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In Real Time, a Virus Learns a New Way to Infect

By CARL ZIMMER

Viruses regularly evolve new ways of making people sick, but scientists usually do not become aware of these new strategies until years or centuries after they have evolved. In a [new study](#) published today in the journal *Science*, however, a team of scientists at Michigan State University describes how viruses evolved a new way of infecting cells in little more than two weeks.

The report is being published in the midst of a controversy over a deadly [bird flu](#) virus that researchers manipulated to spread from mammal to mammal. Some critics have questioned whether such a change could have happened on its own. The new research suggests that new traits based on multiple mutations can indeed occur with frightening speed.

The Michigan researchers studied a virus known as lambda. It is harmless to humans, infecting only the gut bacterium *Escherichia coli*. Justin Meyer, a graduate student in the biology laboratory of Richard Lenski, wondered whether lambda might be able to evolve an entirely new way of getting into its host.

The standard way for lambda to get into a cell is to latch onto its outer membrane, attaching to a particular kind of molecule on the surface of *E. coli*. It can then inject its genes and proteins into the microbe.

Mr. Meyer set up an experiment in which *E. coli* made almost none of the molecules that the virus grabs onto. Now few of the viruses could get into the bacteria. Any mutations that allowed a virus to use a different surface

molecule to get in would make it much more successful than its fellow viruses. “It would have a feast of E. coli,” Dr. Lenski said.

The scientists found that in just 15 days, there were viruses using a new molecule — a channel in E. coli known as OmpF. Lambda viruses had never been reported to use OmpF before.

Mr. Meyer was surprised not just by how fast the change happened, but that it happened at all. “I thought it would be a wild goose chase,” he said.

To see if this result was just a fluke, Mr. Meyer ran his experiment over again, this time with 96 separate lines. The viruses in 24 of the lines also evolved to use OmpF.

The researchers then sequenced the genomes of the evolved viruses and were surprised to find that this transformation always required four mutations. In all the lines that could grab OmpF, those four mutations were identical, or nearly so. No single mutation could allow the viruses to start latching onto OmpF. Even three out of four mutations brought no change. Only after they developed all four mutations could the viruses make the switch.

The results from the experiment suggest that the mutations initially help the viruses do a better job of hooking onto the original molecules after they became scarce. “When you put all four together, you get this entirely new function,” Mr. Meyer said.

The new experiment provides a surprising glimpse at how easily viruses can evolve entirely new traits — and thus give rise to new diseases. A debate has swirled around whether a dangerous strain of avian influenza called H5N1 could turn into a global killer. H5N1 spreads easily from bird to bird, but it infects humans only rarely. Last year, however, a team of scientists ran experiments in which a highly lethal H5N1 virus gained the ability to spread among mammals. In response to the urging of a federal advisory board, the scientists will withhold key details when they publish their research. But according to news reports, the team, based at the Erasmus Medical Center in the Netherlands, found that it took five mutations to

transform [the flu](#).

Some critics have argued that full-blown evolution would not be able to mimic the highly artificial Dutch experiment. The chances that a single virus would acquire so many mutations at once are certainly small. In the case of lambda viruses, Mr. Meyer estimates the chance of all four mutations arising at once is roughly one in a thousand trillion trillion.

Yet the lambda viruses repeatedly acquired all four mutations in a matter of weeks. The mutations each arose one at a time in that compressed time frame. “There’s this thinking that it all has to come together at once,” Dr. Lenski said. “But that’s just not how evolution works.”

Paul Turner, an evolutionary biologist at Yale University who was not involved in the research, said, “I really love this paper.” He said such experiments may allow scientists to forecast evolution in viruses and bacteria at the molecular level — potentially helping to prepare for new diseases.

“It gives us hope of making evolution more predictive,” Dr. Turner said.

This article has been revised to reflect the following correction:

Correction: January 26, 2012

A previous version of this article misstated the probability that all four mutations for lambda viruses would arise at once. It is roughly one in a thousand trillion trillion, not one in a thousand billion billion.

