# Antiviral activity of interferon-induced transmembrane proteins (IFITM) in cells infected with tick-borne encephalitis virus and hepatitis C virus

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The first line of host defence against viral infection is the production of interferons type I. These cytokines trigger the expression of hundreds of IFN-stimulated genes (ISGs), which leads to the production of proteins directly limiting viral infections. IFITM proteins (Interferon Induced Transmembrane Proteins) belong to ISG proteins and inhibit replication of viruses belonging to the various families, e.g. *Ortomyxoviridae, Flaviviridae, Lentiviridae, Coronavidae, Reoviridae*. The mechanism of their actions is still not clear. It has been shown that these proteins block the virus entry into the cell at the initial stage of the infection cycle.

TBEV (*tick-borne encephalitis virus*) and HCV (*Hepatitis C virus*) belong to the *Flaviviridae* family. TBEV is a pathogen causing neuroinfection in humans. In recent years an increase in hospitalization due to TBE has been observed in both Europe and Asia. This situation is caused by spread of ticks - vectors for TBEV. There is no effective therapy available against tick-borne encephalitis and the treatment is symptomatic. The working vaccine against TBEV is available but the percentage of vaccinates population is low in most affected countries.

HCV is transmitted by blood and infection leads to acute or chronic liver inflammation. The effective therapy has been recently developed against hepatitis C, but because of the high cost, its availability is limited. Preventive vaccination against HCV is of high need and numerous attempts have been made to generate a vaccine capable to protect against all genotypes of this highly variable virus. Also, more knowledge about virus-host interactions is needed.

The main goal of my study is to investigate the role of IFITM proteins (IFITM1, IFITM2 and IFITM3) in TBEV and HCV infections. In the first part of the project, I obtained cell lines stably overexpressing IFITM proteins by lentivirus transduction and cell lines with IFITM-loss-of-function constructed by CRISPR/Cas9 method. Obtained cell lines are being validated by Western blot and sequencing. In the next part of the project, I will use constructed cell lines as targets of TBEV and HCV infection to analyse the impact of IFITM proteins on various steps of the virus infectious cycle.

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