

Moving towards a universal flu vaccine

Israeli company reports good results with supplemental shot in elderly.

Amber Dance

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Multimeric-001, an influenza vaccine now in clinical trials, boosts immunity in elderly people when given as a supplement to the seasonal shot. But supplementation is just a short-term goal: eventually the drug's maker, BiondVax Pharmaceuticals of Ness Ziona, Israel, believes that Multimeric-001 alone could protect against all strains of flu.

The company will present the results from its second phase II trial of the shot on 3 April at the Second Annual Vaccines Congress in London. The 90 people aged 65 and older who got the pair of shots, compared to 30 who received only the annual vaccine, mounted a stronger immune response to the three seasonal flu strains, as well as to a few other strains not in the seasonal vaccine.

For most infectious agents, one exposure teaches the body's immune system to recognize and destroy the virus or bacterium. The standard flu vaccine teaches the body to recognize the virus's outer coating. But influenza is constantly changing its stripes, mutating from year to year and forcing scientists to guess which three strains to include in the seasonal vaccine. "This is crazy," says Vincent Racaniello, a virologist at Columbia University in New York, who is not involved with the BiondVax trials. If there were one vaccine that worked for any kind of flu, no matter how it mutated its coat, the costs of protection would drop and pandemics could disappear, he says.

The Multimeric-001 vaccine comprises nine linked sections from three flu proteins from different parts of the virus. These represent a "common denominator" shared by more than 10,000 flu strains since 1940, says the company's chief scientist Tamar Ben-Yedidia. Racaniello says that, in theory, this combination of proteins should be universal, because every strain of flu would have them.

In a study published in February in the *Journal of Clinical Immunology*¹, BiondVax reported that its Multimeric-001 vaccine was safe and conferred immunity on its own. However, BiondVax thinks that a universal flu vaccine would be a tough sell to regulatory agencies. Part of the challenge is that the standard test for a vaccine's efficacy is based on the presence of antibodies to the ever-changing parts of the haemagglutinin protein on the outside of the virus in a vaccinated person's blood. It's a test their universal vaccine is designed to fail, because Multimeric-001 does not confer immunity to these proteins.

Instead, the company hopes to obtain approval for Multimeric-001 as a supplement to the three-strain annual vaccine, then track the first recipients of the shot to see if they suffer from fewer flu infections. The company is focusing on people aged 65 and older, who tend not to get much benefit from the regular shot — Ben-Yedidia says that only 30% of older people achieve immunity after the seasonal vaccine, and they account for 90% of flu deaths.

In the latest trial, the proportion of older people with a good antibody response to the annual shot increased by more than 10% when they got Multimeric-001 first. Their blood T cells also pumped out antivirals such as interferon gamma in response to several flu strains after receiving only Multimeric-001, Ben-Yedidia says.

BiondVax's approach is just one in the hunt for a universal flu vaccine. Other researchers are looking in human sera for naturally occurring universal flu antibodies². These antibodies could be used as a treatment, but would be unlikely to have widespread use, Racaniello says, because it is too expensive to generate large quantities of them.

Scientists could also use natural universal flu antibodies to reverse-engineer a vaccine. However, "these are tough antibodies to



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Flu viruses evolve quickly, making it difficult to create a universal vaccine.

induce because they're rare," Racaniello notes. "Designing an immunogen that will give rise to them is not easy," he says, because the immune system usually stops trying to make new antibodies once it has one that works well enough against the current infection..

But there is an advantage to this approach, says Gregory Stoloff, chief executive of SEEK, a drug company in London that is also working on a universal vaccine. Researchers know the pan-flu antibody exists, and confers protection if they can just convince the body to make it. The potential antibodies that could arise from BiondVax's peptide chain are unknown targets, and may or may not offer protection. He thinks going after a known target is a better approach.

"We have to wait and see who is going to be the first to reach this goal," Ben-Yedidia says.

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References

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2. Corti, D. *et al.* *Science* **333**, 850–856 (2011).