

Liver Immunology



Magdalena Filipowicz Sinnreich

SNSF Ambizione-SCORE
Department of Biomedicine
University Hospital Basel

Group Members

Martin Lett (PhD Student)

Characterization of mucosal-associated invariant T cells in liver diseases

Accumulating evidence suggests that the gut microbiome (i.e. gut resident bacteria) is involved in the pathogenesis of various liver diseases. Interestingly, a specialized T cell subset belonging to the family of innate-like lymphocytes is highly abundant both in the gut mucosa and the liver. These mucosal-associated invariant T (MAIT) cells respond to bacterial metabolites produced in the vitamin B2 (riboflavin) synthesis pathway, what places them at a central position in the immunological gut-liver axis. Antigen presentation to MAIT cells involves the highly conserved MHC-related protein MR1. Since these MR1-restricted T cells were identified in the liver only recently, little is known about their function in healthy and diseased liver.

Our aim is to elucidate the role of MAIT cells in selected liver diseases, including autoimmune liver diseases, steatohepatitis and viral hepatitis, and in the fibrogenic response in the liver. Our studies address a largely unexplored area of human liver physiology and pathology. Due to their location and high abundance in the liver, and their responsiveness to bacterial products and various cytokines, we hypothesize that liver-resident MAIT cells play a role in the pathogenesis of liver diseases and that changes in MAIT abundance, activation status, and cytokine expression profile influence disease development and outcome.

Our study has three main goals:

1. To characterize liver-resident MAIT cells using patient-derived liver biopsies and blood samples. Using both cellular and molecular approaches, we are determining MAIT cell location and abundance in the liver and blood in different pathological conditions, and analyzing their functional and transcriptional profiles.
2. To determine how the gut microbiome influences MAIT cells present in the liver, gut, and blood. By analyzing tissue and stool samples from patients with liver diseases, we aim at establishing whether changes in bacterial composition parallel changes in the functionality of MAIT cells.
3. To identify and characterize interactions of MAIT cells within the liver environment. In cell culture experiments, performed with distinct purified subpopulations of primary human liver cells, we are defining the cellular and cytokine milieu contributing to MAIT cell activation.

The anticipated outcome of our experiments is identification of disease-specific changes and patterns that will allow us to draw conclusions about how MAIT cells influence liver physiology and pathology.

Connection to Clinical Practice

Most liver diseases are characterized by an inflammatory response in the liver, driven by numerous triggering conditions, such as exposure to alcohol, excess fat, medication, infection or autoimmunity. A prolonged inflammatory state leads to progressive fibrosis that can result in liver cirrhosis associated with serious complications including loss of liver function or development of hepatocellular carcinoma. To date little is known about the function of MAIT cells in healthy and diseased liver and very few studies have addressed a role of these cells in human liver tissue and using primary human material. Our projects are being performed in close collaboration with the Laboratory of Experimental Immunology, headed by Prof. Gennaro De Libero, and the Department of Gastroenterology and Hepatology at the University Hospital in Basel, headed by Prof. Markus Heim.