

2. Protocol Synopsis: 1 page maximum

Note: This synopsis fits best a prospective clinical trial. Adapt as needed for other type of studies.

PROJECT TITLE	Investigation of "Natural Killer" (NK) cells before and after liver transplantation
BACKGROUND	<p>Presently liver transplantation is the only available treatment for end-stage liver disease. As compared to other organs human liver allografts are less susceptible to rejection but still require long-term immunosuppression. It is well known that "Natural Killer" (NK) cells play an important role in host defense against infections and malignant diseases; however, their role in transplantation is only emerging. NK cells are a heterogenous subgroup of lymphocytes present in the blood and even more abundant in the liver contributing to innate immunity, particular by controlling viral infections, but also regulating adaptive immune responses. NK cells are important for the outcome of hematopoietic stem cell transplantation and for rejection mechanisms in xenotransplantation. In contrast, the role of NK cells in liver transplantation with respect to rejection and viral control is poorly understood and currently becoming increasingly a focus of research. In particular, the potential of NK cells to provide protection from recurrent hepatitis C is of interest. Therefore, the overall goal of this project is to study NK cells before and after human liver transplantation, in particular to address the question of whether NK cell distribution, phenotype and function correlate with the pathology and severity of liver injury leading to end-stage liver disease, graft rejection, immunosuppressive protocols and posttransplant infectious diseases such as recurrent hepatitis C, CMV reactivation and EBV associated lymphoproliferation.</p>
PRIMARY OBJECTIVE(S)	<p>The following specific aims will be addressed:</p> <p>Aim #1: To characterize the patients' peripheral blood and intra-hepatic NK cells before and after liver transplantation with regard to numbers, phenotype, cytotoxicity and cytokine production.</p> <p>Aim #2: To correlate the results of the NK cell analyses obtained under aim #1 with clinical parameters and outcome including immunosuppression, viral infections, graft function, rejection, and survival.</p> <p>The results of this research project will provide a better understanding of the function of NK cells during chronic liver disease and their evolution under immunosuppression after liver transplantation. This will allow us to develop better immunosuppressive and anti-viral strategies for liver transplantation, by modulating the activity of NK cells in order to reduce the impact of viral infections such as the recurrence of hepatitis C and CMV reactivation. Ultimately, together with the advent of novel anti-viral drugs and immunosuppressive protocols this research will contribute to improving the clinical outcome of liver transplant recipients.</p>
REQUESTED BUDGET	<p>CHF (total for three years) 200 000 CHF TOTAL YEAR 2011-12 43 000 CHF TOTAL YEAR 2012 -13 78 000 CHF TOTAL YEAR 2013-14 79 000 CHF</p>

3. Project Description (5 pages maximum with fond size 12, for parts a. to d (annexe))