



Theraclone Sciences Technology Uncovers Rare Anti-Influenza Antibodies

Discovery Could Lead to Development of Novel Products to Prevent or Treat Seasonal and Pandemic Disease

SEATTLE, WA —June 28, 2010— Scientists have identified a new, highly conserved molecular target on the influenza A virus and demonstrated that human antibodies against this target are protective in animal models of seasonal and highly-pathogenic avian influenza. The work was conducted by researchers at Theraclone Sciences, with collaborators at University of Wisconsin-Madison, University of Tokyo and Johns Hopkins University; and is reported this week in the online Early Edition of the *Proceedings of the National Academy of Sciences*.

Each year in the United States, 5% to 20% of the population is infected with influenza virus, and over 200,000 people are hospitalized as a result of influenza-related complications. Of the different types of influenza virus, influenza A viruses typically cause more serious infections and also pandemics, with potentially severe impacts on global health. Current preventative and therapeutic approaches are only partially effective due to the ability of influenza viruses to multiply and mutate rapidly, making it difficult to identify a universal target for an anti-viral agent.

The newly identified influenza target is on the outer tip of the external portion, or “ectodomain,” of the influenza matrix 2 protein (M2e). Using Theraclone’s I-STAR™ technology, the researchers found rare, naturally occurring, human antibodies in healthy volunteers that targeted this highly conserved part of the influenza virus. When they mass produced the human anti-M2e antibodies and administered them to infected mice, they showed 60-80% recovery in the treated animals, compared with 10% or less survival of the untreated animals. Notably, the antibodies protected against two structurally distinct influenza strains - a highly pathogenic avian (H5N1) strain and a seasonal human (H1N1) strain.

“The ability of these antibodies to protect mice from highly lethal strains of influenza is encouraging,” said Yoshihiro Kawaoka, Professor of Virology at University of Wisconsin-Madison and University of Tokyo, and a co-author on the study. “Such antibodies may be especially useful during outbreaks of newly emerging, highly pathogenic influenza viruses.”

M2 is known to be essential for the normal function of the influenza virus; in fact, one class of existing influenza drugs – adamantanes – are M2 inhibitors, and researchers have previously studied the therapeutic potential of antibodies specific for other regions of the M2 protein. Unfortunately, in most cases, M2 mutations have evolved that evade these therapeutic approaches. The fact that the M2 target discovered in this new research study comprises a region where very few changes have been

observed means that antibodies that target it have the potential to be successful against multiple types of influenza A, and suggests that viral escape from such antibodies could be minimal.

Last year, Theraclone scientists identified two novel antibodies that potentially neutralize a broad range of HIV-1 viruses, described in a paper published in the journal *Science*. “We have now found human antibodies that identify novel viral targets for two completely different viral pathogens for which development of effective therapeutic agents has proven to be challenging,” noted Matthew Moyle, Theraclone’s Chief Scientific Officer. “Unlike other antibody technologies, our approach enables rapid functional screening of human antibody repertoires which captures the work that the human immune system has already invested in pathogen defense.” The company is currently pursuing the development of therapeutic antibodies against influenza as its lead program.

Papers published in the PNAS Early Edition are available online at: <http://www.pnas.org/content/early/recent>. Because PNAS publishes daily online, this article may appear later in the week.

This paper is dedicated to the memory of David J. Fanning.

ABOUT INFLUENZA

Influenza is a contagious disease affecting the respiratory tract and sometimes other organs, which typically causes mild to severe illness, but, at times, can lead to death. Approximately 36,000 people die each year from flu-related causes in the US. Certain populations, including the elderly, young children, and people with certain health conditions, are at particularly high risk for serious flu complications.

Influenza A viruses can replicate and mutate very rapidly. Reassortment or recombining of viral genetic material from human, swine, and avian influenza strains presents the dangerous possibility of pathogenic strains capable of causing widespread infection including pandemics, as was the case with the swine-origin influenza virus pandemic last year. To date, international governments have established multibillion dollar stockpiles of drugs and vaccines in an effort to provide protection against future influenza pandemics. The development of new, complementary therapeutic approaches is a high international public health priority.

ABOUT I-STAR™ TECHNOLOGY

The human immune system responds to pathogens, like viruses and bacteria, by evolving highly protective proteins, called antibodies, in real time. The immunological history of these protective responses is archived in human memory B cells, a specialized type of blood cell. The I-STAR™ platform allows comprehensive interrogation of this memory B cell archive. Theraclone’s technology is unique, because it enables rapid functional screening of tens of thousands of natural human antibodies to find those with exceptional biological activities. The antibodies identified through this discovery process are appropriate for further study as novel therapies to help patients fight disease.

ABOUT THERACLONE SCIENCES

Teraclone Sciences is a Seattle-based, discovery-stage biotechnology company focused on the development of novel therapeutic antibodies for the treatment of infectious disease, inflammation and cancer. The company's technology harnesses the power of the human immune system to identify rare, naturally evolved antibodies from the blood cells of immunologically relevant human subjects. Human monoclonal antibodies can be rapidly isolated using the I-STAR™ discovery platform and scaled for industrial production. Such human antibody drug candidates may be uniquely safe and relevant to combating disease across broad patient populations. Teraclone is a privately held company with venture investment from ARCH Venture Partners, Canaan Partners, Healthcare Ventures, Amgen Ventures, MPM Capital, and Alexandria Real Estate Investment.

For additional information, please visit www.theraclone-sciences.com.

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