Title: **Investigating tissue engineering to create nerve allograft scaffolds for the repair of peripheral nerve injuries.**

Summary: Peripheral nerve injuries are devastating, life-altering injuries. Autologous nerve grafts are the current elective therapy for the repairs of nerve injuries. However, their clinical application is restricted by the limited tissue supply and their use is accompanied by 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 scaffolds that act as a guide for the regenerating nerves have been developed. In this approach, cadaveric allografts are decellularized to eliminate cells and maintain an extracellular matrix that provides a three-dimensional support the self-repair process and axonal growth without generating an immune response. Recently, in collaboration with the group of Prof. Lengelé, we have investigated the use of perfusion decellularization methods for the generation of scaffold of vascularized engineered allografts (2). We have demonstrated that perfusion decellularization may facilitate removal of cellular material preserving the structure and regenerative potential of the extracellular matrix. Now we will assess the possibility to use perfusion decellularization to create vascularized peripheral nerve scaffold for the repair of nerve injuries. We hypothesized that the use of vascularized nerve scaffolds will allow an effecting decellularization process and, on another hand, lead to a faster regeneration process with better functional recovery as compared to not-vascularized conduits. To test this hypothesis we retrieve vascularized porcine sciatic nerve grafts, which are decellularized using perfusion decellularization. The structure and vascularization of these decellularized scaffolds is thoroughly characterized using state of the art tissue-imaging techniques (i.e., immunofluorescence, confocal microscopy, electronic microscopy), analysis of the vascular tree (fluoroscopy, micro-CT), and measurement of growth factor concentration by Luminex technology. Moreover, *in vitro* recellularizion protocols are developed using porcine and human endothelial cells under physiological flow. To this aim, endothelial progenitor cells are isolated and characterized and the recellularization process is monitored and characterized *in vitro* using imaging techniques and functional assessment.

Requirements: Students selecting this module are interested in tissue engineering and state of the art methodologies for characterizing the extracellular matrix component of decellularized scaffold and develop and asses the recellularizeation process. The topic does not involve animal experimentation but graft-procurement from animal models.

Literature:
(1) Pabari A, et al. Nerve Conduits for Peripheral Nerve Surgery. *Plast. Reconstr. Surg.*133: 1420, 2014
(2) Duisit J, Maistriaux L, Taddeo A, et al. *Bioengineering a Human Face Graft: The Matrix of Identity. Ann Surg.* 2017 Jul 24.

Time-slots & # of students:
Elective module series I : 1 student
Elective module series II: 1 student

Location: Department for BioMedical Research, Murtenstrasse 50, CH-3008 Bern

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