POLSKY Center for Entrepreneurship and Innovation
THE UNIVERSITY OF CHICAGO

Cross-Reactive Antibodies Neutralize H1N1 Influenza Virus

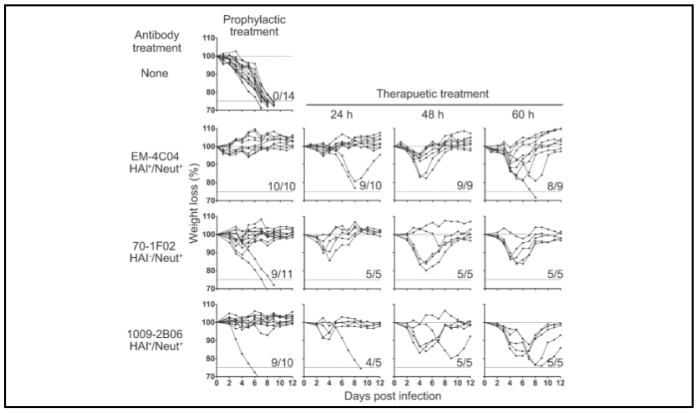
SUMMARY
Monoclonal antibodies recognize the most recent H1N1 strain of influenza as well as highly pathogenic 1918 and avian H1N1. These antibodies target the conserved HA epitopes to provide protection against H1N1 infection.

KEY RESULTS
These antibodies displayed hemagglutination inhibition and neutralization activity against pandemic H1N1 influenza and several other annual H1N1 strains. The antibodies demonstrated efficacy in a lethal mouse model of influenza when administered prior to infection or 3 days post infection. Researchers are seeking development and efficacy of antibodies in clinical trials.

ADVANTAGES
- Targets the head and stalk-region of hemagglutinin for a pan-influenza therapeutic.
- Broad-neutralizing capacity against antigenically distinct H1N1.
- Humanized monoclonal antibodies for safe administration in humans.

APPLICATIONS
- Prophylactic and therapeutic efficacy against pandemic H1N1 influenza.

Monoclonal Antibodies Are Protective Against Pandemic H1N1 Influenza Virus



Mice were infected with 3xLD50 dose of H1N1 influenza. Mice treated with monoclonal antibodies (EM-4C04, 70-1F02, or 1009-2806) prior to infection (prophylactic) or treated with antibodies 24, 48, or 60 hours post- infection (therapeutic) maintained weight and survived infection compared to mice treated with a placebo.

TECHNICAL DESCRIPTION
Hemagglutinin (HA) is a trimeric glycoprotein, composed of a globular head domain and a stalk domain, on the surface of influenza viruses that enables the virus to bind to host cells. Unlike the variable HA head domain, the stalk domain retains conserved antigenic sequences across multiple influenza strains, making it an attractive therapeutic target. Drs. Wilson and Ahmed examined a panel of monoclonal antibodies induced by an H1N1 infection of human plasmablasts to identify effective neutralizing antibodies. Select antibodies demonstrated superior hemagglutination inhibition and neutralization. High avidity and specificity to the stalk region was demonstrated and characterized to the precise amino acid residues. In a lethal mouse model of influenza infection, prior and post administration of the H1N1 monoclonal antibodies provided protection against antigenically distinct H1N1 influenza strains (A/CA/04/09, A/NewCal/20/99, A/Solls/3/06, A/Brisb/59/07), providing both a prophylaxis and therapeutic treatment. These antibodies are thus promising therapeutics against pandemic H1N1 as well as most other H1N1 and H5N1 strains, especially in high-risk populations such as immunosuppressed patients and the elderly.

REFERENCE
UCHI 1835, 1842

DEVELOPMENT STAGE
Pre-clinical trial

THERAPEUTIC AREAS
Influenza

PUBLICATIONS
Wrammert J, et al. Broadly cross-reactive antibodies dominate the human B cell response against 2009 pandemic H1N1 influenza virus infection. Journal of Experimental Medicine. 2011 208(1); 181-193.

INTELLECTUAL PROPERTY
US 9,458,226
US 9,469,685

INVENTOR(S)
Patrick C. Wilson, PhD

Dr. Wilson is an associate professor of medicine and innovator in the field of immunology for translational medicine. He heads a research group focusing on antibody specificity and differentiation of B cells, developing powerful approaches to generate antibodies for various diseases such as autoimmune and infectious diseases.

Rafi Ahmed, PhD

Dr. Rafi Ahmed, a member of the National Academy of Science, is a world-renowned immunologist whose work during the past decade has been highly influential in shaping our current understanding of memory T cell differentiation and anti-viral T and B cell immunity.

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