Engineering self-destructing Salmonella to make better vaccines

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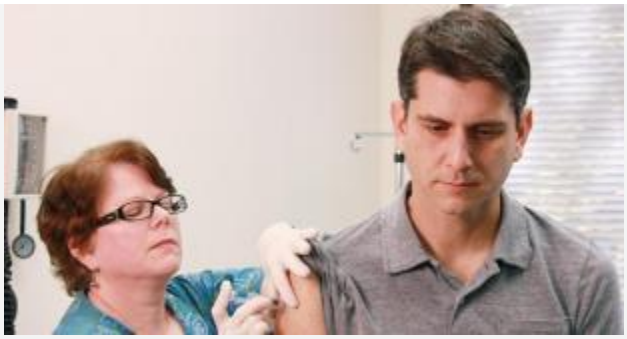

A nurse is giving this man a traditional vaccine. New developments in DNA vaccines could change how we deliver vaccines by eliminating the need for needles (Image: CDC)

Researchers at Arizona State University are doing an amazing thing. Wei Kong and others in Roy Curtiss's lab are engineering Salmonella to turn it into a delivery system for DNA vaccines. They recently published their advances in the Proceedings of the National Academy of Sciences. Hypothetically such vaccines could be used against not just viruses but also fungal or parasitic infections and could also be a key defense against bioterrorism.

There are several advantages to using a bacteria-based DNA vaccine. For one, such a vaccine can be taken orally (a big plus for those of us who hate needles). Additionally, whereas traditional vaccines are targeted against specific viral strains, DNA vaccines have the flexibility to provide immunity more broadly. This is an important advance for fighting against both the seasonal flu and possible bioterrorism agents. DNA vaccines are also faster to produce than traditional vaccines. A newly engineered vaccine vector can be produced in less than two weeks. According to the PNAS paper, this means that a new vaccine could be "manufactured in billions of doses at a low cost within several months from the time a decision is made to change the antigenic components." This is a major advance over traditional vaccine production methods which take longer to develop and are limited to a certain scale—sometimes causing rationing of vaccines.

Other benefits of DNA vaccines come directly from the way such vaccines work. Most vaccines are still produced the old fashioned way—by injecting specific viral strains into fertilized chicken eggs which then produce many copies of the virus. Next, the virus is extracted from the egg and is deactivated. The viral proteins maintain their shape even when deactivated, allowing our immune system to produce antibodies against them in preparation for possible exposure to the actual virus. There are two major problems with this system: 1) you need to guess right about which viral strains will be a public health threat (and you need to do this more than 6 months in advance) and 2) you are limited by the number of fertilized eggs you have to work with.

DNA vaccines aren't limited by these factors. They work by introducing the DNA that codes for an antigen (the part of the protein that the antibody recognizes) rather than requiring the production of an entire virus. So researchers can make a DNA vaccine that codes for an antigen found in many strains of flu, for example, meaning that the antibodies produced in the host after receiving the vaccine are ready to fight off all flu strains containing that antigen. And you also don't have that whole egg problem.

That's not to say that engineering the actual bacteria-based DNA vaccines is trivial. The Curtiss lab and other labs working in this field had two main challenges: 1) creating a self-destruction feature in the bacterium to prevent it

from multiplying widely outside its host and, on the other hand, 2) engineering the bacterium so it reaches the cells needed to produce immunity. So far these tweaks seem to have been a success. The Curtiss lab developed a Salmonella-based DNA vaccine against infant pneumonia that is currently in a phase 1 clinical trial. If this vaccine is approved, it could be the beginning of a wave of new DNA vaccines.

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