

Title: Extremity preservation by cytoprotective drugs (C1-INH) in a porcine model

Introduction: Trauma is the main cause of lower limb amputation in the developing countries. Usually the traumatic amputees are young with long life expectancy. Revascularization of the amputated limb within 4-6 hours is essential to avoid extensive reperfusion injury due to vascular leakage, edema and tissue necrosis. Ischemia / reperfusion injury (IRI) is a pathological inflammatory condition that occurs during reperfusion of an organ after prolonged ischemia. Clinical and experimental studies showed that ischemia over 4-6 hours can adversely affect the success of revascularization surgery as well as lead to damage of distant organs like lungs and kidneys. However, it is not always possible to maintain that time period especially if the patient has to be treated first for a life threatening condition. Several strategies have therefore been tested to reduce IRI, including extracorporeal perfusion before replantation of the amputated extremities. Our lab has used extracorporeal perfusion of amputated porcine extremities using the heart lung machine as a potential limb preserving technique in addition to cytoprotective agents to prevent reperfusion injury.

Research work: Wild type porcine forelimbs will be amputated and exposed to prolonged cold ischemia. One forelimb will be treated with cytoprotective agent 2 hours after amputation and both limbs will be reperfused with autologous blood for 12 hours. Tissue samples will be collected at baseline and end of perfusion. Blood samples will be collected at baseline and different time points during perfusions. In this module the students will work hand-in-hand with a PhD student to perform immunofluorescence staining analyses of cryosections from pig forelimbs as well as performing ELISA on plasma samples from pig blood which were subjected to prolonged ischemia and perfusion on the heart lung machine.

Relevance: The above study is proposed to examine the protective effects of cytoprotective agents against complement- and coagulation-mediated humoral responses during reperfusion injury after replantation of amputated limb.

References: Müller S et al., Journal of Surgical Research 2013; 181: 170-182.
Perkins ZB et al., British Journal of Surgery 2012; 9(1): 75-86.

Requirements: Ideally, Students selecting this module should be interested in translational biomedical research. Some background knowledge on complement, coagulation and the endothelium are a plus. The students will get a thorough introduction into state-of-the-art immunofluorescence analysis as well as testing of activation markers of innate immunity in general. The topic involves no animal experimentation, but will be based on pig limb reperfusions.

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

Date of start: The master thesis can be started upon mutual agreement (June 2015). Perfusions will be performed in March and April and interested students are welcome to attend these experiments.

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