

4th International Conference on

Vaccines & Vaccination

September 24-26, 2014 Valencia Convention Centre, Spain

In vivo electroporation for improvement of therapeutic DNA vaccine against chronic hepatitis B infection

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Despite the existence of an effective prophylactic vaccine, chronic hepatitis B virus (HBV) infection remains a major public health problem. DNA-based vaccination has emerged as promising immunotherapeutic approach against chronic hepatitis B, although its efficacy needs to be increased as indicated by the results of first clinical trials. In this regard *in vivo* electroporation (EP)-mediated delivery appears of particular interest to improve therapeutic potency of DNA vaccines against chronic viral diseases. However, little was known of the ability of EP to improve DNA vaccine for therapy of chronic hepatitis B infection. We explored EP-mediated DNA vaccine delivery for hepatitis B immunotherapy using the duck HBV (DHBV) infection model, which is a reference for novel anti-HBV approaches evaluation. We first demonstrated in naïve animals that EP was able to dramatically enhance neutralizing potency of DNA vaccine leading to highly neutralizing, multi-specific B-cell response at clinically feasible DNA dose. Next, the therapeutic benefit of EP-mediated DNA vaccine delivery was investigated. The therapy of chronic DHBV-carrier ducks with EP-delivered DNA vaccine encoding viral proteins (envelope, core) and IFN- γ resulted in a marked and sustained decrease in viremia titers as compared with standard needle DNA injection. Importantly, a significant decrease in intrahepatic covalently closed circular viral DNA (cccDNA) form, responsible for chronicity of infection, was observed following EP of DNA vaccine. In addition a break of immune-tolerance was observed after DNA vaccine administration by EP. Collectively, our data indicate that electroporation is able to dramatically enhance therapeutic potency of DNA vaccine targeting hepadnaviral proteins supporting clinical application of this approach against chronic hepatitis B.

Biography

Lucyna Cova obtained her PhD in Biochemistry at the University Claude Bernard in Lyon, France. She held a Post-doctorate position at the Wistar Institute in Philadelphia. Thereafter she joined Institut National de la Sante et Recherche Medicale (INSERM), which is a French medical research institute (equivalent of NIH). Currently she is a research Director at INSERM and a co-leader of a team working on Novel approaches against Hepatitis B and C infections at Cancer Research Center of Lyon. She has expertise in viral hepatitis. Over the past decade her research focused on the development of therapeutic DNA vaccines against chronic hepatitis B.

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