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Bioengineering approach to artificial tracheas

A new paper reports an approach to growing tracheas by coaxing cells to form three distinct tissue types after assembling them into a tube structure.

The research, led by Eben Alsberg, professor in Biomedical Engineering and Orthopaedic Surgery and director of the Alsberg Stem Cell & Engineered Novel Therapeutics (ASCENT) Lab at Case Western Reserve University, is published in Advanced Science (Dikina et al. 2018).

Patients with damaged tracheas have limited options currently. Other techniques for artificial tracheas use a scaffolding approach, in which cells are seeded on the scaffolding. Difficulties have included uniformly seeding cells on the scaffolding, recreating the multiple different tissue types found in the native trachea, tailoring the scaffolding degradation rate to equal the rate of new tissue formation, and recreating important contacts between cells because of the intervening scaffold.

The research at Case Western University uses self-assembling rings that can fuse together to form tubes of cartilage and 'prevascular' tissue types (i.e., tissues potentially ready to participate in the formation of blood vessels). The cartilage rings are formed by aggregating marrow-derived stem cells in ring-shaped wells. Polymer microspheres are incorporated that contain a protein that induces the stem cells to become chondrocytes (i.e., cells that form cartilage). The prevascular rings include the stem cells and endothelial cells. The fusion of the different tissue ring modules, along coating the resulting tube lumen with epithelial cells, enables the creation of the complex multi-tissue structure of the trachea: cartilage with ridigity, epithelium for immunoprotection and prevascular tissue to ultimately allow blood flow into the new trachea tissue.

Prof. Alsberg told *ICU Management & Practice* in an email: "A scaffold-free approach has several potential advantages over a scaffold-based approach. The cellular condensations are more mimetic of natural development. A scaffold can interfere with vital cell-cell contact and communication, and it is also necessary to tune its degradation rate to match that of cell growth and tissue production, which can be challenging."

So far the team has engineered highly elastic 'neo-tracheas' of various sizes, including tissues similar to the human trachea. When these were implanted under the skin in mice, there was evidence the prevascular structures could join up with the host vascular supply.

Alsberg confirmed that the research is continuing: "We are working on enhancing vascularization and epithelialization of the constructs, and look forward to testing them in an in vivo model."

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