Bats and Wallabies Have a Lot of NIRV

by Jon Cohen on June 25, 2010 5:46 PM | Permanent Link | 0 Comments

A dead bat stashed in a freezer and a wallaby from a local zoo have helped reveal that relatives of the lethal Ebola and Marburg viruses likely began infecting mammals tens of millions years ago, making this family of viruses far older than scientists had thought. Remnants of genes from these viruses exist in the DNA of bats, marsupials, rodents, and other mammals, a finding that may suggest where these deadly microbes lurk before they emerge to kill people.

ENLARGE IMAGE

Marburg in marsupials? Derek Taylor with a wallaby, which his labhas shown carries fossil filovirus genes.

Credit: Sandra Murray

Although outbreaks are rare, Ebola virus, Marburg virus, and other so-called filoviruses periodically cause massive hemorrhaging in humans, chimpanzees, gorillas, and other primates. Some reports based on the estimated mutation rate of this virus family have suggested that filoviruses are a mere 10,000 years old, but Derek Taylor, an evolutionary biologist at the State University of New York (SUNY),Buffalo, has found a new way to gauge their age.

Just as paleontologists use fossil bones to date when a species originated, paleovirologists can use remnants of viral genes scattered around the genomes of the organisms they infect. Viruses have genes composed of either DNA or RNA, and some integrate their genes into the host cell's DNA. Researchers long have believed that to accomplish this feat, RNA viruses had to carry the gene for an enzyme, reverse transcriptase, to convert their RNA into DNA. Such viruses, which include HIV, are known as retroviruses. Scan any animal's genome, and one will even find "fossil" viral genes, remnants of ancient retroviral infections.

Filoviruses are RNA viruses that don't carry the gene for reverse transcriptase, yet that hasn't stopped them from somehow leaving their mark. Taylor and his colleagues have now found fossil filovirus genes buried within the genomes of a dozen species, but none in any primates. They initially scanned mammalian genome databases to find these viral remnants, but they also confirmed that filoviral gene remnants were present in the DNA from a dead bat stored in a lab freezer and from the zoo's wallaby. "In order to see if this finding was real, we wanted to isolate copies of the genes ourselves," Taylor says.

To try to pin an age on these fossil genes and determine when these ancient infections happened, Taylor and his co-authors—virologist Jeremy Bruenn, and bioinformatics specialist Robert Leach, both also of SUNY Buffalo—compared the viral remnants in different species and found they were nearly identical, indicating that they infected mammals only once early in evolution, and then the viral remnants were passed down as the groups diverged. In a

study reported online this week in *BMC Evolutionary Biology*, the researchers conclude that filoviruses have existed for tens of millions of years. They arrived at that estimate by showing that the Norway rat and the house mouse, which diverged from each other somewhere between 12 million and 24 million years ago, have the same filovirus gene pieces integrated at the same places on the same chromosomes. "The odds of a gene inserting itself in the exact same spot when you have billions of nucleotides are pretty unlikely," Taylor says.

Taylor and Bruenn began these studies after they discovered non-retrovirus viral genes in fungi, which they reported last year. They came up with a catchy acronym for these genetic oddities: NIRVs (non-retroviral integrated RNA viruses). Their discovery of NIRVs in mammalian genomes corroborates a study in the 7 January issue of *Nature* in which John Coffin of Tufts University School of Medicine in Boston and colleagues reported that another group of RNA viruses that lack reverse transcriptase, *bornavirus*, can integrate their genes into mammals.

The SUNY team suggests that the NIRVs in mammals may help clarify perplexing riddles about filoviruses. Ebola virus and Marburg virus regularly surface in remote African locales, seemingly out of nowhere. Many studies have sought species that could harbor these viruses without suffering harm. The NIRVs are "battle scars of an infection," Taylor says, and may point to such "reservoir species." Indeed, bats have long been a prime suspect for a filovirus reservoir. Taylor suggests that finding NIRVs in New World marsupials indicates that there may be unknown filoviruses in South America, where people sometimes die of unexplained hemorrhagic fevers.

Coffin says the discovery of NIRVs in mammals establishes that these and other RNA viruses are ancient. "It gives us grounds for thinking in more appropriate ways about how these things evolved," he says. "And I suspect as better tools become available and we can do even deeper looks into the genomes, we'll find even older things."