

Tracking the evolution of antibiotic resistance

February 1 2013

With the discovery of antibiotics, medicine acquired power on a scale never before possible to protect health, save lives, and reduce suffering caused by certain bacteria. But the power of antibiotics is now under siege because some virulent infections no longer respond to antibiotic drugs.

This antibiotic resistance is an urgent <u>public health threat</u> that a team of researchers from Sabanci University in Istanbul, Turkey, and Harvard Medical School and Harvard University in Cambridge, Mass., aim to stop. Their approach is based on an automated device they created that yields a new understanding of how antibiotic resistance evolves at the <u>genetic level</u>. The team will present its work at the 57th Annual Meeting of the Biophysical Society (BPS), held Feb. 2-6, 2013, in Philadelphia, Pa.

Called the "morbidostat," the device grows bacteria in various concentrations of antibiotic. This enabled researchers to identify the concentrations at which the antibiotics stopped working and the bacteria became resistant to therapy. Next, they targeted key genes involved in creating the drug-resistant states. Their approach documented real-time changes in genes that gave bacteria an advantage in evolving to "outwit" antibiotics.

Knowledge at the gene level can be applied to the molecular design of the next generation of bacteria-killing antibiotics.



"Morbidostat is designed to evolve bacteria in conditions comparable with clinical settings," explains Erdal Toprak of Sabanci University. "Combined with next generation genome <u>sequencing technologies</u>, it is possible to follow the evolution of resistance in real time and identify resistance-conferring genetic changes that accumulate in the <u>bacterial</u> <u>genome</u>."

Data show an unusual survival profile of the common bacteria they used, Escherichia coli. "We identified striking features in the evolution of resistance to the antibiotic trimethoprim," Toprak says. It was these unusual features that helped them isolate the gene involved in conferring <u>antibiotic resistance</u> through multiple mutations.

The team's next steps will involve determining how this genetic information might one day be applied to drug design to develop new antibiotic therapies.

More information: Presentation #3390-Pos, "Evolution of antibiotic resistance through a multi-peaked adaptive landscape," will take place at 10:30 a.m. on Wednesday, Feb. 6, 2013, in the Pennsylvania Convention Center, Hall C. ABSTRACT: <u>tinyurl.com/bfcke65</u>

Provided by American Institute of Physics

Citation: Tracking the evolution of antibiotic resistance (2013, February 1) retrieved 23 April 2024 from <u>https://phys.org/news/2013-02-tracking-evolution-antibiotic-resistance.html</u>

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