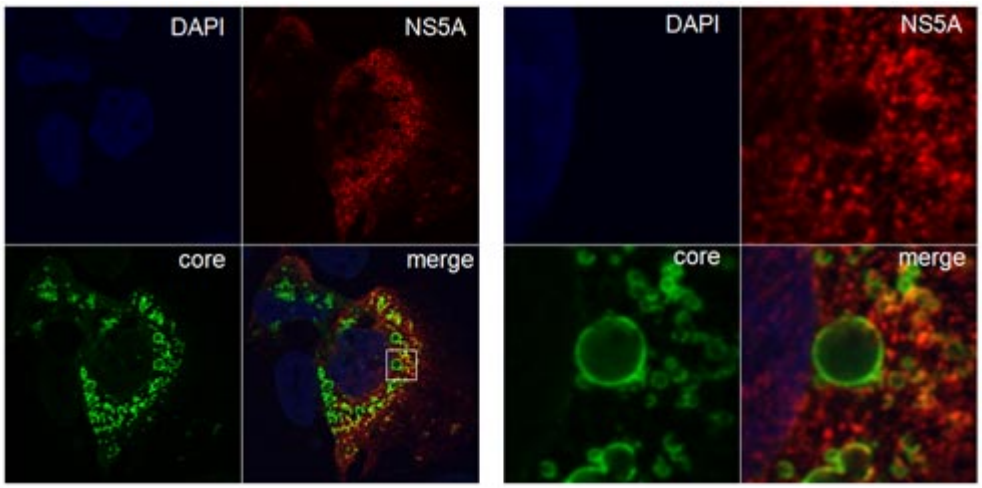
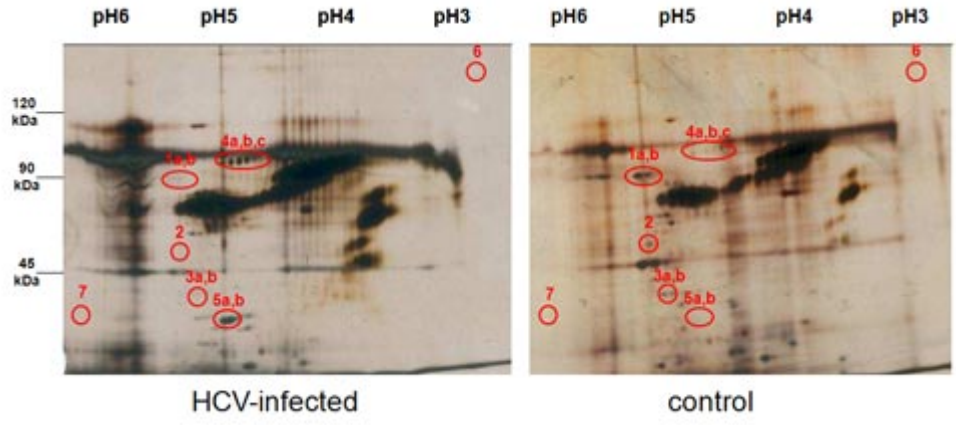
Virus replication and morphogenesis

The focus of this project is to analyze the relevance of intracellular signal transduction cascades for viral genome replication and viral morphogenesis. As mentioned above, both HBV and HCV are known to interfere with a variety of intracellular signal transduction cascades. With respect to HBV, the effect of the HBx and PreS2 regulatory proteins on viral gene expression and the signaling cascades mediating these effects are being characterized. Moreover, we are studying the signaling cascades which modulate the function of the HBV polymerase. Finally, we are investigating the effects of the HBx and PreS2 proteins on various apoptotic pathways.



Replication of hepatitis C virus in cell culture: Confocal laser scanning fluorescence microscopy of HCV producing Huh7.5 cells. The non-structural protein 5A (NS5A) (red fluorescence) was detected by a polyclonal rabbit-derived antiserum. The core protein was detected by a mouse-derived monoclonal (green fluorescence). Nuclei were stained by DAPI (blue fluorescence). Source: PEI

With respect to HCV, we recently identified c-Raf as a novel binding partner of NS5A. Consequently, c-Raf is an integral part of the replicon complex. Furthermore, we could demonstrate that inhibition of c-Raf blocks HCV replication. Currently, the underlying mechanism that eventually mediates the inhibition of HCV replication is being studied. Specifically, we are investigating the effects of c-Raf inhibition on the phosphorylation pattern of NS5A, on the composition of the replicon complex, the formation of lipid droplets and on viral morphogenesis. Regarding the morphogenesis, we could recently identify via proteome analyses two proteins that are associated with intracellular vesicle transport to be deregulated in HCV replicating cells. In this context we are aiming at characterizing the specific role of these proteins in HCV morphogenesis and secretion.



HCV replication affects the protein pattern of the host cell 2d separation of lysate of HCV-replicating Huh7.5 cells and Huh7.5 cells Source: PEI