Zika Researchers Work to Crack Virus’s Genetic Secrets

Scientists in Brazil race to compile more data on how the deadly virus evolves before outbreaks worsen.

In June, a group of international researchers embarked on a Zika-hunting mission in Brazil, where the virus has infected tens of thousands of people and caused a dramatic rise in birth defects. They collected 2,000 samples from people around northeastern Brazil to better understand Zika’s genetics.
“What we know about Zika virus evolution is almost nothing,” said Marcio Nunes, one of the scientists leading the genetic-sleuthing expedition and the director of the Evandro Chagas Institute’s genetic core in Brazil.

As Zika continues its rapid spread across the Americas and into the U.S., scientists like Dr. Nunes are racing to answer a puzzling question: Is the virus evolving in ways that make it more dangerous?

Viruses are packaged strands of genetic material that, once inside cells, get copied over and over. With each replication, the virus can change slightly. Most of the time these changes are benign, but sometimes they can help it infect its hosts more easily or cause new types of health problems.
Several studies suggest Zika’s genome—its repertoire of genes—is relatively stable, but there is some early evidence that certain genes may be changing—in some cases in ways that could, in theory, help it to replicate more efficiently once inside human cells, prompting researchers to seek more data.

Scientists know two main families of Zika exist, the so-called African and Asian lineages.

They think the Asian version hopped from French Polynesia to the Americas in recent years. It was first detected in Brazil in 2015, but scientists think the virus may have made its way there as early as 2013, perhaps during the Confederations Cup soccer tournament. One study suggests Zika has been in Haiti since 2014.

To date, there are few full Zika genomes available to study. The U.S. public genome repository contains just 69. Dr. Nunes and his colleagues say their Brazilian road trip, dubbed ZiBra—short for Zika in Brazil Real Time Analysis—yielded roughly 60 new full genomes and about a hundred partial ones. The goal is to sequence hundreds more.

Some experts say that from what little data are available, it appears that the genetic changes scientists are now detecting are probably just part of Zika’s normal life cycle.

So-called RNA viruses, like Zika, are especially prone to changing because they have no way of checking for mistakes when they copy themselves. Most errors don’t affect virulence. Changes can also be detrimental to viral survival so they are weeded out because the viruses that have them don’t reproduce as effectively.

“This is a natural process. It’s not particularly alarming or scary. [But] it’s something we monitor,” said Ann Powers, a virologist at the U.S. Centers for Disease Control and Prevention’s diseases branch in Fort Collins, Colo. “We’ve not seen anything that would suggest there’s a substantial change.”
The slight tweaks, several scientists say, appear random, which is encouraging. It would be more worrisome, for instance, if they clumped in one particular gene.

Also, Zika isn’t actually well-suited to Aedes Aegypti mosquitoes, one of its primary modes of transmission, according to Paolo Zanotto, a Zika expert at the University of São Paulo. The insect creates a powerful evolutionary filter that keeps the virus pretty stable as it ferries it from one human host to the next.

“The mosquito resets the virus” to its current form, Dr. Zanotto said.

If Zika starts to pass directly from person to person more frequently, through sex for example, that could potentially allow it to change more rapidly, he said. Right now, “the virus has to negotiate
two distinct systems, human and invertebrate, that combined could impose different types of constraints to viral-genetic variation.”

Still, many questions remain. Zika was always regarded as “mild and weak,” said Dr. Zanotto. “How did it turn into a monster?”

One possibility is that past Zika outbreaks in Asia or Africa just weren’t large enough to produce the noticeable effects public-health workers are seeing in the Americas—or that over time, people in Asia and Africa have built up an immunity to the virus that those in countries like Brazil just don’t have. The recent outbreak in Singapore may put that theory to the test.

To get more answers, researchers need to test the virulence of different Zika strains using cells or animal models, not just through genetic analyses, viral-genetics experts said. Scientists could, for instance, make tweaks in the virus they suspect might increase virulence and test if those changes, in fact, have that effect under controlled conditions in a lab, the viral geneticists said.

“These informatics need to be backed up by experimental work,” said Scott Weaver, the director of the Institute for Human Infections and Immunity at the University of Texas Medical Branch in Galveston. “We’re not at the point yet where anyone’s got any good data [on that].”

Part of the problem is the shortage of good animal models for how the pathogen infects cells to cause disease, several researchers said.

It will also be important to get access to strains from different parts of the world, virologists said, otherwise much of its genetic history could remain fuzzy.

The host’s genetics might also matter. For instance, could some people’s immune systems be better equipped to fight off the virus?
Dr. Nunes and the ZiBra crew are planning to test the genes of Brazilians infected with Zika to see if they can tease out any differences that might account for why some people get sick and others don’t. The data will be publicly available so that researchers with access to strains from other parts of the world can make comparisons.

The team is also planning on embarking on another scientific excursion in January as mosquito season ramps up, this time in Brazilian states in the south. They want to better understand Zika and how it causes disease.

“We really don’t know what’s going on with the virus,” he said.