New compound protects 100 percent of ferrets, mice, from H5N1

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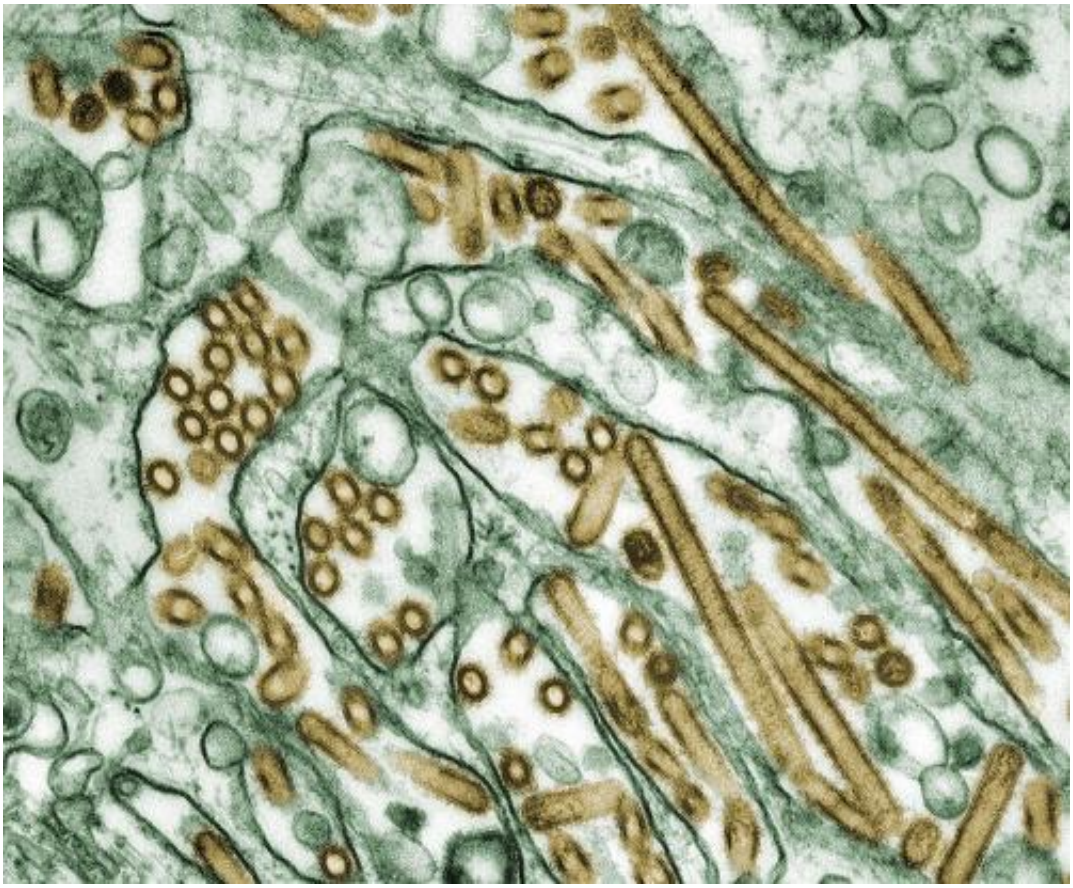

A colorized transmission electron micrograph of Avian influenza A H5N1 viruses. Credit: Wikipedia

Since 2003, the H5N1 influenza virus, more commonly known as the bird flu, has been responsible for the deaths of millions of chickens and

ducks and has infected more than 650 people, leading to a 60 percent mortality rate for the latter. Luckily, this virus has yet to achieve human-to-human transmission, but a small number of mutations could change that, resulting in a pandemic. Now a team of investigators from St. Jude Children's Research Hospital, Stanford University Medical Center, and MacroGenics have developed an antibody which has proven 100 percent protective against the virus in two species of animal models. The research is published ahead of print February 11, in the *Journal of Virology*.

Antivirals have been potential sources of protection, but they are hampered by the propensity of viruses to rapidly mutate, which often results in resistance. "We have seen this in H5N1 viruses," said corresponding author Richard Webby, PhD, a Member in the Infectious Diseases Department at St. Jude Children's Research Hospital, Memphis, TN, and Director of the World Health Organization (WHO) Collaborating Center for Studies on the Ecology of Influenza Viruses in Lower Animals and Birds.

Vaccines, Webby said, must be developed to match each flu virus, something which would likely take at least six months following the emergence of a pandemic. Additionally, vaccines are somewhat ineffective in the elderly and immunocompromised individuals.

The investigators turned to antibodies, which target antigens on viruses as specifically as keys to locks, thus disabling them. Regardless, mutations can render antibodies ineffective. "Our solution was to make a 'dual-specific' antibody by combining two different antibodies that attach strongly to H5N1 viruses into a single antibody-like molecule," said Webby. That, he said, should make it much harder for resistance to emerge. The new compound is called FcDART, for Fc (the type of fusion protein) Dual-Affinity ReTargeting molecule.

A single, low dose of the FcDART provided complete protection against lethal H5N1 viruses in laboratory models of influenza. "This dose could be given one day before infection—for example, to protect healthcare providers—or up to three days after," said Webby.

"Laboratory models are rough approximations of what might happen in humans," said first author Mark Zanin, a post-doctoral fellow in Webby's lab at St. Jude. "We did see complete protection against H5N1 in ferrets, which have long been used as a model for human flu, so we are confident in our results."

Provided by American Society for Microbiology

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