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Clinical Studies of Vaccines for Pandemic Influenza

Project Number
1ZIAAI000997-13

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Awardee Organization
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Description

Abstract Text

Seasonal epidemics and sporadic pandemics of influenza A viruses (IAV) pose a global public health burden. Influenza A viruses are divided into subtypes on the basis of the antigenicity and nucleotide sequence relatedness of their surface glycoproteins, hemagglutinin (HA) and neuraminidase (NA). Hemagglutinin-specific antibodies directly bind the virus and prevent its entry into host cells, providing narrow immunity from reinfection by closely related strains. CD8 T cell responses to IAV generated against highly conserved viral proteins/epitopes contribute to clearance of virus during primary IAV infection and also confer broad heterosubtypic protection in animal models. Recent evidence links the cross-reactive CD8 T cell response in man to reduced viral replication and protection from severe illness in **pandemic** H1N1 infections in European populations, and H7N9 infections in China. Because pre-existing T-cell immunity, independent of baseline antibodies, protects against symptoms and viral shedding associated with influenza, influenza vaccines that stimulate broadly reactive CD8 T cell responses may have the capacity to protect against any **pandemic** influenza A virus. Human infections with H5N1 and H7N9 avian IAV and the 2009 H1N1 **pandemic** have spurred an interest in the development of vaccines against IAV with **pandemic** potential. Major challenges to this effort include our inability to predict which virus will emerge and rapid production and deployment of vaccine if the virus spreads rapidly and vaccine yield is not optimal. In addition, the number of doses of vaccine required depends on whether the population is immunologically naive. Outbreaks of severe respiratory disease in humans in Eastern China due to H7N9 influenza viruses began to occur in 2013. Therefore, development of safe and effective vaccines for H7N9 and other H7 viruses is a critical component of **pandemic** preparedness. High levels of immune memory are achieved by vaccination with repeated doses of a live attenuated influenza virus vaccine followed by vaccination with antigenically matched inactivated influenza virus vaccine. However, the potential effects of vaccinating with live attenuated influenza virus vaccine followed by vaccination with antigenically mismatched inactivated influenza virus vaccine are unknown. This is an important question because it is possible that priming the immune response with a live attenuated vaccine followed by boosting with mismatched inactivated virus vaccine might result in a broader immune response than priming and boosting with the same virus. Therefore, this year we completed a trial entitled A Phase I Study In Healthy Adults To Assess Priming With Antigenically Mismatched Live Attenuated A/H7N3 Influenza Virus Vaccine Followed By Inactivated A/H7N9 Influenza Virus Vaccine. In this study we vaccinated volunteers with two doses of live attenuated H7N3 influenza virus and then boosted them with a mismatched virus (inactivated H7N3). The study has been completed and results are currently being analyzed. This year we also initiated a new clinical protocol "Immunogenicity and Safety Study of Inactivated Subunit H5N1 Influenza Vaccine in Prior Recipients of Live Attenuated H2N2, H6N1 and H9N2 Influenza Vaccines and in H5N1 and Live Attenuated Vaccine Nave Individuals." This study will examine the effect of administering a group 1 **pandemic** inactivated subvirion vaccine (H5N1) vaccine to previous recipients of a different group 1 **pandemic** live attenuated influenza vaccine recipients (H2N2, H6N1 or H9N2 live influenza vaccines). The objective is to determine whether boosting with an inactivated vaccine with shared hemagglutinin (HA) stem region, but a mismatched HA head region will boost the HA stem antibody response more than the HA head antibody response.

Thank you for your feedback!

Public Health Relevance Statement

Data not available.

NIH Spending Category

Biodefense Biotechnology Clinical Research Clinical Trials and Supportive Activities Emerging Infectious Diseases Immunization Infectious Diseases Influenza Pneumonia & Influenza Prevention Vaccine Related

Project Terms

Adult Animal Model Animals Antibodies Antibody Response Attenuated Attenuated Live Virus Vaccine Avian Influenza A Virus Base Sequence Binding CD8-Positive T-Lymphocytes Cells China Clinical Protocols Clinical Research Clinical Trials Development Disease Disease Outbreaks Dose Epidemic Epitopes Equilibrium European Genes Goals Head Hemagglutinin Human Immune response Immunity Immunologic Memory Immunologics Inactivated Vaccines Individual Infection Influenza Influenza A Virus, H1N1 Subtype Influenza A Virus, H5N1 Subtype Influenza A Virus, H7N9 Subtype Influenza A virus

Details

No information available for 1ZIAAI000997-13

Sub Projects

No Sub Projects information available for 1ZIAAI000997-13

Publications

No Publications available for 1ZIAAI000997-13

Patents

No Patents information available for 1ZIAAI000997-13

Outcomes

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