New nanoparticle vaccine is more effective but less expensive

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Good news for public health: Bioengineering researchers from the EPFL in Lausanne, Switzerland, have developed and patented a nanoparticle that can deliver vaccines more effectively, with fewer side effects, and at a fraction of the cost of current vaccine technologies.

Described in an article appearing online September 16 in the journal *Nature Biotechnology*, the vaccine delivery platform is a deceptively simple combination of nanotechnology and chemistry that represents a huge advantage over current vaccine methods. This technology may make it possible to vaccinate against diseases like hepatitis and malaria with a single injection. And at an estimated cost of only a dollar a dose, this technology represents a real breakthrough for vaccine efforts in the developing world.

A vaccination is an injection of a non-virulent form of a pathogen or molecule from a pathogen (known as an antigen), to which the immune system responds, destroying and then developing a “memory” for the pathogen. Later, when a virulent form of the pathogen comes along, this memory kicks in and the intruder is quickly eradicated. Most vaccines protect against viruses or bacteria, but vaccine techniques are also being explored as a way to kill cancer cells.

Thanks to recent advances, an immune response can be triggered with just a single protein from a virus or bacterium. Recent research has also shown that the best way to get sustained immunity is to deliver an antigen directly to specialized immune cells known as dendritic cells

(DCs).

This technique is not yet used clinically because there are two difficulties to overcome in targeting the DCs: first, there are not very many of these cells in the skin or muscle, where injections are usually made, so obtaining an adequate immune response with a single injection is difficult; and second, activating the DCs requires co-delivering a "danger signal" of some sort, otherwise the immune system will just ignore it. Current approaches mimic bacterial molecules already known to the immune system, but this can cause side effects or even be toxic.

EPFL professors Jeff Hubbell and Melody Swartz and PhD student Sai Reddy have engineered nanoparticles that completely overcome these limitations. At a mere 25 nanometers, these particles are so tiny that once injected, they flow through the skin's extracellular matrix, making a beeline to the lymph nodes. Within minutes, they've reached a concentration of DCs thousands of times greater than in the skin. The immune response can then be extremely strong and effective.

In addition, the EPFL team has also engineered a special chemical coating for the nanoparticles that mimics the surface chemistry of a bacterial cell wall. The DCs don't recognize this as a specific invader, but do know that it's something foreign, and so a low-level, generic immune reaction known as "complement" is triggered. This results in a particularly potent immune response without the risk of unpleasant or toxic side effects.

"People have been exploring nanoparticles for a while," says Hubbell. "Our ideas -- to activate complement as a danger signal, and to exploit the slow interstitial flow towards the lymph nodes – are completely new. But it meant that our particles had to be much smaller than anything currently being developed. No other labs have managed to engineer so many levels of functionality into nanoparticles that are smaller than

biologically occurring particles," he adds. "The beauty of it is that once we have developed the recipe, any lab can make them."

Cost and logistics are important factors, especially for use in developing countries. Unlike other nanoparticle vaccine technologies that degrade in water and thus require expensive drying and handling procedures, the EPFL team's nanoparticles won't degrade until they are in the body. They are in liquid form and don't require refrigeration, so preparation and handling costs are reduced, and they are easy to transport.

The group is collaborating with the Swiss Tropical Institute in Basel to determine the strength and duration of the immune response in the context of a nanoparticle malaria vaccine. Toxicity studies are also in the works. Swartz says that the team is also planning to use this technique to target cancer cells.

"If, as we hope, this vaccine technique can confer sustained immunity with a single injection for around a dollar a dose, without toxic side effects, it could have a real impact on public health, in the developing world as well as right here at home," says Swartz. "More study is required to achieve these goals," she adds, "but we have every reason to believe this technique could be in use within five years."

Source: Ecole Polytechnique Fédérale de Lausanne