still searching for the ideal substitute for distal arterial beds when autologous tissue is not available.

Vascular graft tissue engineering has defined and optimized tissue-engineered vascular graft alternatives to replicate native vessels. Tissue-engineered vascular graft focuses on materials, mechanical characteristics, and surface optimization concerning endothelialization and tissue retraction, a complex biological process; interplay between scaffolds and cellular engrafting should determine ideal graft behavior.[8] A thick, irregular, unattached neointima of low quality in terms of compliance and flexibility, as well as subintimal fibrosis, seem to be at the root of the problem.[9]

In this issue of the *Journal*, Tanaka and colleagues[10] present their experience with small-diameter silk fibroin vascular graft (3.5 mm) in a dog model. Graft patency in the femoral artery position was 80%, and the lumen was covered with vascular endothelial cells after 3 months. No aneurysms, calcification, granulomas, or infection was seen at 1 year. The authors stress the graft remodeling capability.

This small-diameter vascular graft in a large animal model brings good news. First is the high patency; second, the improved silk fibroin coating rapidly degrades after implantation. The authors describe smooth muscle cells and elastic fiber layers in the lumen and endothelial cells in the innermost surface of the graft after 3 months with no significant histologic narrowing at 1 year. Endothelial cells may prevent stenosis.

The model has some weaknesses, as the authors did not compare their grafts with other grafts and used pharmacologic support to counteract platelet–graft interaction. On the other hand, antiplatelets are widely used in real-world patients with vascular disease requiring open surgery with great saphenous vein or synthetic grafts.[11]

Silk-based small-caliber grafts have long been used in research using small animal models. Silk fibroin seems to enhance the adhesion and proliferation of vascular cells,[12] as the authors describe. Lack of endothelialization is a major cause of graft and stent failure. Despite some limitations, these experiments confirm smooth muscle cell proliferation

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and rapid growth of extracellular matrix, in line with experiments demonstrating the ability of silk-based small-caliber scaffolds to induce angiogenesis.[13]

Current research pursues the Holy Grail in vascular reconstruction. Experimental vascular grafts have been under investigation and optimization for decades.[14] Previous findings like those of Sauvage[1] remain current today. Let us see how silk and modern technology will help us.[10,13-15]

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