Technique tricks bacteria into generating their own vaccine

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Scientists have developed a way to manipulate bacteria so they will grow mutant sugar molecules on their cell surfaces that could be used against them as the key component in potent vaccines.

Any resulting vaccines, if proven safe, could be developed more quickly, easily and cheaply than many currently available vaccines used to prevent bacterial illnesses.

Most vaccines against bacteria are created with polysaccharides, or long strings of sugars found on the surface of bacterial cells. The most common way to develop these vaccines is to remove sugars from the cell surface and link them to proteins to give them more power to kill bacteria.

Polysaccharides alone typically do not generate a strong enough antibody response needed to kill bacteria. But this new technique would provide an easy approach to make a small alteration to the sugar structure and produce the polysaccharide by simple fermentation.

"We are showing for the first time that you don't have to use complicated chemical reactions to make the alteration to the polysaccharide," said Peng George Wang, Ohio Eminent Scholar and professor of biochemistry and chemistry at Ohio State University and senior author of the study. "All we need to do is ferment the bacteria, and then the polysaccharides that grow on the surface of the cell already incorporate the modification."

The research is scheduled to appear in the online early edition of the *Proceedings of the National Academy of Sciences*.

In vaccines, polysaccharides linked with carrier proteins are injected into the body. That sets off a process that causes the release of antibodies that recognize the sugars as an unwanted foreign body. The antibodies then remain dormant but ready to attack if they ever see the same polysaccharides again - which would be a signal that bacteria have infected the body.

Polysaccharides are chains of sugars, or monosaccharides, and they are targeted for vaccine development because they are the portion of bacterial cells that interact with the rest of the body.

Escherichia coli was used as a model for the study. Wang and colleagues used one of the existing monosaccharides present on the E. coli cell surface polysaccharides, called fucose, to generate this new modification. They manipulated the structure of the fucose to create 10 different analogs, or forms of the sugar in which just one small component is changed.

The scientists then manually introduced these altered forms of fucose to a solution in which bacterial cells were growing, and the bacterial cells absorbed the altered fucose as they would normal forms of the sugar. The presence of these altered forms of fucose then altered the properties of the polysaccharides that grew on the surface of the cells.

"This way, we don't have to do anything to modify the polysaccharides. We let bacteria do it for us," Wang said.

"Bacteria grow lots of polysaccharides - it's similar to the way humans grow hair. But for a vaccine, you need to make the molecules more active, or energetic," he said. "In our method, we feed the bacteria these chemicals while they are growing, and those chemicals end up in the polysaccharides and that makes them more immunogenic. That's the technology."

Wang said the approach is likely to be applicable to many different kinds of bacteria. But each type of pathogen must be tested individually with the alteration of sugars unique to its surface.

"If you want to prevent one type of bacteria, you have to find something very unique for this bacteria because different microbes have different characteristics," he said. "You have to find the oddest thing on the cell surface. It has to be on surface because what the body sees first is the surface."

His lab will next be testing the method's effectiveness on the pneumococcus bacteria under an exploratory $100,000 grant from the Bill & Melinda Gates Foundation. The current vaccine to prevent pneumonia in babies and the elderly combines 23 strains of bacteria, making it complex and expensive to produce. Each injection costs about $50 in the United States. A less expensive way to develop the vaccine would increase its availability in the developing world, Wang said.

Source: Ohio State University

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