Master Project

Bioengineering a vascularized nerve scaffold for nerve repair

Cardiovascular Research Group, Department for BioMedical Research

Introduction / Aims:

Peripheral nerve injuries are devastating, life-altering injuries. Autologous nerve grafts are the current elective therapy for the repairs of these injuries. However, clinical application of autologous grafts is restricted by limited tissue supply and significant donor site morbidity. Tissue engineering methods provide new techniques for the repair of peripheral nerve injuries and engineered nerve conduits have emerged as an alternative to autologous nerve grafting with different formulation used currently in the clinic (1). Among others, the use of decellularized nerve conduits that act as a guide for the regenerating nerves have been developed. Recently, in collaboration with the group of Prof. Lengelé in Brussels, we have investigated into the use of perfusion decellularization methods for the generation of scaffolds of vascularized allografts (2). We have demonstrated that perfusion decellularization may facilitate removal of cellular material, preserving the structure and regenerative potential of the extracellular matrix. The aim of the project is to use perfusion decellularization to obtain vascularized peripheral nerve scaffolds for the repair of nerve injuries. We hypothesize that the use of vascularized nerve scaffolds will lead to a faster regeneration process as well as to a long-term survival and function of the graft with better functional recovery as compared to not-vascularized conduits.

Research Work:

To test our hypothesis we will retrieve vascularized rabbit sciatic nerve grafts, which will be decellularized using perfusion decellularization. The rabbits will be animals which are used and euthanized for other, unrelated experiments. The structure and vascularization of these decellularized scaffolds will be thoroughly characterized using state-of-the-art tissue imaging techniques (i.e., immunofluorescence, confocal microscopy, electron microscopy), analysis of the vascular tree (fluoroscopy, micro-CT), and measurement of growth factor concentration by Luminex technology. Moreover, in vitro recellularization protocols will be developed using porcine and human endothelial cells seeded under physiological flow conditions. To obtain a recellularized allograft compatible with a potential recipient, also rabbit endothelial cells as well as rabbit endothelial progenitor cells from recipient's peripheral blood will be isolated, characterized and the recellularization process will be monitored in real-time using high-end imaging techniques and functional assessment.

Relevance:

Availability of an engineered biocompatible and functional 3D-scaffold of a vascularized nerve may represents an innovative concept and a feasible method for the repair of severe peripheral nerve injuries, helping to eliminate the current limitations associated with the autologous nerve grafting such as limited tissue availability and donor site morbidity.

Selected References:

(1) Pabari A, et al. Nerve Conduits for Peripheral Nerve Surgery. *Plast. Reconstr. Surg.*133: 1420, 2014

(2) Duisit J, et al. Bioengineering *a Human Face Graft: The Matrix of Identity. Ann Surg* 2017;266:754–764

Requirements:

Students selecting this module should be interested in tissue engineering and state-of-the-art methodologies for characterizing extracellular matrix components of decellularized scaffolds and development of recellularization. The topic does not involve animal experimentation but graft-procurement from animals.

Specials:

Based on mutual agreement, a dissertation can be started following the master thesis work.

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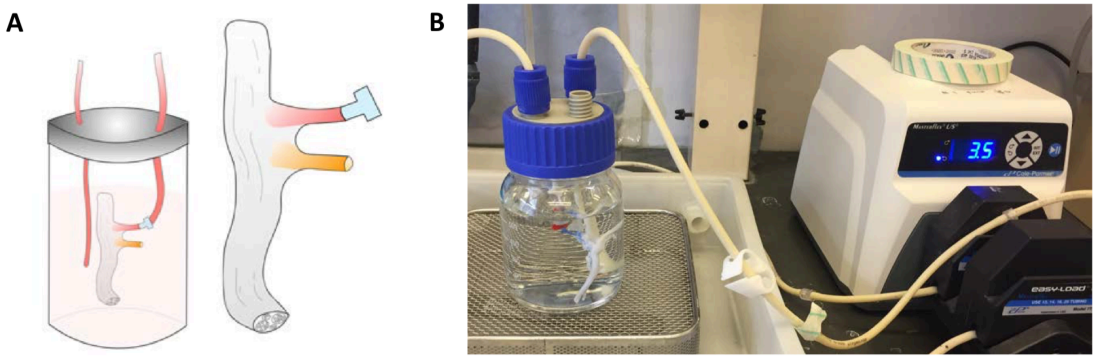

A) Depiction of vascularized nerve and bioreactor for perfusion decellularization. B) A peristaltic pump enables flow of decellularizing solutions through the vascular tree of the graft in a closed-circuit manner.