Hepatitis C virus: How viral proteins interact in human cells

8 May 2014

Scientists at the Helmholtz Zentrum München have for the first time decrypted the interaction network of hepatitis C virus proteins in living human cells. Their findings will contribute to a better understanding of the mechanisms behind inflammatory liver disease caused by hepatitis C viruses and open up new avenues for therapy development. The results are published in the specialist journal *Molecular & Cellular Proteomics*.

Viruses use human cells in order to multiply and spread. This process involves interactions with cellular host factors as well as virus-virus interactions. For example interactions among viral proteins are essential for the assembly of newly produced infectious virions.

Interaction network explains viral mechanisms and opens up possibilities for new treatments

Hepatitis C virus (HCV) forms a precursor protein, which is processed into ten viral proteins. Scientists at the Institute of Virology at the Helmholtz Zentrum have now discovered how these proteins interact with one another and thus regulate important stages in the viral replication cycle. Shedding light on this interaction network creates a better understanding of the mechanisms underlying viral replication and pathogenesis and paves the way for new antiviral therapies.

As part of their investigations, the team led by Professor Michael Schindler, head of the working group at the Institute of Virology, applied the FACS-FRET* technique, which Schindler had developed at the Heinrich Pette Institute in Hamburg. With the aid of FACS-FRET, protein interactions in living cells can be characterized. Furthermore, it allows to unravel the relevance of certain protein interactions for replication. This method also enables screening for antiviral substances.

Finding new antiviral substances with few adverse effects

"Our results show how viral proteins interact within human cells. This provides a basis for identifying new antiviral substances. We propose by specifically targeting virus-virus interactions to find drugs with low cellular toxicity. This hypothesis was already confirmed in first screenings approaches," Schindler explains. "Since our method can be applied in an interdisciplinary manner, we are also aiming to elucidate the networks of other human pathogenic viruses. For instance hepatitis B virus (HBV) or the human immunodeficiency virus (HIV)."

Infections with HCV lead to inflammation of the liver, and in up to 80 percent of cases the inflammation becomes chronic. Hepatitis C is a risk factor for the development of liver cirrhosis and liver cancer.

More information: Hagen, N. et al. (2014), The intra viral protein interaction network of hepatitis C virus. *Molecular & Cellular Proteomics*, DOI: 10.1074/mcp.M113.036301

Provided by Helmholtz Association of German Research Centres