Researchers find new chink in a 'superbug's' armor

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Infections from drug-resistant forms of Staphylococcus bacteria are skyrocketing and have even recently made headlines by debilitating some of the NFL's toughest players. Tools to fight these bugs are few, but now University of Florida researchers have used cutting-edge genetic analysis to find a new weak spot in this "superbug's" armor.

The weak spot is a specialized enzymatic process responsible for producing folate. Among humans, folate is best known for being an essential part of a pregnant woman's diet. This is because folate plays an essential role in cell division.

Humans can't produce folate, so we get it by eating leafy green plants. Bacteria can perform this process, however. This means that the folate manufacturing process within a bacterium is the perfect target for drugs that stop pathogens from growing and spreading—because that drug won't harm humans.

"The problem, of course, is finding the enzymes within that process you want to target," said Valérie de Crécy-Lagard, UF microbiologist and lead author on the research, which appears in the Dec. 8 issue of the *Journal of Biological Chemistry*.

There are millions of chemical reactions that drive the functioning of a cell, she said. Finding the right one is akin to finding a needle in a haystack.

However, the researchers didn't have to look using arduous lab experiments. Instead, Crécy-Lagard used a method known as comparative genomics. For years, researchers around the world have been filling a computer database of bacterial genetic knowledge. By digitally comparing the genetic makeup of more than 100 bacteria, the researchers were able to deduce which gene was responsible for many of the enzymes that produce folate—and thus were able to track down a new enzyme to target for an antibacterial attack.

"This process is far from over, however," Crécy-Lagard said. "We now have to find the best way to attack this new target—and that could take years."

Nonetheless, the resulting antibacterial could one day prove vital, said Dr. Kenneth Rand, a professor of pathology, immunology and laboratory medicine at UF's College of Medicine.

"These pathogens seem to keep adapting to everything we can throw at them," he said. "The bacteria have the opportunity to change in every person that becomes infected. There are a countless number of Staph strains out there. Tomorrow, there are only going to be more."

A 2005 study from Vanderbilt University Medical Center found that nearly 10 percent of children in the U.S. carry drug-resistant Staph bacteria in their noses. In 2002, only 1 percent carried the germ.

The bug is only harmful, however, if it encounters an open cut or other vulnerable area on the body. This makes it especially dangerous in hospital and locker-room settings.

"We do not need to think only about Staph, though," Crécy-Lagard said. "These same enzymes are found in many other harmful bacteria, which could mean that what we design to attack this target could be a more

universal antibiotic."

In fact, the enzymatic target is shared by more than 40 other known pathogens.

"Comparative genomics allowed us to find a very effective target," Crécy-Lagard said. "This is a powerful tool that lets us dissect pathogens from the genome up. In the future, many new drug targets are going to be found this way."

Source: University of Florida