

Genes involved in antibiotic resistance vary within a species

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The recent emergence of multidrug resistance (MDR) in *Acinetobacter baumannii*, a bacteria that causes infections primarily among seriously ill patients in the intensive care unit who may have reduced immune systems, has raised concern in health care settings worldwide. When comparing the genome sequence of three MDR *A. baumannii* isolates and three drug-susceptible *A. baumannii* isolates, Case Western Reserve University School of Medicine found that one variation of bacteria would respond to antibiotics while another variation of the same bacteria may not.

A. baumannii is currently recognized by the Infectious Diseases Society of America as one of the most important pathogens threatening our health care delivery system.

Over the last 10-15 years, *A. baumannii* has become increasingly resistant to antibiotics and now more than one-third of infections are MDR, which means these pathogens are resistant to at least three different classes of antibiotics. This pattern of resistance to many antibiotics limits the ability of physicians to treat serious infections caused by *A. baumannii*.

The study, led by Mark Adams, Ph.D., Associate Professor in the Department of Genetics at Case Western Reserve University School of Medicine, is titled "Comparative Genome Sequence Analysis of Multidrug-Resistant *Acinetobacter baumannii*", and is in the December issue of the *Journal of Bacteriology*.

Adams first sequenced the genome of an MDR isolate and his collaborator in Buffalo, Steven Gill, Ph.D., Associate Professor of Oral Biology at SUNY Buffalo, sequenced two drug susceptible isolates to learn more about the genes (the genome contains the complete set of genes) that control resistance to antibiotics. Adams then compared the new sequence with genomes of other MDR and drug susceptible isolates,

comparing six complete genomes.

What they found is that within a hospital or even a person, there can be a variation within the bacteria which means that it can affect how the infection reacts to antibiotics.

"A key conclusion of our study is that even very closely related isolates of *A. baumannii* can differ significantly in the set of resistance genes that they carry," said Adams. "It is known that resistance genes can be shared between bacteria (horizontal gene transfer), and it appears that this is a frequent event, with genes entering a genome and being deleted even across a single outbreak."

"We used to think—you treat this bacteria with this drug—but now we know that you have to look more carefully not just at the bacteria but at each one's genetic characteristics," said Adams. "This is an argument for targeted therapy in infectious disease because you want to select an antibiotic that will be effective against the particular genetic characteristics of the bug that's causing the infection."

The scientists also found that each isolate has a somewhat different set of genes.

"About three-fourths of the genes are shared by all the isolates, while the remainder are unique to different subsets," said Adams. "We identified 475 genes that are shared by all six clinical isolates of *A. baumannii* but are not present in a closely related *Acinetobacter* species that does not cause infections. These genes merit further study to help figure out what makes *A. baumannii* able to live in association with humans and cause disease."

Source: Case Western Reserve University

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