School in Boston, Mass., and his collaborators. This conclusion is based on viewing how cells change while growing on “microbial evolution and growth arena (MEGA)” plates, following those cells as they spread along large plates containing antibiotics as well as nutrients. Details appeared 9 September 2016 in Science (doi:10.1126/science.aag0822).

The MEGA-plate, which Kishony and his collaborators developed, consists of a 120- by- 60-cm dish filled with agar containing nutrients and different concentrations of antibiotics. Its size enables an antibiotic gradient to be maintained for about 10 days, allowing drug-sensitive *Escherichia coli* cells to grow, evolve, and generate sufficient numbers of mutations to withstand and migrate into higher and higher concentrations of the specific antibiotic to which they are being exposed.

For example, an early set of MEGA-plates contained four-step gradients of either trimethoprim or ciprofloxacin. *E. coli* cells were inoculated onto drug-free regions of plates and allowed to spread. When the inoculant cells reached antibiotic concentrations at which they could no longer grow, resistant mutants emerged and their descendents migrated successively into regions containing stepped-up concentrations of the specific antibiotic to which they are being exposed.

“Importantly, access to intermediate regions of moderate selection enables a range of evolutionary pathways to high-level resistance,” Kishony says. When bacteria were inoculated onto variant MEGA-plates in which they were challenged to go directly from no-drug to high-drug areas, they were unable to adapt. By moving through regions of escalating antibiotic intensity, the *E. coli* ultimately developed high levels of resistance, but it invariably came at the expense of growth rate. Although subsequent mutations compensated, in the absence of sufficient nutrients these very fit mutants became trapped.

“Thus, even though more fit, the bacteria with compensatory mutations were usually spatially restricted from contributing to the ultimate evolutionary success of the population,” says Michael Baym at Harvard Medical School, the project’s lead scientist. “The fitness of a bacterial population confronted by increasing antibiotic levels in natural and clinical setting is not driven by the fittest bacteria but rather by those that are both sufficiently fit and sufficiently close to the advancing front,” adds his colleague Tami Lieberman, also at Harvard Medical School.

These experiments have really captivated people—scientists and regular folks alike—not only because they let people see evolution as it happens, but also because the “films they took of bacteria evolving are just plain cool to watch,” says James Jeffrey Morris at the University of Alabama at Birmingham, adding: “This isn’t the Kishony lab’s first ‘gee whiz’ experiment.” And says Harmit Malik from the Fred Hutchinson Cancer Research Center in Seattle, Washington, there is “amazing value watching evolution in action for students: just like a chemical reaction taking place, seeing is believing.”

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**2016 SCIENCE AWARDS**

**One 2016 Nobel: Yeast-Based Autophagy Work; 3 MacArthurs: Microbiology**

**Jeffrey L. Fox**

The 2016 Nobel Prize in Physiology or Medicine, about $936,000 this year, recognizes Yoshinori Ohsumi of Japan for his efforts to understand autophagy, a fundamental process for degrading and recycling cellular components, research that he began by studying yeast. Separately, among the 2016 MacArthur Foundation Fellows, who receive $625,000 “genius awards,” are microbiologist Dianne Newman, who studies bacteria that played roles in shaping the Earth as well as in modern biomedical contexts; geobiologist Victoria Orphan, whose focus is on microbial communities in extreme environments; and physical biologist Manu Prakash, who invented several devices that can be used for diagnostic work in microbiology. Also noteworthy, the 2016 LaskerDeBakey Clinical Medical Research Award is shared by three scientists whose research on hepatitis C virus (HCV) led to development of drugs for treating HCV infections.

During the 1990s, Ohsumi, who is now a professor at the Tokyo Institute of Technology, identified genes in the yeast *Saccharomyces cerevisiae* that are essential for autophagy, determined its underlying mechanism, and later showed that similar mechanisms are at work in human and other mammalian cells. These studies led to insights about autophagy in mammalian cells, where mutations contribute to various diseases, including type 2 diabetes, cancer, and neurological diseases such as Parkinson’s.

Among the 2016 MacArthur Foundation fellows whose work touches on microbiology, both Newman and Orphan are faculty members at California Institute of Technology in Pasadena, Calif., while Prakash is on the faculty at Stanford University in Stanford, Calif. Both Newman and Orphan are studying microorganisms in extreme or exotic environments, while Prakash works on nanoscale inventions.

Some bacteria use metals such as arsenic and iron instead of oxygen in electron-transfer reactions that are necessary for their metabolism. Indeed, some ancient bacteria depended on iron rather than water for a form of photosynthesis.
sis, consistent with this type of anoxygenic metabolism catalyzing deposition of early banded-iron geologic formations, according to Newman and her collaborators. They also are studying the pathogen *Pseudomonas aeruginosa*, which can use electron-shuttling phenazines as a means for surviving within lungs.

Similar to Newman, Orphan studies microorganisms in places where oxygen is scarce—in this case, deep-sea beds. Some of these microbes depend on anaerobic oxidation of methane, a process that helps to prevent this greenhouse gas, which is being released from underwater seeps, from reaching the atmosphere. Another line of her research focuses on an oxidative, extracellular electron transfer process that couples methane-consuming archaea with sulfate-reducing bacteria.

Among other projects, Prakash recently invented several “frugal science” devices that may prove useful for diagnosing infectious diseases in field settings. For example, he incorporated an origami-based folding design into a lightweight optical microscope that is being field-tested for use in public health and biomedical settings. Meanwhile, a specialized microfluidic chip is being developed to collect nanoliter-scale samples of saliva from mosquito bites to screen for pathogens. Such a device might be used, for example, to collect surveillance data during mosquito-borne disease outbreaks such as the one now involving the Zika virus.

Finally, the 2016 LaskerDeBakey award recognizes three scientists for their research on HCV. Specifically, Ralf F. W. Bartenschlager of the University of Heidelberg in Germany and Charles M. Rice at Rockefeller University in New York, N.Y., developed a means for growing this virus in cells in vitro. The third recipient, Michael J. Sofia, who now is at Arbutus Biopharma, headquartered in Burnaby, British Columbia, Canada, used this in vitro system to evaluate candidate drugs for treating HCV infections. That drug development work was done at Pharmasset, a company acquired by Gilead Sciences of Foster City, Calif.

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