

UC SANTA BARBARA

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Gail Gallesich Brown

## **UCSB Lab Discovers Cross-Protective Vaccine**

New medical research at the University of California, Santa Barbara represents a significant step toward preventing infections through the development of vaccines that elicit protection against several different disease-causing strains.

The work, by UCSB biologists Douglas M. Heithoff, Steve Julio, David A. Low, Robert L. Sinsheimer, and Michael J. Mahan, is an extension of earlier breakthrough research in which a strain of Salmonella was forced, through a new DNA technology, to "show its hand," thus allowing the organism to defend against it. The technology used in this vaccine is called DNA adenine methylase, or "Dam," and was discovered by Mahan's team in 1999.

The new developments are described in articles in the November and December issues of the journal *Infection and Immunity*.

"One of the main obstacles of vaccine development is that there are often many strains that can cause disease in individuals vaccinated against a single strain or a small set of strains," said Mahan. "This is the principle reason why different flu vaccines need to be administered every year, and why disease can occur in vaccinated individuals.

This obstacle is a big problem for Salmonella, which has more than 2500 pathogenic strains. Using Dam technology, we have developed a Salmonella vaccine that is

cross-protective to different salmonella strains."

He said that the development of cross-protective vaccines is paramount to the defense against biowarfare agents wherein pathogenic strains may have been "weaponized" by selecting for strains that overcome the immunity in vaccinated individuals. In effect, this renders many of our current vaccines obsolete.

In the December issue of Infection and Immunity, Mahan explains that "We have expanded the use of Dam technology to *Yersinia pseudotuberculosis* which is a very close cousin of the human plague-causing organism, *Yersinia pestis*.

Dam mutants of *Yersinia* are completely disabled in their ability to cause disease.

Immunized with these Dam mutants fully protects against *Yersinia* infection in other words these immunized mice can't be killed by virulent *Yersinia*."

Mahan noted that his research team is now exploring whether the Salmonella Dam technology can be used to induce immunity to other bacterial and viral pathogens.

This work has been recently funded by a University of California BioSTAR biotechnology grant of \$1 million. (BioSTAR -- Biotechnology Strategic Targets for Alliances in Research -- is a University of California-wide biotechnology matching grants program that forges partnerships among businesses, UC scientists, engineers and students.)

The UCSB research team has formed the company Remedyne, a private biotechnology company focused on developing potent immune stimulating vaccines and antimicrobial agents to treat infectious diseases in humans, companion animals and livestock. The University of California owns the patent for the Dam technology which is licensed to Remedyne. In human health research, the company is focusing on technology to combat cancer, infections of the ear, respiratory and urinary tract.

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draw inspiration from the beauty and resources of our extraordinary location at the edge of the Pacific Ocean.