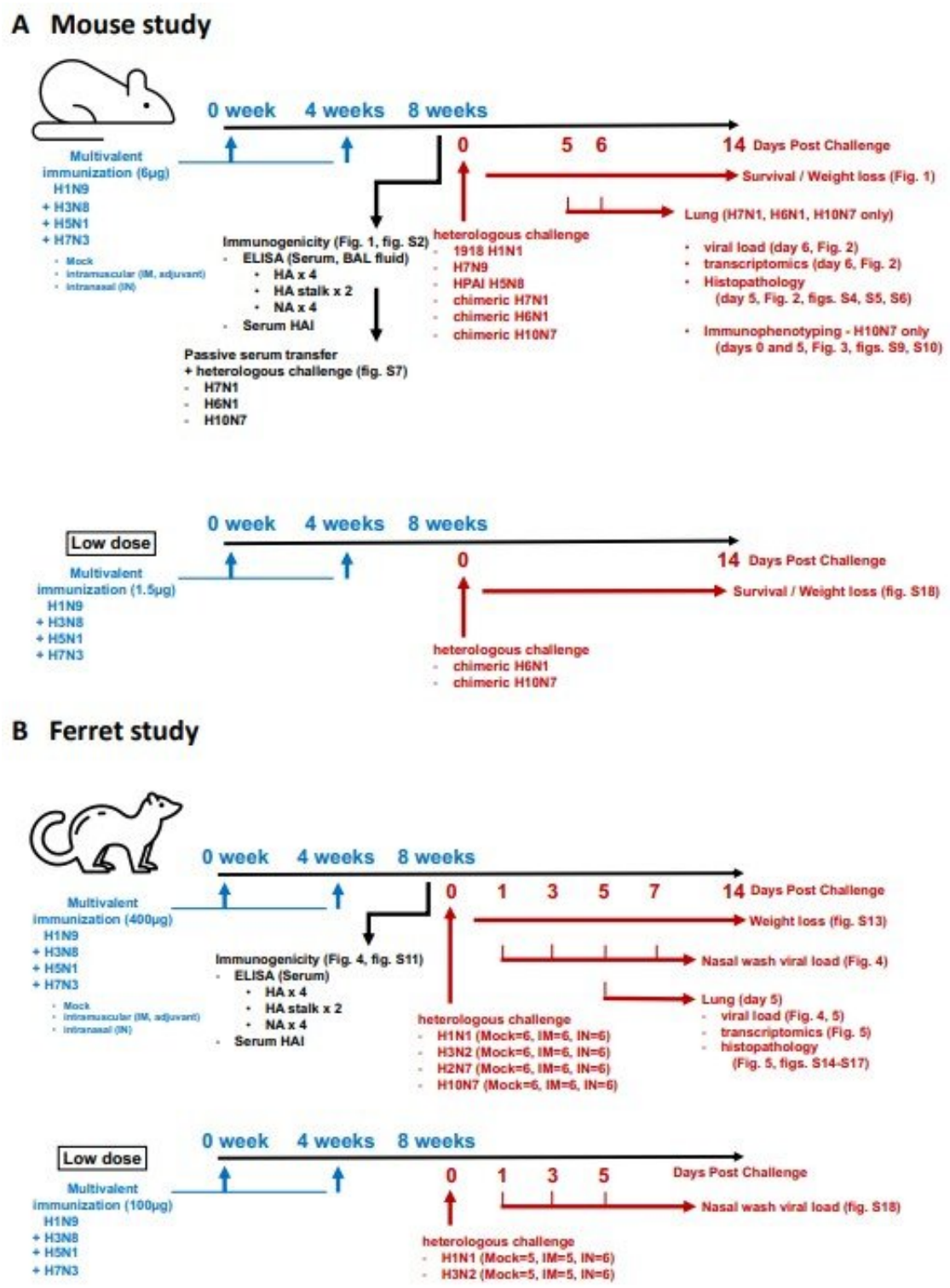
Another tantalizing step closer to a universal flu vaccine

August 16 2022, by Delthia Ricks



Animal study description. Timelines are shown for the (A) mouse and (B) ferret studies. ELISA, enzyme-linked immunosorbent assay; HAI, hemagglutination inhibition. Credit: Science Translational Medicine (2022). DOI: 10.1126/scitranslmed.abo2167

Development of a universal flu vaccine has been a long-sought goal, and as flu scientists begin to see light at the end of a decades-long tunnel, encouraging data have emerged on an experimental shot. It appears effective against multiple A strains of influenza, including zoonotic ones that might jump the species barrier.

Research on several types of universal flu vaccines is underway worldwide in one of the biggest races in science. Several efforts involve developing a universal flu shot that targets A and B strains in a single vaccine. These experiments zero in on a highly conserved region of the flu virus: the stalk of the surface protein hemagglutinin. Picture hemagglutinin as a bulbous head supported on a stalk. That bulbous head mutates frequently, driving the need to change flu vaccines annually. The stable stalk hardly ever mutates.

But while that is an intriguing approach, a team of investigators at the National Institute of Allergy and Infectious Diseases in Bethesda Maryland, is focusing on a type of universal vaccine that is tailored only to A strains of influenza.

History's worst flu epidemics and pandemics have been caused by influenza A viruses, including the highly transmissible and deadly 1918 flu that rapidly circled the globe.

Worse, many zoonotic strains, most circulating in birds are also influenza A viruses, and no one knows if—or when—one of them will jump the species barrier. Developing a universal vaccine that targets A strains of flu viruses would be a scientific godsend, global health experts say.

"Influenza A viruses present major public health threats," writes Dr.

Jaekeun Park of the Viral Pathogenesis and Evolution section of the National Institutes of Allergy and Infectious Diseases.

Park characterizes those threats as running the gamut from annual seasonal flu outbreaks and epidemics to global pandemics that can emerge from any one of several different types of zoonotic sources, such as avian, porcine, and even equine species.

In a new study in *Science Translational Medicine*, Park and colleagues describe a major research project aimed at producing a universal vaccine that would be effective against any A strain of influenza.

"Vaccines that broadly protect against all influenza A viruses, so-called universal influenza vaccines, do not currently exist but are urgently needed," Park added. "We demonstrated that an inactivated, multivalent whole-virus vaccine, delivered intramuscularly or intranasally, was broadly protective against challenges with multiple influenza A viruses…in both mice and ferrets."

Park and colleagues have developed a universal vaccine composed of a quartet of inactivated avian subtypes of influenza A. The vaccine protected laboratory animals from various human, swine, and bird influenza strains, including the 1918 H1N1 pandemic virus and the deadly H5N8 avian strain.

"The vaccine is composed of four β-propiolactone–inactivated low pathogenicity avian influenza A virus subtypes of H1N9, H3N8, H5N1, and H7N3," Park wrote. "Vaccinated mice and ferrets demonstrated substantial protection against a variety of influenza A viruses, including the 1918 H1N1 strain, the highly pathogenic avian H5N8 strain, and H7N9."

Vaccinated animals showed sharp drops in viral titers compared with

unvaccinated controls and additionally displayed less severe inflammation and fewer signs of lung damage, the study showed.

"This vaccine approach could have broad application as both a prepandemic and superseasonal vaccine with low reactogenicity that would be inexpensive, easily distributed worldwide, and could be of value in human influenza virus control," Park continued.

One aim of a universal vaccine would be finally closing the curtain on the annual ritual of choosing vaccine strains for a flu season six months or more into the future. Matching the vaccine to circulating strains has been an imprecise science fraught with guesswork and uncertainty.

Indeed, in many flu seasons the vaccine strains and those in circulation have not matched, resulting in a discrepancy that leaves populations vulnerable.

Along with providing a reliable vaccine to meet seasonal needs, a universal vaccine would eliminate scrambling to figure out the vaccine's critical viral components in the event of an influenza pandemic. Theoretically, production of extra doses could be quickly ramped up. Another advantage is that a universal vaccine would be a flu shot that you get only once or a few times, avoiding the need to roll up your sleeve year after year.

Now, with evidence in hand of a broadly protective vaccine candidate, Park and a large team of collaborators are paving the way toward the Holy Grail, the long-sought universal influenza vaccine for humans. Such a vaccine would go a long way toward addressing the ever-present threat of influenza, which even in its seasonal form can cause anywhere from 290,000 to 650,000 deaths globally, according to the World Health Organization.

The research by Park and colleagues arrives as flu trackers worldwide continue to monitor zoonotic flu strains. None of those highly pathogenic viruses has caused sustained transmission in humans. But that doesn't mean they will continue circulating primarily in birds and other animals.

Among avian A strains of influenza that remain on scientists' short list of potentially lethal viruses are H5N1, H3N8 and H7N9. All are being closely monitored in the event sustained viral transmission occurs in a human population anywhere in the world. While these are under close scrutiny, others that are yet to be identified may emerge without notice.

Avian strain H7N9 had not been seen in either animals or people until its abrupt emergence in birds in March of 2013 in China. Since that time, infections have stricken both humans and birds. Among people who've been infected, the flu triggered by H7N9 is usually severe. The virus doesn't transmit easily from one person to another, and sustained human-to-human transmission has not been reported.

Most human cases involving this avian strain have been reported following recent exposure to live poultry "or potentially contaminated environments, especially markets where live birds have been sold," according to a 2019 WHO report on H7N9.

For Park and colleagues, the investigational vaccine has shown promise in the lab and produced encouraging data that puts it on track for human clinical research. "This vaccine approach indicates the feasibility of eliciting broad, heterosubtypic influenza A virus protection and identifies a promising candidate for influenza vaccine clinical development," Park concluded.

More information: Jaekeun Park et al, An inactivated multivalent influenza A virus vaccine is broadly protective in mice and ferrets,

Science Translational Medicine (2022). DOI: 10.1126/scitranslmed.abo2167