Study: New vaccine delivery system may be more effective

January 25 2010, By Krishna Ramanujan

(PhysOrg.com) -- An interdisciplinary team of Cornell researchers has devised a new way to make vaccines that promises to prevent diseases much more cheaply.

Traditional vaccines can be ineffective and expensive. Now, an interdisciplinary team of Cornell researchers has devised a new way to make vaccines that promises to prevent diseases much more cheaply.

The new technique, described online in the journal Proceedings of the National Academy of Sciences, which involves fusing a novel component to the vaccine to boost its effectiveness, can effectively stimulate antibodies to target bacterial infections, including ulcers, flesh-eating skin infections and leptospirosis. The researchers also are working on modifying the method to create vaccines that stimulate cell-mediated immune responses required to fight viral diseases and some cancers.

"There are a lot of children dying because they can't get a vaccine that is cheap and effective enough," said co-author David Putnam, associate professor of biomedical engineering and chemical and biomolecular engineering. David Chen, a former graduate student in Putnam's lab who is currently a scientist at Wyeth-Ayerst Laboratories in Andover, Mass., is the paper's lead author, while Matthew DeLisa, associate professor of chemical and biomolecular engineering, and virologist Nikolaus Osterrieder in Cornell's College of Veterinary Medicine are also co-authors.

Vaccines introduce a foreign protein (called an antigen) into the body to stimulate an immune response that the body then remembers when faced with the same protein in the future. The body either remembers the antigen's unique structure or the sequences of its amino acids. To boost the immune system's response to an antigen, researchers typically also attach an agent known as an adjuvant.

Researchers have found that the common adjuvant, aluminum hydroxide, can be unreliable because it can destroy the antigen's structure, and the antigen's amino acid sequences may also degrade over time, giving a vaccine limited stability. Purifying vaccines made with aluminum hydroxide involves a complicated and expensive process using specialized equipment.

Now, Cornell researchers from departments across campus have collaborated to substitute aluminum hydroxide with a new adjuvant called ClyA, which can be produced and fused with any desired protein within genetically engineered Escherichia coli bacteria. The E. coli creates a compound of ClyA fused with the desired antigen inside the E. coli cell. The ClyA-antigen then buds off from the E. coli's cell membrane, forming a vesicle containing the vaccine. Since the vesicle is very small compared with the E. coli, purifying this delivery system involves spinning the mixture through a simple centrifuge, which separates the particles and isolates the vaccine cheaply.

"ClyA works as well as aluminum hydroxide without the drawbacks," said Putnam. "There is a strong probability that we can fuse ClyA with any other protein, and it will give a strong immune response."

The researchers tested their method by fusing ClyA with a green fluorescent protein, which is visible inside the vesicles. They also knew that the fluorescent protein retained its structure because the protein only lights up when properly folded. The researchers are collaborating with

Cornell's Baker Institute for Animal Health to develop animal vaccines and with Weill Cornell Medical College to develop cancer vaccines.

Provided by Cornell University