

Hepatitis C virus (HCV) still poses a serious problem to medical systems around the world. The highest reported prevalence rates are observed mostly in the developing countries in Africa and Asia, where medical standards are relatively lower and blood sample testing is not a common practice. Egypt has the highest epidemiological prevalence rate of 22% of its population. Areas with a lower prevalence include the industrialized regions in North America, Northern and Western Europe and Australia. However, there is still a large pool of undiagnosed HCV-infected individuals even in the developed countries, mainly because the infection does not have any early symptoms. WHO estimates that around 3% of the world's population is infected with HCV. In around 80% of HCV-infected individuals the infection progresses from acute to chronic infection that in 20% cases leads to HCV-associated liver diseases such as liver cirrhosis and hepatocellular carcinoma. Patients infected with HCV require extensive medical care and the recently approved therapies are very expensive. Therefore, HCV remains a significant burden to both the patients and governments funding the medical systems. Despite discoveries of highly effective antiviral agents, development of an effective and low-cost prophylactic vaccine is necessary to control the global HCV infection. Unfortunately, such a vaccine is still not available.

Currently it is widely believed that a successful vaccine should trigger both cellular (involving activation of T-lymphocytes) and humoral (involving antibodies) immunological response. Especially the strong cellular response during the acute phase of HCV infection is believed to determine the infection outcome. However, development of the vaccine has proved to be challenging mainly because of the HCV's high genetic diversity. Therefore, the prophylactic vaccine should elicit antibodies against the highly conserved viral regions.

Virus-like particle (VLP) based vaccines are an interesting tool in current vaccinology. VLPs are non-replicating recombinant protein structures morphologically similar to native virions. Due to their structural similarity to the virions and lack of viral genetic material, VLPs are safe and have been already tested as potential vaccine candidates. Moreover, they are highly immunogenic. Hepatitis B virus small surface antigen (sHBsAg) has ability to self-assemble into non-infectious, highly immunogenic particles. Because of its immunogenic potential, sHBsAg was also applied as an antigen carrier to deliver foreign sequences and induce anti-foreign humoral and cellular responses. In our previous studies we proposed a bivalent vaccine candidate against HBV and HCV based on novel chimeric VLPs. In this vaccine, the highly conserved epitope of HCV E2 glycoprotein (residues 412-425) was inserted into the hydrophilic loop of HBV small surface antigen (sHBsAg). We showed that chimeric VLPs are highly immunogenic and able to elicit antibody response against both HCV and HBV. The vaccine candidate was also able to induce cellular response against HBV but we did not observe such a response against HCV. Therefore, the main objective of this project is to obtain a vaccine candidate that would be able to elicit humoral and cellular response against both HCV and HBV. We plan to achieve it by examining immunogenic properties of a panel of highly conserved HCV T-cell epitopes fused into the previously described sHBsAg₄₁₂₋₄₂₅ particles and evaluate the best epitope, or a combination of epitopes, with respect to strong cellular response against HCV. We believe that this approach may contribute to the development of a cost-effective bivalent prophylactic vaccine against the two main hepatotropic human pathogens.