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HCV therapeutic vaccines: Generation of infectious HCV-3a pseudo-particles containing functional E1-E2 envelope protein complexes

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Hepatitis C virus (HCV) causes the most important *Flaviviridae* infections in humans and is the second most common cause of viral hepatitis. Presently, nearly 14% of Pakistani population, 2% of the United States of American (USA) population, and an estimated 250 million people worldwide are HCV carriers. No vaccine is currently available to prevent new infections and the only treatment for chronic hepatitis C is based on interferon alpha (IFN-α) that leads to sustained virological response in 20 to 56% of patients. Obviously, novel therapeutic strategies are required on urgent basis as the health costs for HCV-infected people are predicted to spiral dramatically in the next few decades. Here, we report on the successful generation of infectious pseudo-particles that were assembled by displaying unmodified and functional HCV glycoproteins onto retroviral and lentiviral core particles. The presence of a green fluorescent protein marker gene packaged within these HCV pseudo-particles allowed reliable and fast determination of infectivity mediated by the HCV glycoproteins. Primary hepatocytes as well as hepato-carcinoma cells were found to be the major targets of infection in vitro. High infectivity of the pseudo-particles required both E1 and E2 HCV glycoproteins, and was neutralized by sera from HCV-infected patients and by some anti-E2 monoclonal antibodies. It is anticipated that these pseudo-particles may play a role in investigation the role of putative HCV receptors. Further, pseudo-particles may have the potential to mimic the early infection steps of parental HCV and will be suitable for the development of much needed new antiviral therapies.

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