Immunological evaluation of HCV core and its alternative reading frame protein vaccine prototypes

Irina Sominskaya, Juris Jansons, Anastasija Dovbenko, Ivars Petrovskis and **Dace Skrastina**
Latvian Biomedical Research and Study Center, Latvia

Hepatitis C remains a serious healthcare problem and there is no prophylactic or therapeutic vaccine currently available, although many candidates are in clinical trials. One of the attractive targets is the nucleocapsid protein (core). HCV core (aa 1-191) is highly conserved among HCV genotypes. It binds and packages viral genomic RNA and regulates its translation. The 5' terminus of HCV genome also encodes core+1/ARF protein. This protein possibly participates in HCV morphology or replication, it can be important in gene regulation and it can affect immune response mechanisms. A set of plasmids for eukaryotic and prokaryotic expression carrying different in length variants of the 5' terminus of HCV genome were constructed. Obtained DNA and proteins were purified and used in immunization of BALB/c mice in different schemes of immunization by protein and naked DNA (*in vivo* electroporation). Specific immune response was determined and immunization with HCV core aa 1-159 and full length ARFP proteins expressed in E. coli induced the specific immune response. The antibody titers against HCV core reached 104 and maximum antibody titers against ARFP reached 103. Immunization with HCV core and ARFP genes also induced the specific immune response. Both natural and mutated HCV core genes with prohibited frame-shift provide the same levels of specific cellular responses. Thus, a higher expression of HCV core from the mutated or optimized genes compared to the wild type sequence could not provide for its better immunogenicity. Efficacy of ARFP expression by the natural ribosome frameshift mechanism was low and obviously insufficient to induce a specific immune response. Thus, anti-ARFP immune response is not competing with that against HCV core, and cannot explain low immunogenicity of core in DNA-immunization performed with the virus-derived genes. The immunization by DNA-prime and protein-boost seems to combine the advantages of both approaches and improve the immune response.

Recent Publications

- Sominskaya I, Jansons J, Dovbenko A, et al (2015) Comparative immunogenicity in rabbits of the polypeptides encoded by the 5' terminus of hepatitis C virus RNA. J Immunol Res. http://dx.doi.org/10.1155/2015/762426.
- Dishlers A, Skrastina D, Renhofa R, et al (2015) The hepatitis B virus core variants that expose foreign C-terminal insertions on the outer surface of virus-like particles. Mol Biotechnol. 57(11-12):1038-49.
- Ivanov A V, Smirnova O A, Petrushanko I Y, et al (2015) HCV core protein uses multiple mechanisms to induce oxidative stress in human hepatoma Huh7 cells. Viruses 7(6):2745-70.
- Sominskaya I, Skrastina D, Petrovskis I, et al (2013) A VLP library of C-terminally truncated hepatitis B core proteins: correlation of RNA encapsidation with a Th1/Th2 switch in the immune responses of mice. PLoS One. 8(9):e75938.
- Skrastina D, Petrovskis I, Petraityte R, et al (2013) Chimeric derivatives of hepatitis B virus core particles carrying major epitopes of the rubella virus E1 glycoprotein. Clin Vaccine Immunol. 20(11):1719-28.

Biography

Irina Sominskaya has completed her Doctor of Biology Degree from Latvian University, Riga, Latvia in 1992. She is the Head of Viral hepatitis group of Latvian Biomedical Research and Study Center, Riga, Latvia. Using a multidisciplinary approach, including molecular biology, cell biology, and immunology technologies, the objective of group research is to gain a deeper understanding of virus-host interactions at a fundamental level. She has 25 publications and was a project Leader of several Latvian and international projects. She was supervisor of four doctoral degree students.

irina@biomed.lu.lv

Notes: