Cell-Seeded Synthetic Scaffold for Esophageal Regeneration

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Statement of Purpose. Esophageal diseases may require resection of the damaged portion. Current standard of care requires the replacement of the esophagus with stomach or the intestine. Such procedures have high rates of mortality and morbidity and highly affect the quality of life of patients. The use of alternative conduits is needed. A tissue engineering approach that allows for the regeneration of esophageal tissues would have significant clinical application. In this study, we describe a bioengineered construct that is comprised of a synthetic scaffold laden with autologous cells that can be surgically implanted to guide regeneration of the esophagus.

Methods. The tubular synthetic scaffold was created with electrospun polycarbonate based polyurethane. This was designed to provide a microenvironment conducive to cellular proliferation, with special attention given to the morphological properties, microstructure characteristics, and surface chemistry. In our preclinical model, autologous adipose-derived mesenchymal stem cells were isolated, expanded, and seeded on the scaffold. Scaffolds were then incubated in a disposable bioreactor for 7 days at 37 °C to obtain an autologous combination construct. The 6 cm scaffold was implanted in big animal models in place of a 5 cm circumferential resection of the esophagus. Functional, biochemical and histological techniques tracked host tissue growth and stability.

Results. In vitro, the construct dependably carried metabolically active cells that released bioactive molecules supportive of surgical repair and restoration of esophageal function. In vivo trials resulted in tissue growth that were observed to reconstitute the esophagus with a high degree of continuity and integrity after circumferential full thickness surgical resection. Full mucosal regeneration on the inner lumen was observed within a span of 2.5 months post-implantation.

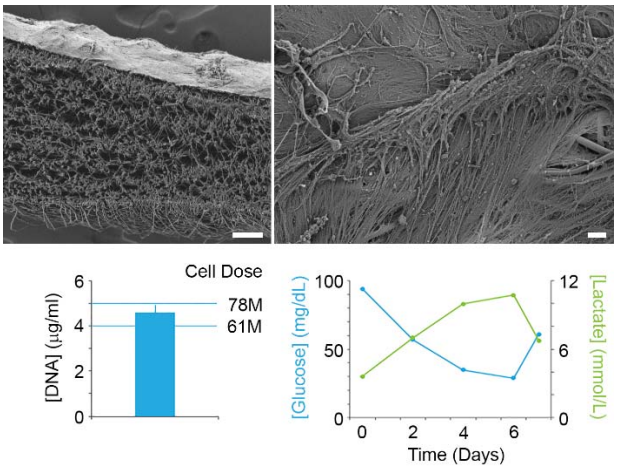

Figure 1. Ultrastructural and biochemical characterization of a combination device for restoring circumferential resections of the esophagus.

Conclusions. We describe an innovative bioengineeered construct that combines autologous cells with a synthetic scaffold for the treatment of patients with esophageal disease. The results demonstrate the feasibility of this approach to facilitate the regeneration of full thickness circumferential defects after esophageal resection as would be clinically required for esophageal malignancy. In addition to the esophagus, we expect the same approach to help patients with disorders of other hollow organs, such as the trachea and bronchus.

References.

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