MedicalXpress

Multi-tasking flu vaccine could provide better protection against outbreaks

October 27 2015

Australian researchers have found a way to boost the effectiveness and cross-protective capabilities of an influenza A vaccine by adding a simple component. Published this week in *mBio*, an online open-access journal of the American Society for Microbiology, the research in mice could lead to better seasonal flu vaccines for humans, and also vaccines that could provide community protection in the early stages of an outbreak of a novel flu virus strain.

"Influenza infections cause 250,000-500,000 deaths every year. Our best protection comes from the seasonal flu vaccine, which induces antibodies that neutralize the virus," notes Brendon Chua, a research fellow at the University of Melbourne. However, each year the seasonal flu vaccine is developed based on a prediction of the handful strains that are likely to be circulating the globe.

"The holy grail would be to develop a vaccine that cross-protects against different strains, which would be beneficial for the whole community, even if the prediction of circulating strains is wrong", says Chua. Such cross-protection could also be beneficial if a flu virus evolves to jump from another species to humans, such as what happened in recent years with the H5N1 strain from birds and the H1N1 strain from pigs. It currently takes at least six months to produce a new flu vaccine on a global scale.

The research team led by Chua and professor David C. Jackson, believed that using an additive, or adjuvant, with the flu vaccine might stimulate

other types of antibody-independent immune responses, resulting in a much improved and cross-protective vaccine.

"We had an adjuvant that worked well to stimulate both innate and adaptive immunity," says Chua. Innate immunity is the body's first wave of defense of non-specific short-lived responses that can help protect cells from infection. Adaptive immunity is the body's longer-term response, which is specific to the invader and can 'remember' it later. "Harnessing both types of immunity would provide protection in that period during an outbreak when no [new] vaccine is available."

The adjuvant is a synthetic lipopeptide—a string of fat molecules mimicking a natural component found on the outer membrane of a pathogenic microorganism. Human immune cells recognize this component as a danger signal.

"This danger signal is the key to the front door of innate immunity," says Jackson, a vaccine expert at University of Melbourne. "It initiates the non-specific innate response that says, 'Get the SWAT squad out here!' "

The team added this adjuvant to an inactivated influenza A vaccine and vaccinated mice, then exposed them three days later to both the virus contained in the vaccine and another strain. The mice given the adjuvanted vaccine were better protected compared to mice that received vaccine without the adjuvant. Mice given the adjuvanted vaccine also survived what is normally a lethal dose of flu virus.

In addition, mice given a low dose of the adjuvanted vaccine as a nasal application produced 600 times more neutralizing antibodies compared to a similar low dose of vaccine alone. Importantly, the adjuvant-vaccine combo also activated more T cells that are responsible for clearing flu-infected cells in the lungs.

"The culmination of all these responses is that it reduces the ability of the virus to infect cells, reproduce, and spread," explains Chua.

Next, the team gave mice the low-dose adjuvant-vaccine combo and challenged them with flu virus strains 35 days later. The mice were completely protected against the strain contained in the vaccine, and against an unmatched strain not contained in the vaccine. In contrast, mice receiving the low-dose vaccine alone were not significantly protected from either flu strain.

Finally, the team demonstrated that the adjuvant could greatly reduce the transmission of the unmatched flu strain from vaccinated mice to unvaccinated mice housed in the same cage for 2 days.

"The biggest advantage is that this approach doesn't rely on getting a match between the strains used in the vaccine and circulating virus—you can still get some protective effect at the population level," says Chua.

Provided by American Society for Microbiology