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**Murine and human tissue-engineered esophagus form from sufficient stem/progenitor cells and do not require microdesigned biomaterials.**

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**Public Summary:**

Purpose: Tissue-engineered esophagus (TEE) may serve as a therapeutic replacement for absent foregut. Most prior esophagus studies have favored microdesigned biomaterials and yielded epithelial growth alone. None have generated human TEE with mesenchymal components. We hypothesized that sufficient progenitor cells might only require basic support for successful generation of murine and human TEE. Methods: Esophageal organoid units (EOU) were isolated from murine or human esophagi and implanted on a polyglycolic acid/poly-L-lactic acid collagen-coated scaffold in adult allogeneic or immune-deficient mice. Alternatively, EOU were cultured for 10 days in vitro prior to implantation. Results: TEE recapitulated all key components of native esophagus with an epithelium and subjacent muscularis. Differentiated suprabasal and proliferative basal layers of esophageal epithelium, muscle, and nerve were identified. Lineage tracing demonstrated that multiple EOU could contribute to the epithelium and mesenchyme of a single TEE. Cultured murine EOU grew as an expanding sphere of proliferative basal cells on a neuromuscular network that demonstrated spontaneous peristalsis in culture. Subsequently, cultured EOU generated TEE. Conclusions: Tissue-engineered esophagus forms after transplantation of mouse and human organ-specific stem/progenitor cells in vivo on a relatively simple biodegradable scaffold. This is a first step toward future human therapies.

**Scientific Abstract:**

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