Final Report

Project title: Influenza vaccine candidate with codon-optimized hemagglutinin

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Summary

Codon usage pattern of influenza virus as well as many other viruses has been shown to be different from that of efficiently expressed human genes. This codon bias can limit translation efficiency of viral genes. Changing codon usage to match that of efficiently expressed human genes can dramatically increase gene expression in human cells. This approach of humanized codon or humanized gene has been widely used for new vaccine design especially for DNA vaccines. Theoretically, the approach can be combined with live-attenuated influenza vaccine (LAIV) in order to increase expression of this gene in nasal epithelium. We have generated reverse genetic influenza virus carrying codon-optimized hemagglutinin (HA) from the 2009 pandemic H1N1 virus and the highly pathogenic H5N1 virus in the genetic background of A/Puerto Rico/8/34 (PR8). The viruses have been sent to the Institute of Experimental Medicine (IEM) for reassorment with the cold-adapted A/Leningrad/134/57. Although the PR8-based viruses could be successfully generated, they did not grow well in eggs and cell culture. Excessive cytopathic effect in cell culture despite low viral titers suggested that there was a viral release defect, which might be due to an imbalance between the viral HA and neuraminidase (NA).