Scientists create first successful libraries of avian flu virus antibodies

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An international group of American and Turkish research scientists, led by Sea Lane Biotechnologies, has created the first comprehensive monoclonal antibody libraries against avian influenza (H5N1) using samples from survivors of the 2005/2006 "bird flu" outbreak in Turkey.

These antibody libraries hold the promise for developing a therapy that could stop a pandemic in its tracks and provide treatment to those infected, as well as potentially pointing the way towards the development of a universal flu vaccine. The expanded treatment and containment options offered by Sea Lane's antibody libraries could help provide healthcare officials, researchers, and governments with unprecedented resources to combat this serious global health threat.

"Three global influenza pandemics have occurred within the past 100 years, each with devastating consequences," said Richard A. Lerner, the Lita Annenberg Hazen Professor of Immunochemistry at, and President of, the Scripps Research Institute (La Jolla, CA) who collaborated with Sea Lane on the study. "Our study holds out the hope that a new outbreak could potentially be stopped at an early stage, and that effective treatment could be available to those infected."

The study is being published in this week's Early Edition of the journal *Proceedings of the National Academy of Sciences*.

So far, the new antibody libraries reported in the study have yielded more than 300 unique monoclonal antibodies that are active against

H5N1 antigens—foreign substances that produce an immune system response. From this group, the authors identified several broadly neutralizing antibodies that were effective against a number of contemporary subtypes of H5 (avian) flu.

Moving Towards A Universal Influenza Vaccine

The new research reported here suggests that the antibodies recovered from the avian flu survivors may point to an exploitable weak spot in the virus, offering the tantalizing possibility that a "universal" vaccine against all strains might be made.

Remarkably, three of the more than 300 antibodies catalogued have been found to neutralize both the H1 (common seasonal flu) and H5 (avian) subtypes. "The antibodies we have isolated have the potential to be used directly as therapeutic agents against multiple influenza subtypes, permitting the resolution of infection upon administration to an infected individual," said Peter Palese, the Horace W. Goldsmith Professor & Chairman of Microbiology at The Mount Sinai School of Medicine (New York, NY), another collaborator on the project.

"Perhaps most importantly, these antibodies may be used to identify cross-reactive epitopes on the hemagglutinin protein of an influenza virus. Identification of such epitopes may allow the rational design of vaccines with cross-subtype neutralizing activity. Such vaccines would constitute a major advance on current technology, and would be a first step towards the design of a universal influenza vaccine," noted Palese.

Preventing The Worst-Case Scenario – Another Global Influenza Pandemic

Human infection with the avian flu virus H5N1 was first reported in

1997. Since 2003, according to the World Health Organization, more than 370 confirmed cases of human infection have been reported in 14 countries.

While overwhelmingly confined to bird populations in Asia and Europe, the H5N1 avian flu virus has shown its ability to infect humans and has killed more than 230 people around the world. Epidemiologists remain concerned that the virus will one day mutate and be able to spread more readily between people, sparking a global pandemic. The 1918-1920 Spanish flu, which shows evidence of originating in birds, killed somewhere between 40 and 100 million people.

The antibodies recovered from these H5N1 survivor libraries, described in the report, provide opportunities for passive immunization with monoclonal antibodies that could help future individuals infected with H5N1 successfully overcome infection. Monoclonal antibody therapy is known as passive immunotherapy because patients are treated with antibodies that were made outside of their own immune systems instead of those actively made internally.

The potential for passive immunization against influenza has been evident since the Spanish influenza pandemic nearly a century ago, where the benefits of transfused blood reduced the risk of mortality by more than 50 percent. Additionally, the benefits of treatment with convalescent plasma have begun to be reported in instances of H5N1, while passive immunization with human and mouse monoclonal antibodies have been shown to protect animals from death, even when given after H5N1 infection.

Offers Additional Therapeutic Potential

“The antibodies we recovered from Turkey have important and broad potential," said Michael Horowitz, Chief Operating Officer for Sea

Lane. "They could lead the way to providing significant protection against a broad reach of influenza—perhaps as protection to first responders and those at immediate risk, and then as treatment for those infected."

According to Ramesh Bhatt, Vice President for Research at Sea Lane, "The combination of the team's innovative antibody library techniques and tremendous scientific rigor enabled the recovery of this extensive collection of antibodies from the avian flu survivors. Because of the large number of antibodies obtained, we were able to perform a detailed immunochemical analysis of these survivors' antibody solutions against avian influenza virus during an actual outbreak."

The resulting antibody libraries—collections of genetic antibody material—were not dependent on whether an important antibody was being produced by the body at the time of the sample collection. Instead, the scientists were able to obtain the entire immunologic history of an individual's response, which offered a clearer picture of the relationships between antibodies and their relative effectiveness. These insights may help scientists determine prescient strategies for therapies as the virus mutates in the future.

"Our libraries create a roadmap for improving the efficacy and/or specificity of therapeutic influenza antibodies," Arun Kashyap, Director of Influenza and Antibody Libraries for Sea Lane said. "As a result, we might be able to engineer the best features of different antibodies into a single antibody that may not only treat contemporary strains of influenza, but also future influenza strains which normally would escape through simple mutations."

Innovative Research Driven by International Effort

"None of this research could have been accomplished without the

participation of the Turkish scientists who were responsible for the processes for collection of the bone marrow and their shipment to the laboratories in the United States preserved in a way that made recovery of the antibodies possible. This shows the value of international cooperation in basic scientific research," said Lawrence Horowitz, CEO of Sea Lane. "Infectious diseases know no national boundaries and treatments will only be developed if the pooled efforts of all scientists are harnessed, regardless of where they happen to reside."

Source: Scripps Research Institute