Title:	Novel therapeutic approaches for immunomodulation in composite tissue allotransplantation
Introduction:	Composite tissue allotransplantation (CTA), including hand transplantation, has become a promising clinical treatment. Sixty-nine hand, forearm and arm transplantations have been performed over the past 12 years. The major hurdle of hand transplantation is health complications associated with immunosuppressive drugs. Thus, the future of CTA will depend on discovery of novel strategies, which can be used in the clinics as a replacement for current immunosuppressive protocols. A composite tissue allograft is readily accessible for local immunosuppression, which may reduce overall systemic immunosuppression. Therefore, one potential method is to develop an efficient local immunosuppressive drug delivery system. Such a system increases bioavailability of drugs locally over many weeks while minimizing systemic drug concentrations. This aids to avoid many drawbacks associated in current immunosuppressive drugs. Our current research aim is to investigate therapeutic potentials of an injectable self-assembling nanofibrous hydrogel system in which immunosuppressive agents are encapsulated. The hydrogel-laden drug delivery system is capable of releasing active immunosuppressives in response to enzymes that are significantly upregulated as a result of inflammation elicited by transplantation procedure and the immune responses from the recipient (on demand drug delivery).
Research work:	An MHC-mismatched orthotopic rat hind-limb transplantation model will be used in this study. Rats will be treated with different therapeutic substances and the graft survival will be routinely evaluated. The master students may be involved in treating and sampling the animals. Tissues will be analyzed by routine histological and immunofluorescence techniques. In addition, flow cytometer analysis of chimerism, mixed lymphocytes reaction assay, Bio-Plex analysis of serum cytokines, and ELISA will be performed. Setting up of qRT-PCR will also be an important part of the project. The student will be introduced to above techniques in the laboratory.
Relevance:	The finding of this study has a great potential in further development of an optimal local immunosuppression protocol in composite tissue allotransplantation.
References:	Gajanayake T. et.al. Am J Transplant. 2008 Jun;8(6):1151-62. Banz Y. et.al J Vasc Surg. 2009 Jul;50(1):161-70. Spirig, R. et al. J Immunol. 2008 Jul 15;181(2):878-90
Requirements:	Students selecting this project should be interested in research, which covers transplantation, immunology, pharmacology and vascular biology. Our research is performed in close collaboration with clinical partners and we use methods ranging from molecular analyses of inflammation markers to animal experiments.
Specials:	Based on mutual agreement and availability of funding, a dissertation can be started following the master thesis work.
Date of start:	The master thesis can be started upon mutual agreement.
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