Compound boosts effect of vaccines against HIV and flu

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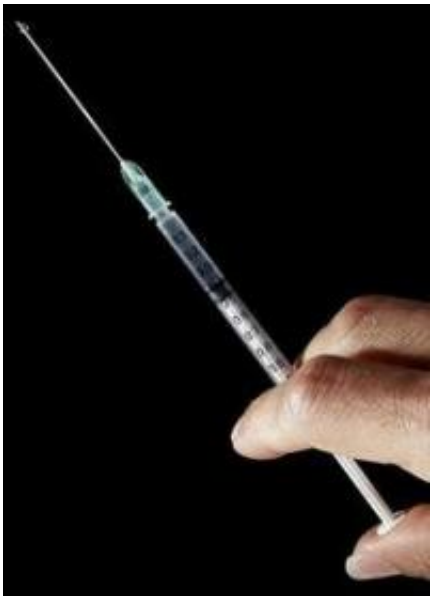

(Medical Xpress)—Oxford University scientists have discovered a compound that greatly boosts the effect of vaccines against viruses like flu, HIV and herpes in mice.

An 'adjuvant' is a substance added to a vaccine to enhance the immune response and offer better protection against infection.

The Oxford University team, along with Swedish and US colleagues,

have shown that a type of polymer called polyethyleneimine (PEI) is a potent adjuvant for test vaccines against HIV, flu and herpes when given in mice.

The researchers were part-funded by the UK Medical Research Council and report their findings in the journal *Nature Biotechnology*.

Mice given a single dose of a flu vaccine including PEI via a nasal droplet were completely protected against a lethal dose of flu. This was a marked improvement over mice given the flu vaccine without an adjuvant or in formulations with other adjuvants.

The Oxford researchers now intend to test the PEI adjuvant in ferrets, a better animal model for studying flu. They also want to understand how long the protection lasts for. It is likely to be a couple of years before a flu vaccine using the adjuvant could be tested in clinical trials in humans, the researchers say.

'Gaining complete protection against flu from just one immunisation is pretty unheard of, even in a study in mice,' says Professor Quentin Sattentau of the Dunn School of Pathology at Oxford University, who led the work. 'This gives us confidence that PEI has the potential to be a potent adjuvant for vaccines against viruses like flu or HIV, though there are many steps ahead if it is ever to be used in humans.'

HIV, flu and herpes are some of the most difficult targets to develop vaccines against. HIV and flu viruses are able to change and evolve to escape immune responses stimulated by vaccines. There aren't any effective vaccines against HIV and herpes as yet, and the flu vaccine needs reformulating each year and doesn't offer complete protection to everyone who receives it. Finding better adjuvants could help in developing more effective vaccines against these diseases.

Most vaccines include an adjuvant. The main ingredient of the vaccine – whether it is a dead or disabled pathogen, or just a part of the virus or bacteria causing the disease – primes the body's immune system so it knows what to attack in case of infection. But the adjuvant is needed as well to stimulate this process.

While the need for adjuvants in vaccines has been recognised for nearly 100 years, the way adjuvants work has only recently been understood. The result has been that only a small set of adjuvants is used in current vaccines, often for historical reasons.

The most common adjuvant by far is alum, an aluminium-containing compound that has been given in many different vaccines worldwide for decades. However, alum is not the most potent adjuvant for many vaccine designs.

'There is a need to develop new adjuvants to get the most appropriate immune response from vaccines,' says Professor Sattentau, who is also a James Martin Senior Fellow at the Oxford Martin School, University of Oxford.

The Oxford University team found that PEI, a standard polymer often used in genetic and cell biology, has strong adjuvant activity.

When included in a vaccine with a protein from HIV, flu or herpes virus, mice subsequently mounted a strong immune response against that virus. The immune response was stronger than with other adjuvants that are currently being investigated.

The team also showed that PEI is a potent adjuvant in rabbits, showing the effect is not just specific to mice and could be general.

Another potential advantage of PEI is that it works well as an adjuvant

for 'mucosal vaccines'. These vaccines are taken up the nose or in the mouth and absorbed through the mucus-lined tissues there, getting rid of any pain and anxiety from a needle. Mucosal vaccines may also be better in some ways as mucosal tissues are the sites of infection for these diseases (airways for respiratory diseases, genital mucosa for HIV and herpes).

Professor Sattentau suggests that: 'In the best of all possible worlds, you could imagine people would have one dose of flu vaccine that they'd just sniff up their nose or put under their tongue. And that would be it: no injections and they'd be protected from flu for a number of years.

'It's just a vision for the future at the moment, but this promising adjuvant suggests it is a vision that is at least possible.'

More information: Polyethyleneimine is a potent mucosal adjuvant for glycoproteins with innate and adaptive immune activating properties, *Nature Biotechnology*, 2012. www.nature.com/nbt/journal/vao … t/full/nbt.2344.html

Provided by Oxford University