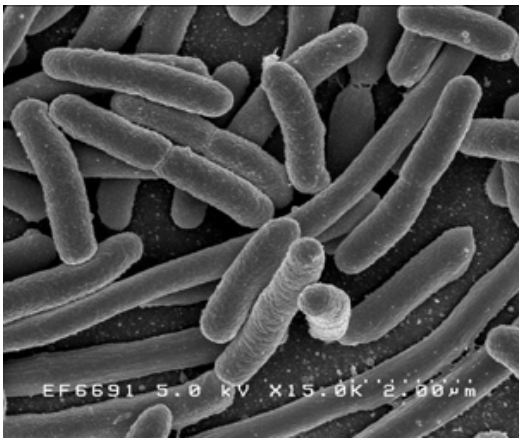
Press Release
An antibiotic effect minus resistance
Friday, October 28, 2011



Bacteria Credit: NIAID

After 70 years, antibiotics are still the primary treatment for halting the spread of bacterial infections. But the prevalence of antibiotic resistance is now outpacing the rate of new drug discovery and approval.
A microbiologist at the University of Wisconsin-Milwaukee (UWM) has discovered a different approach: Instead of killing the bacteria, why not disarm them, quashing disease without the worry of antibiotic resistance?
Ching-Hong Yang, associate professor of biological sciences, has developed a compound that shuts off the "valve" in a pathogen's DNA that allows it to invade and infect.
The research is so promising that two private companies are testing it with an eye toward commercialization.
"We analyzed the genomic defense pathways in plants to identify all the precursors to infection," says Yang. "Then we used the information to discover a group of novel small molecules that interrupt one channel in the intricate pathway system."
Yang and collaborator Xin Chen, a professor of chemistry at Changzhou University in China, have tested the compound on two virulent bacteria that affect plants and one that attacks humans. They found it effective against all three and believe the compound can be applied to treatments for plants, animals and people.
The work was published online this month in the journal *Antimicrobial Agents and Chemotherapy*.
Urgent concerns about antibiotics
The economic costs and health threats of antibiotic resistance have become

so serious that the World Health Organization (WHO) this year dedicated World Health Day to call global attention to the issue.

Antibiotics are routinely sprayed on crops and widely used in factory farming of animals, which causes resistance to develop quickly. That antibiotic resistance is then transferred to humans who eat the food containing antibiotic-resistant bacteria.

Among the bacteria tested by the researchers is Pseudomonas aeruginosa, which is resistant to a broad range of antibiotics. It causes infections in people with compromised immune systems, such as HIV and cancer patients. It's also responsible for lung infections in patients with cystic fibrosis, and hospital-related infections such as urinary tract infections, pneumonia and infections from burns.

The fatality rate from these is about 50 percent. Hospital-acquired urinary tract infections by P. aeruginosa alone cost more than $3.5 billion a year in the U.S.

Road to the market

The research has attracted interest from two companies. Creative Antibiotics, a Swedish pharmaceutical company, is testing the compound and derivatives for human therapeutic uses and Wilbur-Ellis Agribusiness Division, based in Washington and California, is examining them for agricultural uses.

Despite the constant threat of disease in agriculture, says John Frieden, a biologist and R&D manager with Wilbur-Ellis, the industry has not had access to any new antibiotics in many years. U.S. regulatory agencies do not allow agribusiness to use antibiotics that are also used for human health – even if they would be effective.

"The thing that caught my attention," Frieden says, "was that this was not an antibiotic, but it accomplishes the same thing as an antibiotic."

Although he says it is too soon to tell if a product could spring from the research, the approach is "incredibly unique. I've never seen anything that is even close to a commercial application like this. It could be very big."

The researchers have filed two patents on the work through the UWM Research Foundation (UWMRF), and Yang is partially funded through two UWMRF Bradley Catalyst Grants and a UWM Research Growth Initiative (RGI) grant.

Virulence factors

The compounds Yang and Chen have developed are unique because they take aim at one component of a cluster that makes pathogenic bacteria harmful.

One of those components, the type III secretion system (T3SS), gives pathogens their ability to invade a cell, letting in a host of proteins that enhance the bacterium's ability to cause disease.

"These bacteria are very smart," says Yang. "They grow a narrow appendage that acts as a 'needle,' injecting the virulence factors, such as toxins, into the host cell. The host cell cannot recognize the pathogen's 'needle,' so its defense mechanism is not triggered."

Yang and Chen's compounds block the production of T3SS. Although they have tested the compounds on only three pathogens, they have reason to believe the compounds will be effective against far more.

"T3SS exists in many different kinds of disease-causing bacteria," says Yang, "so the compounds can target multiple pathogens. That's the beauty of it."

He and his lab members are now working on developing more derivatives that could be effective against different kinds of harmful bacteria.
Yang also believes that their therapeutic compounds, like antibiotics, can offer both a broad spectrum of activity and be unique to a specific pathogen, depending on which virulence elements are targeted.
###
University of Wisconsin - Milwaukee: **http://www.uwm.edu**

Thanks to University of Wisconsin - Milwaukee for this article.