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OESOPHAGUS

Tissue-engineered oesophagus successfully transplanted in rats

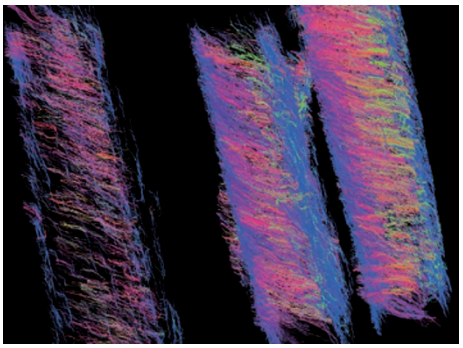
An international research team has developed a functional tissue-engineered oesophagus that can be transplanted into rats. In the future, this protocol could be used for reconstruction purposes in patients who undergo resection of the oesophagus.

Current practice is to use a patient's stomach or intestinal tissue to replace resected segments of the oesophagus. Oesophageal resection and reconstruction is complex surgery that often has poor outcomes. Following positive results with tissue-engineered trachea, Paolo Macchiarini and colleagues attempted to replicate the findings with the oesophagus. "Our tissue-engineered approach would eliminate the need to use the patient's own tissues and potentially could lead to better outcomes," explains Macchiarini.

The researchers decellularized oesophagi from adult Sprague–Dawley rats to create a biological scaffold, which bone marrow stem cells were then added to. These seeded stem cells differentiated into epithelial-like and muscle-like cells to populate the scaffold and create the functional tissue-engineered oesophagus. As the scaffold is not immunogenic, it can be transplanted into a donor without the need of immunosuppressant drugs.

Imaging techniques revealed that the decellularized organ generally retained the fibre structure of the native organ, although fewer tracts were present. Immunohistochemical analysis demonstrated that elastin, fibronectin, laminin and collagen were still present in the decellularized oesophagi. An intact vasculature was also identified in the scaffold, suggesting that it would have a functional blood supply if transplanted.

The seeded oesophagi sections were then transplanted into rats, which were followed up for 14 days. All the animals survived during the follow-up period and the transplanted oesophagi segments were functional. Interestingly, the rats that underwent transplantation gained more weight after surgery than sham-operated rats.



Using MRI and subsequent tractography, the decellularized organ (left) was shown to largely retain the general fibre orientations of the native organ (the two structures to the right). Image courtesy of P. Macchiarini.

All major cell and tissue components regenerated in the grafts, including nerves and vasculature. "We believe that our approach was successful due to large retention of bioactive proteins in the decellularized scaffold in combination with the known immunomodulatory effect of the stem cells that we seeded," says Macchiarini.

The team are now conducting several follow-up studies, including a study to determine the function of the bone marrow stem cells. "We will investigate the possibility of decellularizing oesophagi from larger animals and humans," concludes Macchiarini. "Furthermore, we will study how cells on the scaffolds are affected by a dynamic cell culture, which more closely mimics the *in vivo* environment."

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Original article Sjöqvist, S. *et al.* Experimental orthotopic transplantation of a tissue-engineered oesophagus in rats. *Nat. Commun.* doi:10.1038/ncomms4562