Antibiotic Resistance and Bacterial Evolution: Using a Big Tool to Visualize a Big Problem

Antibiotics are drugs that are designed to stop bacteria from growing. Doctors use antibiotics to treat bacterial infections and prevent illness and death. However, populations of bacteria often evolve **resistance** to antibiotics over time, which makes the antibiotics less effective at treating infections.

Bacteria possess certain characteristics that allow them to quickly evolve antibiotic resistance. A bacterial cell replicates by copying itself, including its DNA. During the process of DNA replication, mistakes sometimes occur which leads to **mutations**, or changes in the DNA sequence. Some of these mutations may change the bacteria so that antibiotics are no longer effective. When the population of bacteria is exposed to an antibiotic, bacteria without these mutations will die, while bacteria with these mutations will survive and replicate, passing on the ability to resist the antibiotic. As a result, the proportion of individuals within the population that contain these mutations will increase over time, as seen in **Figure 1** below.

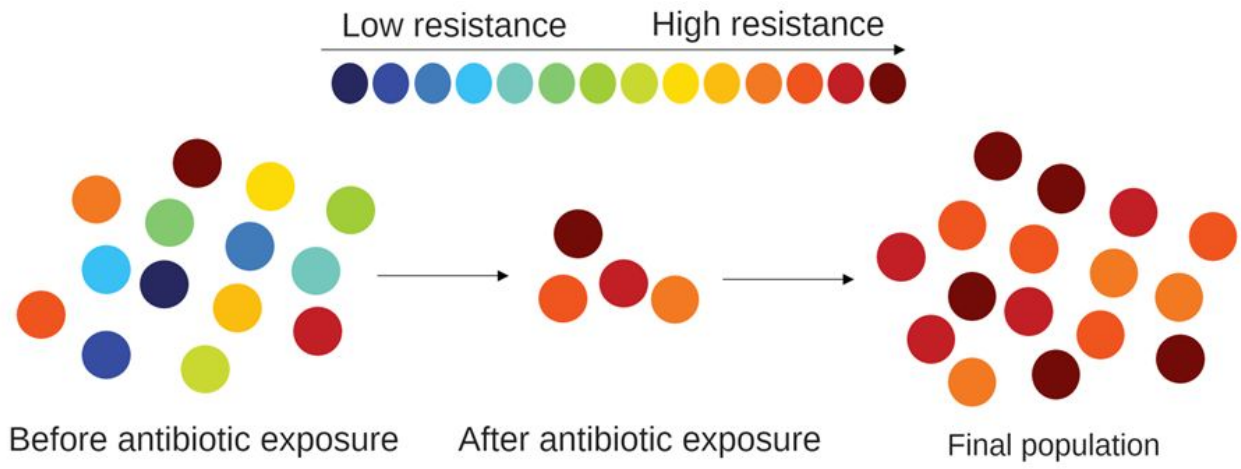

Figure 1. Bacteria Evolve Antibiotic Resistance Over Time. Within a population of bacteria, some organisms have mutations in their DNA that give them resistance to an antibiotic. In an antibiotic-free environment, these mutant organisms are present in the population at low proportions. When exposed to an antibiotic, however, bacteria without these mutations will die, and the resistant bacteria will survive and continue to replicate. Eventually the proportion of mutant bacteria will increase, and the population will be resistant to the antibiotic.

To study bacterial evolution and antibiotic resistance, researchers at Harvard Medical School and Technion–Israel Institute of Technology built a 60-cm x 120-cm dish called the Microbial Evolution and Growth Arena, or “MEGA-plate.” This large MEGA-plate, drawn below in **Figure 2**, is filled with a substance called agar, which contains nutrients that the bacteria need to grow. The lower level is solid agar, stained black so that the bacteria are easier to see. On top is a thinner Jello™-like agar that the bacteria can move through. The agar is divided into

sections that contain an antibiotic called Trimethoprim. There is no antibiotic at either end of the plate, and the concentration increases toward the center of the plate. *E. coli* bacteria, which can move through the Jello™-like agar using their flagella, are added to both ends of the MEGA plate, and a camera records their movement.

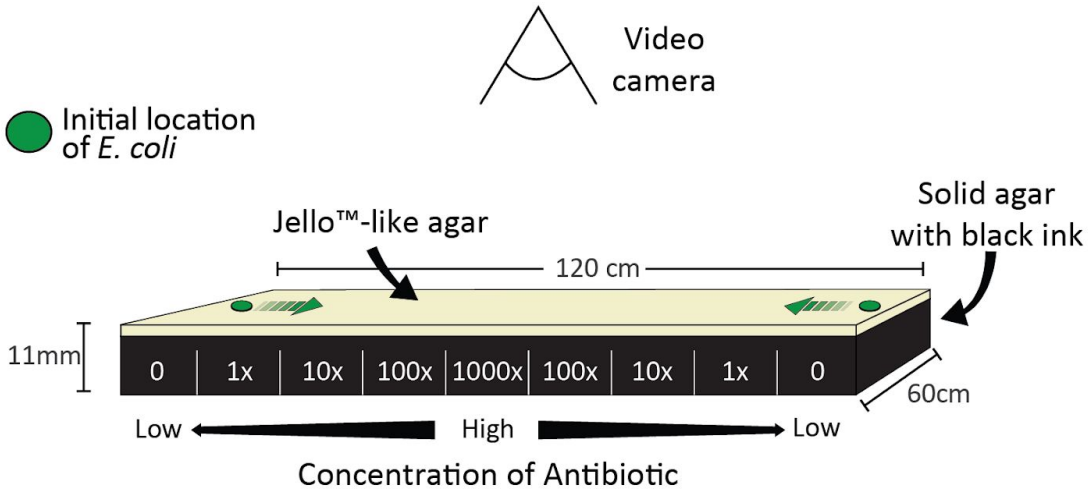

Figure 2. The MEGA-plate. The Microbial Evolution and Growth Arena (MEGA) plate is filled with agar, a specialized substance that contains all of the ingredients necessary for *E. coli* to grow. The concentration of trimethoprim, an antibiotic, increases towards the center of the plate. Scientists added bacteria at the outside edge of the plate, then videotaped the *E. coli* from above the MEGA-plate as the bacteria grew and spread toward the center of the plate. *Source:* Figure modified from Baym, *et al.,* 2016

When the *E. coli* reached a section with a higher concentration of antibiotic, the bacteria that do not have resistance mutations are unable to grow, while the mutant bacteria continue to replicate and spread. In only eleven days, resistant populations of bacteria traveled to the center of the MEGA-plate and had evolved resistance to the highest concentration of antibiotic that the researchers tested. The MEGA-plate is a useful tool that will allow scientists to observe bacteria as it evolves in different environments over time.

Reference

Baym, Michael, Tami D. Lieberman, Eric D. Kelsic, Remy Chait, Rotem Gross, Idan Yelin, and Roy Kishony. 2016. “Spatiotemporal microbial evolution on antibiotic landscapes.” Science 353: 1147-1151. doi: 10.1126/science.aag0822

BiteScientist Profiles

Rebecca Clements studies parasites, in particular the parasites that cause malaria, *Plasmodium falciparum*. She is currently a graduate student at Harvard University where she is researching the genes of *P. falciparum* to better understand how the parasite causes disease and to identify new targets for antimalarial drugs. When she's not in the lab, she spends her time dancing, cooking, and playing soccer.

David Mangus is a molecular biologist and former research scientist whose work focused on understanding how Baker's yeast, *Saccharomyces cerevisiae*, regulate their genes. He currently leads the biotechnology program at Brockton High School in Brockton, Massachusetts. If you can't find him in the lab, he's likely outside gardening or kayaking.