

CPB 69700 RESEARCH SEMINAR

DEPARTMENT OF COMPARATIVE PATHOBIOLOGY

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3:30 pm

“Development Of Adenovirus Vector Based H5N1 Influenza Vaccine”

Abstract:

The emergence of a highly pathogenic influenza A strain H5N1 in the past several years, beginning in Southeast Asia and then spreading into Africa, the Middle East, and Europe has evoked the fear of a global influenza pandemic. Outbreaks have been reported in humans, domestic and migratory birds in several Asian, European and African countries. One of the most important ways to combat the threat of influenza pandemic is to develop an effective vaccine. Adenoviral vectors have been shown to have some of the important properties of a vaccine delivery system in terms of efficacy, safety and stability. Earlier we have demonstrated the potential of an adenoviral vector-based delivery system, where we generated a replication-incompetent, human adenoviral vector (HAd-H5HA) expressing subtype 5 hemagglutinin. Immunization of mice with HAd-H5HA induced both humoral and cell-mediated immune responses and effectively protected the mice from H5N1 disease, death, and primary viral replication upon lethal challenge with H5N1 influenza virus. In order to broaden the protection coverage of human adenoviral vector- based H5N1 vaccine against antigenically divergent H5N1 viruses, we developed human adenoviral vector-based vaccine candidates expressing hemagglutinin protein from clade 1 and clade 2 viruses, as well as conserved nucleoprotein and evaluated the protective efficacy of these vaccine candidates in mouse model. Due to high prevalence of adenovirus infections in humans, it is believed that the preexisting adenoviral neutralizing antibodies (popularly known as ‘vector immunity’) may reduce the antigen expression by human adenoviral vectors and thereby negatively impact the resultant immune response. To address the issue of preexisting vector immunity we developed a bovine adenoviral vector based H5N1 vaccine, BAd-H5HA [BAd3 vector expressing the hemagglutinin (HA) gene from H5N1 influenza virus] and evaluated its immunogenicity and protective efficacy in absence and presence of high levels of pre-existing vector immunity in a mouse model.