Universität Basel

Research Project

Interferon Regulated Immune Responses in Viral Hepatitis

Third-party funded project

Project title Interferon Regulated Immune Responses in Viral Hepatitis
Principal Investigator(s) Heim, Markus H. ;
Organisation / Research unit
Departement Biomedizin / Hepatology Laboratory (Heim)
Bereich Medizinische Fächer (Klinik) / Hepatologie (Heim)
Department
Project start 01.04.2016
Probable end 31.03.2019
Status Completed

Interferons (IFNs) are central regulators of the host immune response to viral hepatitis. T-cell derived IFNγ is a major antiviral effector controlling both hepatitis C virus and hepatitis B virus infection. IFNα is being used since 30 years for treatment of chronic hepatitis B (CHB) and C (CHC). More recently, IFNλ4 has been identified as a key regulator of the immune response to HCV. The IFNλ4 gene exists in two major allelic variants. The ancestral allele encodes a fully functional IFNλ4. An insertion mutation (changing a G to a TT) disrupts the open reading frame of IFNλ4. Genome wide association studies discovered a highly significant association of the TT allele with spontaneous clearance of HCV. It is presently unclear why IFNλ4 is a liability in case of an HCV infection.

We hypothesize that IFNλ4 negatively regulates the cellular immune response to HCV.

In this application, we propose three subprojects that investigate different aspects of the IFNλ system in viral hepatitis, with a focus on the specific role of IFNλ4 in the host response to HCV.

In **subproject 1**we will study the biochemistry, physiology, tissue distribution and natural regulation of IFNλ4.

In **subproject 2**we will study the regulation of the IFNλ receptor. Contrary to the ubiquitous expression of the IFNα receptor in all cell types and organs, IFNλ receptor expression is restricted mainly to epithelial cells. However, its expression can be induced in other cell types such as hepatocytes or dendritic cells. A better understanding of the regulation of IFNλ receptor expression should provide important insights into the biological function of the IFNλ system.

In **subproject 3** we plan to identify the IFNλ responsive immune cells and to elucidate the cell-cell network and the cytokines involved that regulate the immune response to HCV.

Simultaneously with these subprojects focused on the IFNλ system, we plan to develop human biopsy derived liver organoids as an experimental model to study inter-individual differences in cellular responses to HCV and HBV in **subproject 4**. Current in vitro models for HCV and HBV are based on few hepatoma derived cell lines and primary human hepatocytes. Both systems have major limitations. Human liver biopsy derived organoids might overcome some of these limitations. Because they can be derived from individual patients they have a unique potential to enable the study of inter-individual differences in cellular responses to hepatitis viruses.

Financed by
Swiss National Science Foundation (SNSF)

Add publication

Add documents

Specify cooperation partners