New Synthetic Compound Message to Drug-Resistant Bacteria: 'Resistance is Futile'

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(PhysOrg.com) -- Scientists at the University of Massachusetts Amherst and the University of Illinois have developed a smart new synthetic compound that not only targets some drug-resistant bacteria and kills them, but the new antibiotic takes away the germs' most potent defense - the mutation that could provide new resistance will also kill them, leaving no escape.

As polymer scientist Gregory Tew at UMass explains, “This newly designed molecule inserts into the cell wall of bacteria and changes its curvature. Instead of forming stable membranes, cells treated with the new antibiotic have increased curvature which makes a hole form in the wall, killing the cell.” Tew says the new antibiotic uses compounds called phenylene ethylnylenes that mimic the body’s own antimicrobial proteins.

“Understanding the details of how this antibiotic works is essential for expanding our tools for fighting infectious diseases,” Tew notes. Bacterial resistance to conventional antibiotics is a major public health problem. Penicillin could once be counted on to kill bacteria that can cause pneumonia, for example, but germs in the Staphylococcus and Enterococcus families have evolved so penicillin no longer works. Now, they’ve also learned to resist newer antibiotics such as tetracycline, streptomycin and gentamicin.

The new compound’s hole-punching ability depends strongly on the presence of a lipid or fat molecule, phosphoethanolamine (PE), found in

bacterial cell membranes, he adds. “This new antibiotic likes PE-rich membranes, which is ideal because gram-negative bacteria are rich in PE while human cells are not.”

In their experiment reported in the last 2008 issue of the *Proceedings of the National Academy of Sciences*, Tew and co-author Gerard Wong of the University of Illinois compared survival rates in two strains of E. coli bacteria grown in separate Petri dishes. One group was engineered so it lacked the PE lipid in its membranes while the other group had the PE layer.

The researchers treated both groups with the new synthetic hole-punching antimicrobial, at the same time giving two more groups a traditional antibiotic, tobramycin that does not attack the PE membrane but rather a cell structure called a ribosome. Results show that the new antibiotic successfully attacked the E. coli strain rich in PE, but it did not work against the other strain without PE. By contrast, tobramycin killed both strains, pinpointing that the bacteria’s vulnerability to the new compound lies in its PE layer.

Provided by University of Massachusetts Amherst