Liver disease is responsible for considerable morbidity and mortality. There is a great need for treatment of both chronic and acute liver failure. Also, many congenital metabolic liver diseases are not treatable today. Orthotopic liver transplant (OLT) remains the only curative treatment for end-stage liver failure. Hepatocyte transplantation has been proposed as a complementary therapy in the treatment of a variety of liver diseases, predominantly metabolic liver diseases with enzymatic defect or deficiencies that are manageable with the replacement of only a small percentage of the parenchymal hepatocytes. The hepatocytes are transplanted through an infusion via the portal vein using invasive radiology approach. Hepatocyte transplantation is a much less invasive procedure with fewer risks compared to whole organ transplantation. The challenge and difficulty in hepatocyte transplantation is cell engraftment, proliferation and long-term maintenance and function. We will study the two contrasting strategies of injury affliction and protection approach to improve the outcome of hepatocyte transplantation.

Objectives
We recognize the potential gain in hepatocyte transplantation but also the hurdles and current limitations hampering progress and full potential of the method. Therefore, in this thesis we would like to address these issues and compile different strategies to overcome some of these obstacles, such as viability and engraftment. We intend to focus on preconditioning strategies in the pre- and peritransplant stages. These strategies will range from different compounds to be tested on primary human hepatocytes in vitro and subsequently in animal models where we intend to explore different technical and surgical preconditioning strategies. All these strategies could be applicable in the clinic. We also aim to evaluate the effect of hepatocyte transplantation and whole organ transplantation in alpha-1 antitrypsin deficiency (A1AT-d) patients. By translating in vitro studies to animal models and ultimately bringing new insights to the clinical setting, we aim to use different preconditioning strategies to improve hepatocyte transplantation to benefit patients with liver disease.