New biologic approach may protect against any influenza strain

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A new biologic drug prevented death when administered to mice a week in advance of lethal challenge with influenza H7N9, a disease that has shown a roughly 30 percent mortality rate in humans. The biologic had previously proven protective in mice against the pandemic 2009 H1N1 and the highly pathogenic H5N1 influenza viruses. "This suggests that our approach could work for any strain of the influenza virus," says corresponding author Elena Govorkova, of St. Jude Children's Research Hospital, Memphis, Tennessee. The research is published ahead of print in *Antimicrobial Agents and Chemotherapy*.

Influenza viruses are notoriously mutable, making it a huge annual challenge for scientists to predict each new year's strain, and to formulate an effective vaccine. Collaborators Garry Taylor and co-corresponding author Helen Connaris at the University of St. Andrews, United Kingdom came up with an ingenious approach to thwart influenza viruses. Rather than predicting which antibodies would work against each new strain, they developed a way of "barring the door" to the respiratory tract cells.

"Influenza viruses attach to a very specific sugar molecule that decorates all the cells that line the respiratory tract," coauthor Robert Webster of St. Jude's explains. "Following attachment, the virus is engulfed by the cell and then replicates therein to produce more viruses that are released to infect even more cells." So Taylor and Connaris developed a novel engineered protein, which goes by the unwieldy moniker, Sp2CBMTD. This biologic binds to those sugar molecules, blocking the viruses from

entry.

The investigators engineered Sp2CBMTD using multiple copies of a small sugar-binding section, or "domain" of a protein they isolated from Streptococcus pneumoniae, which the bacterium, a normal inhabitant of the human throat, also uses to bind to those cells.

In the study, the investigators administered the biologic nasally to mice, either as a single large dose, or repeated low doses, up to a week in advance of lethal influenza challenge. "In most cases, the mice were fully protected," says Govorkova.

"Our findings suggest that this preventive approach could protect people during periods of flu vaccine development, particularly in the case of a pandemic, or in situations where vaccine efficacy may vary amongst specific populations groups such as the elderly, immunocompromised individuals, or those with pre-existing respiratory diseases," says Connaris. "Several other respiratory diseases attach to the same sugar molecule as influenza virus, suggesting that our biologic has an even broader potential in preventing respiratory disease."

Govorkova says that even after administration of the biologic, there is sufficient viral replication to stimulate an immune response, and speculates that this might provide protection against repeat infection.

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