

Research provides insight into new drug resistance in hospital microbes

July 13 2011

Hospitals struggle to prevent the infections that complicate treatment for cancer, joint replacement, heart surgery and other conditions. Hospital-acquired infections are often resistant to multiple antibiotics, leading to approximately 100,000 deaths and more than \$30 billion in additional health care costs yearly. New drugs are being developed to combat these infections, but resistance invariably emerges to these last-line drugs.

Daptomycin, a new antibiotic approved by the FDA in 2003, is used to treat infections caused by multi-drug resistant bacteria, including staph and microbes known as enterococci. Scientists in the Department of Ophthalmology at Mass. Eye and Ear and Harvard Medical School, and the pharmaceutical company Cubist, which produces daptomycin under the trade name Cubicin, teamed up to discover the basis for resistance that has now begun to emerge to daptomycin in the enterococci. Their discovery of a new mechanism of resistance is described in an article in the current (July) issue of [Antimicrobial Agents and Chemotherapy](#).

In a two-week experiment, investigators were able to recreate the development of resistance in the laboratory in a manner similar to that which occurred in the hospital. Using new genome sequencing technology, they resequenced the entire genome of the resistant enterococcus strain to identify all of the [genetic changes](#). The researchers found changes in genes that they were also able to identify in hospital daptomycin resistant strains. Mutations in a gene encoding an enzyme called cardiolipin synthase were able by itself to confer daptomycin resistance to a laboratory strain of enterococcus.

"Knowing the changes that correspond with resistance not only tells us what happens in [resistant strains](#), it tells us much about how exactly how the antibiotic works, providing new ideas for better treatment and next generation drugs," observed Dr. Michael S. Gilmore, a scientist at Harvard Medical School and the Mass. Eye and Ear, and the corresponding author.

Provided by Massachusetts Eye and Ear Infirmary

Citation: Research provides insight into new drug resistance in hospital microbes (2011, July 13) retrieved 25 April 2024 from

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