

Currently, there are 170 million people infected with hepatitis C (HCV) worldwide. 80% of cases develop chronic infection, leading to liver fibrosis and ultimately to the of hepatocellular carcinoma. Extensive research performed in the last couple years allowed for a better understanding of virus biology, resulting in the discovery of the new, highly effective antivirals. Although, the high cost of both therapy and hospitalization and the low rate of infected people detection, confirm the need of an effective prophylactic vaccine.

The biggest obstacle in the vaccine against HCV design is the high variability of the virus. At present, we can distinguish 7 HCV genotypes and at least 67 subtypes. The HCV variability manifests primarily in the sequence of HCV envelope glycoproteins – E1E2, which because of their localization on the viral particle surface, are the primary target for the neutralizing antibodies.

Currently there are many identified highly conserved E2 epitopes capable of inducing broadly-neutralizing antibodies. The induction of immune response against not one but many highly conserved epitopes seems to be crucial in the development of the rationally designed vaccine against HCV.

One method to elicit immunogenic response against single epitope is exposing it on the surface of the virus-like particles (VLPs), which due to their highly organized structure are able to elicit potent immune response. One of the best known protein assembling into VLPs is hepatitis B virus small surface protein (sHBsAg), widely used as a commercial prophylactic vaccine against hepatitis B virus. sHBsAg tertiary structure forms a hydrophilic loop and because of its immunogenic potential and ability to tolerate insertions, sHBsAg was applied before as an antigen carrier to deliver foreign sequences.

In the course of this project the highly conserved sequences of the HCV E2 glycoprotein will be inserted into sHBsAg hydrophilic loop. After HCV_sHBsAg particles assembly confirmation and purification they will be used for mouse immunization. In the next step we will characterize mouse sera binding to the sHBsAg protein and HCV epitopes peptides. The final step will be to evaluate the mouse sera ability to neutralize cell-culture-derived HCV *in vitro*.

To summarize, the objective of this project is to examine the immunogenic properties of the panel of highly conserved HCV E2 glycoprotein epitopes exposed individually or/and in the combinations on the surface of the sHBsAg VLPs and evaluate their potential utility in the development of a rational prophylactic vaccine against hepatitis C.