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University of Texas lab works on new generation of vaccines

By Mary Ann Roser

When many people think about E. coli, they think of tainted burgers. Researchers at the University of Texas see the future of vaccines.

M. Stephen Trent, a professor of molecular biosciences, and doctoral candidate Brittany Needham were among the UT researchers who published a paper a year ago that explains how they re-engineered 61 strains of Escherichia coli bacteria as a way to make vaccines more potent. They are now building on that work, which showed that a molecule on the E. coli bacteria called lipid A can be changed and purified to become an adjuvant, a chemical added to vaccines to trigger a stronger immune system response.

Although vaccines — reviled by some — are considered one of the 20th century's greatest inventions, some lose their punch over time, while others are less than 100 percent effective when new. Stronger adjuvants that use pieces of a disease-causing organism can change that. They rally more disease-fighting soldiers to flood the bloodstream and attack the threatening virus or bacteria.

"That's why we call adjuvants 'vaccines' dirty little secret,'" said Trent, associate director of UT's new Center for Infectious Disease.

His lab didn't invent the adjuvant, but they devised a novel way of using it. They won praise for their paper in the journal Proceedings of the National Academy of Sciences and have since piqued the interest of pharmaceutical companies. They are moving their research to the next step by tweaking the formula to make any potential new vaccines even stronger. To do that, they are adding a foreign substance, called an antigen, to the cocktail to trigger the body's production of disease-fighting antibodies.

The ingredients have to be measured out just right to produce a healthy immune response. If Trent's lab did not engineer the adjuvant, for example, the resulting vaccine could

overwhelm a person's immune system and be toxic, Trent said. If there's not enough adjuvant, the vaccine's power is too limited.

Needham is testing the re-jiggered formulas on mice and is getting good results, she said.

Some of the 61 E. coli strains are more promising than others. "We are focusing more on five," Needham said. "Hopefully, we provided options … so you have a selection to choose from" when making a vaccine.

Trent said the goal is to create a library of lipid A adjuvants for making future vaccines. The research team obtained funding from the National Institutes of Health, the Texas Higher Education Coordinating Board and the Army Research Office.

A partnership with a pharmaceutical company would be the next step, Trent said.

Trent and Needham's work was heralded as smart and sophisticated by national vaccine experts who are eager to see where it goes.

"There's a lot of potential … but a lot of things need to be done" before a product can go to market, said Shahida Baqar, a program officer at the National Institute of Allergy and Infectious Diseases.

Her colleague, program officer Robert Hall, called the research "new and exciting."

Trent has been working with lipid A since 1999, when he was at Duke University. Ten years later, the U.S. Food and Drug Administration approved its use as part of the human papilloma virus vaccine. It was the first new adjuvant in more than 70 years.

Lipid A is attractive because it activates multiple parts of the immune system.

Other labs also are working with lipid A, said Alan Barrett, director of the Sealy Center for Vaccine Development at the UT Medical Branch in Galveston. Some researchers at Sealy, a comprehensive vaccine development center, are using tiny fibers called nanofibers in their vaccine development work.

"In the 20th century, vaccine development was all about making childhood vaccines so children would survive to adulthood," Barrett said. "In the 21st century, we're really interested in making adults live longer."

The Trent lab's research is "an exciting step forward," he said, adding that he is seeing an emphasis on developing vaccine cocktails. He anticipates a time when vaccines can be personalized so that people who need a bigger immune system boost — the elderly, for example — get a more potent vaccine.

In November, UT applied to patent the process by which Trent's lab re-engineered E. coli. Trent is hopeful it will lead to new vaccines to fight numerous infectious diseases, including flu, whooping cough, pneumonia and cholera.

Further, he believes the same re-engineered bacteria can be used to make drugs to fight cancer and sepsis, a potentially deadly blood infection.

He hopes that his lab's work will lead to new vaccines in the next 10 years that are cheap and easy to use — given orally, rather than injected. That would make the vaccines attractive to health care providers in the developing world, where costs and refrigeration are factors.

"If you want to do really good in the world, you need to have a really cheap vaccine," Trent said. "I like the idea of doing something good."