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Breakthrough On Microbial Disease Published In Science

When it comes to bacterial disease, the wake-up call has been sounded, -- Michael J. Mahan

(Santa Barbara, CA) A discovery with profound implications for human health was announced today by biology researchers at the University of California, Santa Barbara.

In a major breakthrough in the treatment and prevention of infectious disease, the researchers have found a way to disarm microbial pathogens using the discovery of a "cloaking" device, effectively stopping them in their tracks in animal studies.

The findings, published in the May 7 issue of the journal Science, will be applied toward the development of a new generation of vaccines and antibiotics, according to the researchers.

Michael J. Mahan, associate professor of biology, and three colleagues -- graduate student Douglas M. Heithoff and professors Robert L. Sinsheimer and David A. Low -- report that they have identified a Ômaster switch' that controls the production of many of the weapons that are required for bacterial infection.

When they knock out the switch, the bacteria are completely disabled in their ability to cause disease.

The master switch is the same within many pathogenic bacteria, including Vibrio cholerae (cholera), Yersinia (plague), Salmonella (typhoid fever), and Shigella (dysentery), and may apply to the treatment of these bacterial infections as well as others that are a major cause of death of AIDS and cancer patients.

Currently, microbial infections are the leading killer worldwide, responsible for 17 million deaths each year (almost three times the annual deaths due to cancer).

The discovery will eventually be a major aid in the fight against newly emerging, drug resistant pathogens.

"When it comes to bacterial disease, the wake-up call has been sounded," said Mahan.

"Our microbial defenses are crumbling as superior pathogens have emerged that can no longer be controlled by available antibiotics.

There are numerous warning signs including the recent emergence of drug resistant tuberculosis, staphylococcus, and streptococcus."

Mahan studies salmonella, a rod-shaped bacteria that causes food poisoning in 4 million people in the United States every year.

There are 2,500 different strains of salmonella, and they are responsible for diseases ranging from food and blood poisoning to typhoid fever.

Young children are the most vulnerable, with infants being 15 times as susceptible as adults.

The Science paper describes the results of using a novel approach to identify genes in bacteria that come alive when they infect mice, but are "cloaked" in the petri dish.

Mahan compares the bacteria to a Trojan horse to describe the way they hide their destructive weapons until they are inside a cell. "You can't fight what you can't see," said Mahan.

But Mahan has discovered a way to get the bacteria to reveal itself fully to the immune system, to show its hand. "Bacteria are great poker players," he said. "But no matter how good a poker player you are, if you lay your cards down, you're dead."

Mahan's new mutated strain of Salmonella, with the master switch on, now shows all its "cards," its tricks for getting past the gut and into organs and tissues. "This has two important consequences," Mahan said, "the bacteria are completely disabled in their ability to cause disease and these crippled bacteria work as a vaccine since they stimulate immune defenses to defend against subsequent infections."

Vaccines and antibiotics developed out of this discovery are expected to provide a major boon to human health worldwide, particularly in countries where many people die from bacterial infections.

While application to human vaccines and antibiotics may be down the road a few years, Mahan sees significant impact on human health happening very soon -- through the food supply.

It might be possible, for example, to vaccinate chickens and cows to develop Salmonella-free poultry and E. coli-free beef.

Such vaccines are sorely needed as the level of contamination in the food supply is expected to worsen due to large scale animal processing and distribution practices, according to Mahan.

"We are proud of professors Mahan, Sinsheimer, and Low as well as Mr. Heithoff for this important and exciting discovery," said UCSB Chancellor Henry T. Yang. "These UCSB scientific colleagues have our respect and appreciation for their dedication in studying the causes of human and animal disease."

Mahan joined the faculty at the University of California, Santa Barbara in 1993 after four years as a post-doctoral fellow at Harvard University Medical School.

He shared the prestigious Association for the Advancement of Science Newcomb-Cleveland Prize for the top paper published in the journal Science.

He is recipient of an American Cancer Society Junior Faculty Science Research Award and a Beckman Young Investigator Award.

At UC Santa Barbara, he received the Plous Award in 1998, which honors the assistant professor in the College of Letters and Science who has made the greatest contribution to the intellectual life of the university through outstanding teaching, research, and community service.

He received a B.S. in biochemistry and a M.S. in genetics from the University of California at Davis. In 1988 he received his Ph.D. in genetics from the University of Utah.

Editors: An audio version of the research announcement described in this release will be available immediately following the press announcement on May 6.

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