

## Neutralization of Hepatitis C Virus (HCV)

### Technology Summary

Most hepatitis C virus (HCV)-infected patients fail to clear the virus and despite the presence of neutralizing antibodies (nAbs), develop chronic infections. Although standard treatments cure approximately 50% of patients, those that do not clear the virus continue to suffer from chronic HCV infections, exposing them to higher risk of developing cirrhosis and liver cancer. Currently, no antibody-based prophylaxis nor an effective vaccine is available.

**This technology is a composition consisting of recombinant EI and EII envelope glycoproteins and a method to treat and/or prevent HCV infections.** To study the mechanism by which HCV persists in the presence of nAbs, FDA inventors sequenced the antigenic regions of the E2 envelope glycoprotein of HCV which contains two epitopes, epitope I (EI) and epitope II (EII). Epitope I (neutralizing epitope) is an important HCV neutralization site and epitope II (interfering epitope) was discovered to interfere with the binding of antibodies to EI, inhibiting the neutralization of HCV. The interfering effects of EII binding were demonstrated by removing the antibodies to EII in plasma from a chronically infected HCV patient. When EI was left unhindered, the HCV neutralizing activity was not only enhanced but also broadened to include additional genotypes of the virus. In another study, recombinant E1 and E2 peptides, that disrupt the binding of the inhibitory antibodies to EII, were used to vaccinate two chimpanzees, both of which displayed monotypic immune responses containing cross-neutralizing capabilities. These novel recombinant E1 and E2 glycoproteins could potentially be used to improve a patient's immune response during HCV infections and immunotherapeutic products by enhancing the neutralizing activity by preventing the binding of EII.

#### Potential Commercial Applications

- HCV Vaccines
- Preventing HCV infection

#### Competitive Advantages

- Generate post exposure prophylaxis
- Generate the first effective vaccine for HCV

#### Development Stage:

- *in vivo* chimpanzee vaccine studies demonstrate a monotypic immune response that contained cross-neutralizing capabilities to HCV

**Inventors:** Pei Zhang, Marian Major, Stephen Feinstone

#### Publications:

- Zhang, P., et. al. Depletion of interfering antibodies in chronic hepatitis C patients and vaccinated chimpanzees reveals broad cross-genotype neutralizing activity. Proc Natl Acad Sci U S A. 2009 May 5;106(18):7537-41. PMID: [19380744](#)
- Zhang, P. et. al. Hepatitis C virus epitope-specific neutralizing antibodies in Igs prepared from human plasma. Proc Natl Acad Sci U S A. 2007 May 15;104(20):8449-54. PMID: [17494735](#)

#### Intellectual Property:

United States Patent No. US [8,603,468](#) issued 12.10.2013

**Product Area:** Hepatitis, HCV, virus, antibodies

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#### Licensing Contact:

Ken Millburne, J.D.  
FDA Technology Transfer Program  
Email: [FDAInventionlicensing@fda.hhs.gov](mailto:FDAInventionlicensing@fda.hhs.gov)  
Phone: 301-346-3964