Project 3: Interference of HCV with chemokine-mediated intercellular communication processes of the host (Projektleiter Johannes Bode)

Although there are now very potent treatment options, hepatitis C virus (HCV) infection remains one of the leading causes of chronic liver disease worldwide. In about 70% of cases, HCV infection leads to the development of a persistent infection which, despite continuous viral replication, lasts for decades without significantly affecting the host. This is mainly due to the fact that HCV has developed potent mechanisms during co-evolution that enable it to interfere with and modify the inter- and intracellular signal transduction of the host. This enables the virus to undermine processes such as the antiviral host response, to influence the inflammatory response of the host and to use the infrastructure of the host cell without significantly affecting the viability of the host cell.

Based on preliminary findings of the research group, which show that HCV influences () the basal as well as the inducible synthesis of chemokines of the host cell and thereby modifies the recruitment of immune cells, the continuation of the project aims to further investigate which communication signals are released by the host cell during infection with the hepatitis C virus and how this changes over time. Initially, the influence of a HCV infection on the gene expression of the host cell will be analyzed using NGS RNA sequencing. Further processing of the resulting data aims to identify chemokines, cytokines or other factors that have chemotactic activity and whose expression is influenced by HCV. The regulation of the expression of identified factors will then be further validated at transcript and protein level.

Since elevated serum levels of inflammatory cytokines such as IL-1b and TNFa are observed in patients infected with HCV, a comparable approach will also be used to investigate the influence of HCV infection on the expression of intercellular signals induced by inflammatory cytokines such as IL-1b and TNFa, which influence the migration behavior of cells.

In the continuation of the project it is planned to further elucidate the molecular mechanisms by which HCV influences the basal and/or inducible expression of identified signal molecules and to further investigate the influence of identified factors on viral replication, the production of infectious particles or the migration behavior of cells of innate or adaptive immunity.

The results of the work will contribute to a better understanding of the spectrum of mechanisms through which viruses that establish a persistent infection influence the intercellular and intracellular communication of their host.