

# Hunting Fossil Viruses in Human DNA

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Published: January 11, 2010

The borna virus is at once obscure and grotesque. It can infect mammals and birds, but scientists know little about its effects on its victims. In some species it seems to be harmless, but it can drive horses into wild fits. The horses sometimes kill themselves by smashing in their skulls. In other cases, they starve themselves to death. Some scientists have even claimed that borna viruses alter human behavior, playing a role in [schizophrenia](#) and [bipolar disorder](#), although others say there is no solid evidence of a link.

The virus now turns out to have an intimate bond with every person on Earth. In the latest issue of *Nature*, a team of Japanese and American scientists [report](#) that the human genome contains borna virus genes. The virus infected our monkey-like ancestors 40 million years ago, and its genes have been passed down ever since.

Borna viruses are not the only viruses lurking in our genome. Scientists have found about 100,000 elements of human DNA that probably came from viruses. But the borna virus belongs to a kind of virus that has never been found in the human genome before. Its discovery raises the possibility that many more viruses are left to be found.

Scientists who hunt for these viruses think of themselves as paleontologists searching for fossils. Just as animals get buried in rock, these viruses become trapped in the genomes of their hosts. While their free-living relatives continue to evolve, fossil viruses are effectively frozen in time.

“We can really dig fossils out of the genome and literally put them back together,”

said Cédric Feschotte, a genome biologist at the [University of Texas](#), Arlington. “It’s like putting a hominid back together and asking it if it can walk upright.”

When scientists sequenced the human genome in 2001, they noticed many segments that bore a striking resemblance to genes in retroviruses, a class of viruses that includes [H.I.V.](#)

Retroviruses carry their genetic material in a single-stranded version of DNA, called RNA. To make new viruses, they make DNA versions of their genes, which are inserted into a host cell’s genome. The cell then reads the retrovirus’s genes as if they were its own, and manufactures new retroviruses.

Scientists speculated that every now and then a retrovirus inserted itself into a host cell and then failed to turn it into a virus factory. If the trapped retrovirus happened to be in sperm or egg cells, its DNA might be passed down to the host’s descendants. From generation to generation, the virus’s DNA would mutate. It would lose its ability to produce normal viruses. For a while it might be able to make new viruses that could re-infect the same cell, but over enough time, the viruses would become disabled.

In recent years, scientists have found several lines of evidence to support this idea. . Koala retroviruses, for example, appear to be in the [middle of the journey](#). The viruses can move from one koala to another. But in some populations of koalas, the virus’s DNA is permanently lodged in their genomes.

Thierry Heidmann of the Gustave Roussy Institute in France and his colleagues put the fossil virus hypothesis to a spectacular test: they tried to resurrect a dead retrovirus. They first identified a number of copies of the same virus-like stretch of DNA in the human genome. Each version had its own set of mutations that it acquired after the virus had invaded our ancestors.

By comparing the copies, Dr. Heidmann and his colleagues were able to figure out what the original sequence of the virus's genes had been. When they synthesized the genes from scratch and injected the genetic material into cells, [the cells produced new viruses](#).

“It was a tour-de-force of an experiment,” said John Coffin, an expert on fossil viruses at [Tufts University](#).

Now fossil virus hunters are moving beyond the human genome. They're taking advantage of the growing number of mammal genomes piling up in online databases and helping to flesh out the evolutionary history of viruses, reaching back tens of millions of years. Aris Katzourakis, an evolutionary biologist at the University of Oxford, and his colleagues recently went on a hunt for fossils of foamy viruses in mammals. Foamy viruses infect some mammals, including monkeys and apes. Primate foamy viruses can infect humans harmlessly, but researchers fear they may evolve to become dangerous. [Dr. Katzourakis and his colleagues](#) discovered hundreds of foamy virus copies in the DNA of the two-toed sloth. They then found the same virus lurking in the genome of the three-toed sloth. Before Dr. Katzourakis's fossil hunt, scientists had never found a foamy virus infecting any sloths, or any of their relatives like armadillos and anteaters.

Sloths and their relatives branched off from all other placental mammals about 100 million years ago. Dr. Katzourakis's discovery thus reveals the great antiquity of foamy viruses. They were already infecting the common ancestor of all placental mammals back when dinosaurs ruled the Earth.

These fossils are also offering clues to how viruses evolved. Dr. Katzourakis and his colleagues have found fossil viruses that are helping shed light on the deep history of H.I.V., for example.

H.I.V. evolved about a century ago from a chimpanzee virus known as simian

immunodeficiency virus, or S.I.V. Many apes and monkeys carry their own strain of S.I.V, but it's not clear how long the viruses have been infecting primates.

In 2008, Dr. Katzourakis and his colleagues discovered fossil S.I.V. in the genome of the gray lemur, a primate that lives in Madagascar. Last May, Dr. Feschotte and his colleagues reported that they had found the same fossil virus in the fat-tailed lemur.

Scientists had never before found S.I.V. in lemurs, which branched off from all other living primates some 50 million years ago. The fossil virus is also missing one of the genes found in all other forms of S.I.V. and H.I.V. It may be a transitional form of the virus, akin to the fossils paleontologists have found of feathered dinosaurs that couldn't fly.

Fossil viruses are also illuminating human evolution. Scientists estimate that 8.3 percent of the human genome can be traced back to retrovirus infections. To put that in perspective, that's seven times more DNA than is found in all the 20,000 protein-coding genes in the human genome.

But that figure may be too low, according to Dr. Katzourakis. "The measurable diversity of viruses may go up, and the true diversity may be much higher," he said.

For one thing, some viruses may be too well hidden for scientists to see. The discovery of borna viruses in the human genome is another reason to wonder if we're actually more viral than we know. All fossil viruses discovered until now have been retroviruses, but borna viruses are not.

Unlike retroviruses, borna viruses do not insert themselves into host genomes. Instead, they take up residence inside the nucleus, the chamber that holds our DNA. There, they manipulate the cell's proteins to make new copies of

themselves.

Keizo Tomonaga, a virologist at Osaka University, discovered the borna virus DNA by accident. He had been comparing the virus genes with human genes to see if the virus might have evolved to mimic our own proteins. Instead, he discovered four segments of human DNA that clearly had descended from a borna virus gene. "I was surprised when I found them," Dr. Tomonaga said.

He and his colleagues found the same borna virus DNA in apes and monkeys. In other words, borna virus first invaded the common ancestor of humans, apes and monkeys about 40 million years ago. But primates were not the only targets for borna viruses. Dr. Tomonaga and his colleagues have found independent invasions in other mammals, including ground squirrels, guinea pigs and elephants.

Dr. Tomonaga and his colleagues suspect that borna viruses didn't actually invade mammal genomes. Instead, the genomes kidnapped them.

Mammal genomes contain thousands of stretches of DNA called LINEs. LINEs sometimes make copies of themselves that get reinserted back into the genome. Dr. Tomonaga's research indicates that LINEs grabbed the genes of borna viruses and pulled them into their genome.

The discovery raises the possibility that LINEs have kidnapped other viruses floating near their host's DNA, like flu viruses.

Two of the four copies of the borna virus gene carry crippling mutations. It's impossible for our cells to make proteins from them. But the other two genes look remarkably intact, perhaps suggesting that our bodies use them for our own benefit. Exactly what they do isn't clear though.

Studies on other captive viruses have revealed that some help ward off viral invasions. One virus protein, syncytin, is essential for our being born at all.

“The only place it’s expressed is in the placenta,” Dr. Heidmann said. To understand its function, he and his colleagues disabled the gene in mice. Without syncytin, mice developed deformed placentas, and their embryos died.

Syncytin started as a surface protein on retroviruses that fused them to cells. When mammals captured the gene, they used it in the placenta to create a layer of fused cells through which mothers can send nutrients to their embryos.

Dr. Heidmann and his colleagues have discovered that over the past 100 million years, mammals have repeatedly harnessed viruses to make syncytin. “Wherever we search for them, we find them,” Dr. Heidmann said.

But the syncytin genes we use today may have actually replaced an ancestral one that a virus bequeathed to the very first placental mammals. In fact, that infection may have made the placenta possible in the first place. “It was a major event for animal evolution”, Dr Heidmann said.