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Densified Collagen Tubes for Human Tissue Replacement

Customisable, mechanically robust collagen hydrogel-based grafting material.

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The problem – unsuitable materials

Synthetic material grafts do not imitate the extracellular niche, have limited or no bioactivity, limiting the physiological cell response, and have poor patency rates.

Grafts sourced from decellularised tissue are limited by donor availability, are not customisable, can have highly variable mechanical properties and cells can only be seeded from the surface.

Fibrous or freeze-dried bioengineered scaffolds are mechanically weak, porous, or made from weakly bioactive or non-degradable polymers.

The solution – Densified Collagen Tubes for Human Tissue Replacement and Disease Modelling

The inventors Dr Justin and Dr Markaki of the Department of Engineering at the University of Cambridge have developed a novel method for generating human-size tubular scaffolds made of densified collagen.

Application – Tissue Replacement

Cardiovascular: grafting material for replacement coronary and peripheral arteries.

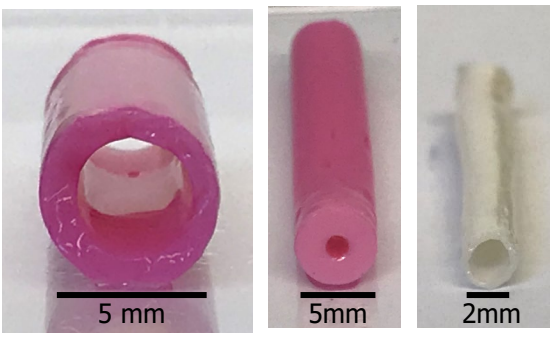
Gastrointestinal: replacement of bile duct, small and large intestine, oesophagus.

Genitourinary: replacement of ureter, urethra, fallopian tubes.

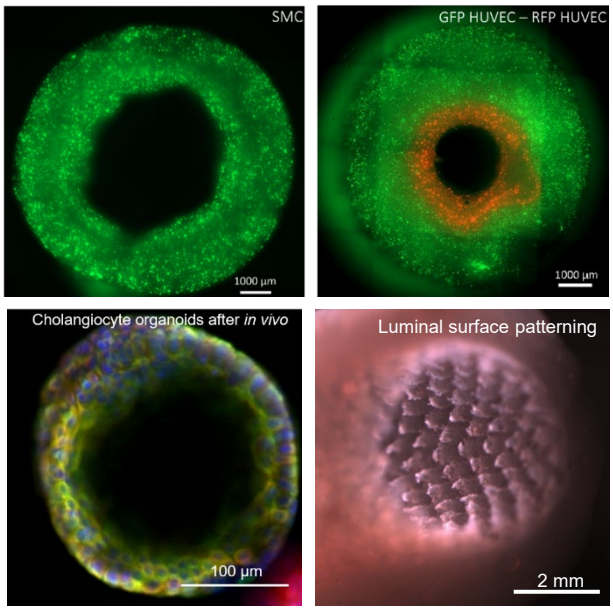
Neuroregeneration: Peripheral nerve repair.

Key Benefits

- Collagen hydrogel biomaterial – bioactive and biocompatible with high densities of functional cell populations and mature organoids. Fully replaceable by native tissue over time.
- Custom tubes fabricated de novo to a range of diameters and wall thicknesses. Tubes with uniform or gradient of collagen density.
- Uniform bulk and surface seeding of cells. Multiple cellular domains within same tube.
- Suitable for surgical implantation as an acellular or cellularised graft material.
- Seamless tube with comparable mechanical strength to native tissue when crosslinked with biocompatible genipin.
- Luminal surface patterning. Potential for patterned vasculature. Potential for drug elution from collagen tube in situ.



Custom tubes fabricated de novo.



Cells and organoids embedded in the walls of the tubes. Patterned luminal surface.

Commercialisation

We are looking to licence the collagen tube fabrication technology to meet the wide range of clinical applications. Currently seeking commercialisation partners to help undertake extensive in vivo studies.

Further information

Please view second page for further information including a materials comparison and mechanical testing graphs.

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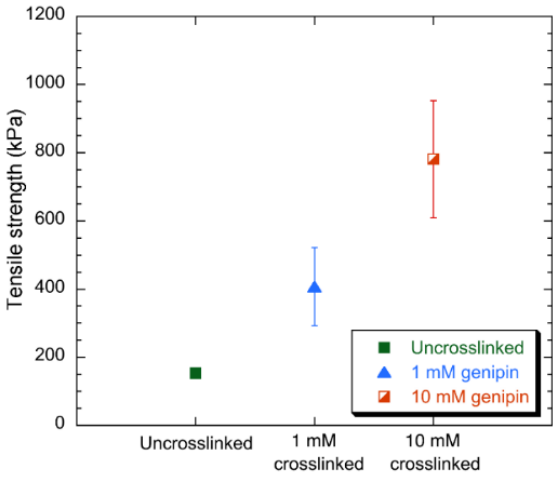
Product comparison:

Tubular grafts have been fabricated from a range of different materials, most notably synthetic material-based tubes (e.g. polyester, polyurethane), decellularised tissue-derived scaffolds (e.g. porcine, bovine), and other collagen-based grafts (e.g. macroporous freeze-dried, dense electrospun, membranes). Each have specific limitations within the required parameters for a clinically-viable graft.

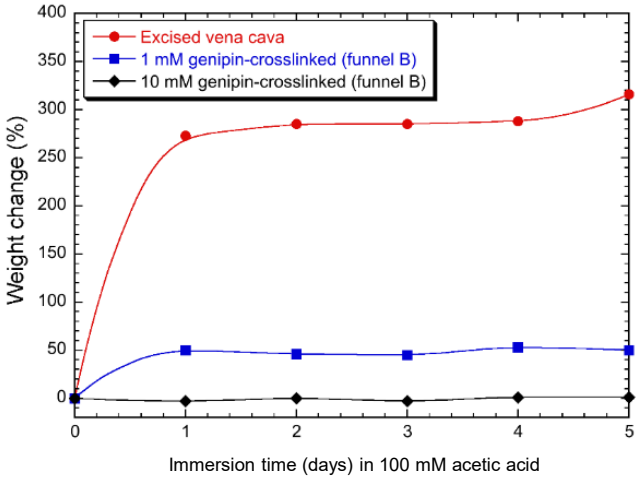
	Customisable	Availability	Mechanical Strength	Biocompatibility and Bioactivity	Cell Distribution
Densified Collagen Tubes	**yes**	**high**	**strong / tuneable**	**High**	**uniform, surface and bulk**
Synthetic Tubes	yes	high	strong (porosity dependent)	limited	surface only
Decellularised Scaffolds	no	limited (donor dependent)	highly variable	high (potential transmission of pathogens)	surface, non-uniform bulk (low cell survivability)
Other Bioengineered Scaffolds	yes	high	weak	high	surface only

Tensile testing:



Biocompatible genipin crosslinking results in increased tensile strength.

Acid solubility and swelling:



Biocompatible genipin crosslinking results in acid- and swell-resistant tubes.

Patent & Publications:

AW Justin & AE Markaki, “Tissue equivalent scaffold structure, and methods of production thereof”, PCT application number: PCT/EP2020/060068, filing date: 8th April 2020, priority date: 9th April 2019.

F Sampaziotis, AW Justin et al. "Reconstruction of the mouse extrahepatic biliary tree using primary human extrahepatic cholangiocyte organoids." Nature medicine 23.8 (2017): 954.

OC Tysoe, AW Justin et al. "Isolation and propagation of primary human cholangiocyte organoids for the generation of bioengineered biliary tissue." Nature protocols 14.6 (2019): 1884.

AW Justin et al., “Densified Collagen Tubes for Human Tissue Replacement and Disease Modelling Applications, in preparation.