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No-refrigeration, spray vaccine could curb diseases in remote areas

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A new kind of single-dose vaccine that comes in a nasal spray and doesn't require refrigeration could dramatically alter the public health landscape—get more people vaccinated around the world and address the looming threats of emerging and re-emerging diseases. Researchers presented the latest design and testing of these "nanovaccines" at the 247th National Meeting & Exposition of the American Chemical Society (ACS), the world's largest scientific society.

Their talk was one of more than 10,000 presentations at the meeting, being held here through Thursday at the Dallas Convention Center and area hotels.

"Our nanovaccine approach could be instrumental for containing future outbreaks of recently emerged and re-emerging diseases, such as SARS, new flu strains and multi-drug resistant tuberculosis," said Balaji Narasimhan, Ph.D., the project's lead researcher.

He noted that most of today's vaccines require needles, boosters and refrigeration, all of which pose challenges for doctors and patients. Other than the pain factor, which can lower the chances that someone will seek out a vaccine, follow-up shots and refrigeration further reduce the reach of these vitally important preventive treatments. In some places with limited resources, refrigeration simply isn't available. Thus, many people who need vaccinations the most aren't getting them at all. The good news is that the vaccines Narasimhan's team is developing don't need to be kept cold and are easy to administer.

"Our nanovaccines can be stored at room temperature for as long as six to 10 months and still work," said Narasimhan, professor of chemical engineering at Iowa State University. "Also, we're designing them so they get delivered in one dose through a nasal spray, which could potentially allow patients to give the vaccine to themselves."

Another major limitation of traditional vaccines is the way they work, he said. Most current vaccines help a person develop disease immunity by introducing part of a virus or bacteria and triggering the body's humoral response—the part of the immune system that produces antibodies to fight off a harmful pathogen. Later, if the person gets infected by that microbe, the body immediately knows how to respond.

But increasingly, evidence is emerging that the other component of the body's immune system, what's called the cell-mediated arm, also plays an important part in some emerging and re-emerging diseases, such as whooping cough. This side of the immune system depends on a group of cells called T cells, rather than antibodies, to fight viruses and bacteria.

Part of the elegance of these nanovaccines is their simplicity and versatility, Narasimhan explained. They are made of only two components: bits of proteins from a virus or bacteria packed into nontoxic, biodegradable polymers that can be custom-designed.

When administered through the nose or by a shot, these tiny packages enter the body and flag the immune system. Sentinels called antigen-presenting cells that keep watch in the body for foreign invaders gobble up the nanovaccine particles, chop up the polymers and pathogen proteins, and appropriately put pieces of the proteins on their surfaces. Depending on the chemistry of the nanovaccine, this triggers the body's cell-mediated or humoral immune response and trains it to recognize the pathogen and attack it quickly in case of future infections.

"We have exciting results that attest to the ability of the nanovaccine formulations to do a very good job of activating cell-mediated immunity," said Narasimhan. "We've shown that it works with rodents, and we're moving forward to show that in larger animals, as well."

More information: Presentation: Pathogen mimicking nanovaccine platform technology: A new paradigm

Abstract

The design of vaccines and therapeutics to address infectious diseases is fraught with challenges ranging from the need for cold storage to poor immunogenicity to the need for multiple doses to the need for needle-based methods that require medical professionals to administer. We have developed a cross-disciplinary approach at the intersection of polymer chemistry, nanotechnology, and immunology for the molecular design of a safe, needle-free, and efficacious nanoparticle-based platform that can address these challenges and provide a robust technology to address both pre- and post-exposure to respiratory pathogens. These biodegradable nanoparticles are based on amphiphilic polyanhydrides, which degrade by hydrolytic cleavage of the anhydride bond. We have shown using a bottom-up approach that vaccine adjuvants based on amphiphilic polyanhydride nanoparticles are capable of mimicking a natural infection and inducing a robust immune response with long-lived protection against a subsequent challenge. The nanoparticles possess the unique ability to mimic pathogens with respect to persisting within and activating immune cells as well as rapidly distributing to tissue sites distal to the site of administration. Furthermore, these particles can be targeted for uptake by immune cells by functionalizing their surface with carbohydrates, enabling more efficient delivery of antigen to dendritic cells and macrophages.

Our studies have shown that the nanoparticles are safe when administered via multiple routes – intranasal, subcutaneous, and intramuscular. These particles are stable at high temperature for

extended periods of time obviating the "cold chain", which is a major hurdle in the deployment of vaccines to remote regions of the globe. The nanoparticles can be designed to encapsulate fragile protein antigens and deliver them in a sustained manner to immune cells, facilitating the maintenance of antigen-specific CD8+ and CD4+ T cells. We have demonstrated that these nanovaccines confer full protection in a single intranasal dose ten months prior to lethal challenge by several respiratory pathogens. Additionally, these particles can be used for effective intracellular delivery of antibiotics in a single administration, which results in lower toxicity, enhanced patient compliance, dose sparing, and cost savings. This rational approach for designing novel amphiphilic materials as nanoscale adjuvants and therapeutics has the tantalizing potential to catalyze the development of next generation technologies against emerging and re-emerging diseases.

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