# Chimeric HBV – HCV virus-like particles as a potential vaccine against Hepatitis C

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Hepatitis C virus (HCV) infection is a major health problem worldwide, affecting an estimated 2-3 % of human population. An HCV vaccine, however, remains unavailable. The major obstacle in the development of a protective immunity against HCV is the high genetic diversity of the virus, manifesting primarily in the sequence of HCV envelope glycoproteins – E1E2. E1E2 glycoproteins heterodimer plays an important role in the virus-host interaction and is the main target for the neutralizing antibodies. Because of that, the ideal prophylactic vaccine should induce strong humoral response from the neutralizing antibodies against the highly conserved epitopes accessible on the surface of the HCV E1E2 glycoproteins. One method to elicit immunogenic response against single epitope is to expose it on the surface of the virus-like particles (VLPs). The small surface antigen (sHBsAg) of hepatitis B virus (HBV) has the ability to form highly immunogenic subviral particles which are currently used as an efficient anti-HBV vaccine. sHBsAg tertiary structure forms a hydrophilic loop containing the major B-cell epitopes also known as the "a"- determinant. Because of its immunogenic potential and ability to tolerate insertions, sHBsAg represents an attractive antigen carrier for the delivery of foreign sequences.

In my PhD study, I designed a bivalent vaccine candidate based on novel chimeric particles in which highly conserved epitope of HCV E2 glycoprotein (residues 412-425) was inserted into the hydrophilic loop of sHBsAg. The expression of this chimeric protein was performed in an unconventional, *Leishmania tarentolae* expression system resulting in an assembly of particles which retained immunogenicity of both HCV epitope and sHBsAg protein. Furthermore, it was proved that 412-425_sHBsAg particles are highly immunogenic in mice and able to elicit cross-reactive and neutralizing antibody response against HCV.

However, because of the HCV ability to create escape mutants it is now generally recognized that the future anti-HCV vaccine must induce antibody response against not one, but multiple epitopes. Because of that, the aim of my PhD project is to design the panel of chimeric HCV_sHBsAg particles, in which multiple highly conserved epitopes of HCV E2 glycoprotein will be inserted into the hydrophilic loop of the sHBsAg protein individually or in multi-epitope combinations.

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 and in the combinations on the surface of the sHBsAg VLPs and to evaluate their potential utility in the development of a rational prophylactic vaccine against HCV.