

Adjuvant Combo Shows Potential for Universal Influenza Vaccine

Killer T Cells Activated to Bring Extra Protection

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DENVER — Researchers at National Jewish Health have discovered how to prime a second arm of the immune system to potentially boost influenza vaccine effectiveness. A combination of two adjuvants, chemicals used to boost the effectiveness of some vaccines, induced CD8, or killer, T cells to join antibodies in response to influenza infection. Since the killer T cells targeted a highly conserved protein that does not change from year to year, the adjuvant strategy suggests potential for a universal flu vaccine.

“Most vaccines protect against disease by boosting antibody protection,” said lead author post-doctoral fellow Megan MacLeod, PhD. “We have shown that the two adjuvants work in concert to generate memory CD8 T cells, which can kill infected cells. We believe that this strategy of stimulating both the cellular and humoral immune responses holds promise for better vaccines.”

Vaccines prepare the immune system to respond quickly to an infection with antibodies, Y-shaped molecules that neutralize or otherwise inactivate pathogens.

Aluminum salts, or alum, have been used for nearly a century as an adjuvant to boost the effectiveness of many vaccines. Surprisingly no one is sure even today exactly how it works. The only other adjuvant approved for use in the United States, monophosphoryl lipid A (MPL), is used by GlaxoSmithKline to boost the antibody response of some of its vaccines.

Dr. MacLeod, senior author Philippa Marrack, FRS, PhD, and their colleagues evaluated the responses of mice immunized with influenza vaccines containing no adjuvant, each adjuvant alone and both together. They engineered the vaccine so that any immune defense would be provided by killer T cells, not antibodies. Several weeks after the immunization, they infected the mice with influenza A virus.

They found that unvaccinated mice lost about 15 percent of their body weight in the first eight days after infection, then regained some of that weight by 20 days after infection. Mice whose vaccines contained either alum or MPL adjuvants lost less weight but did not fully regain their original weight. Mice whose vaccines contained both adjuvants together lost about 5 percent of their original weight and regained it all back rapidly.

The researchers also found that mice receiving vaccines with both adjuvants had the fewest viral particles in their lungs four days after infection.

Further experiments revealed that alum promoted long-lived CD8 memory cells, but that MPL was required to produce activated cells, ready and able to kill. The findings were published in the May 10, 2011, issue of the *Proceedings of The National Academy of Sciences*.

Current influenza vaccines use antigens against two proteins on the viral surface, neuraminidase (N), and hemagglutinin (H), to which antibodies can bind. Because these cell-surface proteins mutate frequently, new vaccines must be formulated each year to recognize a viral strains.

Killer T cells instead recognize viral fragments displayed on the surface of infected cells. The researchers used as their vaccine a fragment from the viral nucleus, which rarely changes. This suggests the possible development of a universal flu vaccine that would not have to be reformulated and administered every year.

National Jewish Health is the leading respiratory hospital in the nation. Founded 121 years ago as a nonprofit hospital, National Jewish Health today is the only facility in the world dedicated exclusively to groundbreaking medical research and treatment of patients with respiratory, cardiac, immune and related disorders. Patients and families come to National

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