

Unexpected viral 'fossils' found in vertebrate genomes

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Over millions of years, retroviruses, which insert their genetic material into the host genome as part of their replication, have left behind bits of their genetic material in vertebrate genomes. In a recent study, published July 29 in the open-access journal *PLoS Pathogens*, a team of researchers have now found that human and other vertebrate genomes also contain many ancient sequences from Ebola/Marburgviruses and Bornaviruses - two deadly virus families.

Because neither virus family inserts their genetic material into the host genome during replication, as <u>retroviruses</u> do, the discovery was all the more unexpected.

"This was a surprise for us," says author Anna Marie Skalka, Ph.D., Director Emerita of the Institute for Cancer Research at Fox Chase Cancer. "It says that the source of our genetic material is considerably wider than we thought. It includes our own genes and unexpected viral genes as well."

The team, which included lead author Vladimir A. Belyi, Ph.D., and coauthor Arnold J. Levine, Ph.D., both at the Institute for Advanced Study in Princeton, compared 5,666 viral genes from all known non-retroviral families with single-stranded RNA genomes to the genomes of 48 vertebrate species, including humans. In doing so, they uncovered 80 separate viral sequence integrations into 19 different vertebrate species. Interestingly, nearly all of the viral sequences come from ancient relatives of just two viral families, the Ebola/Marburgviruses and



Bornaviruses, both of which cause hemorrhagic fevers and neurological disease.

"These viruses are RNA viruses," Skalka says. "They replicate their RNA and are not known to make any DNA. And they have no known mechanism for getting their <u>genetic material</u> integrated into the DNA of the host genome. Indeed, some of them don't even enter the nucleus when they replicate."

That the sequences, some of which may have been integrated into the genomes more than 40 million years ago, have been largely conserved over evolutionary time suggests that they give the host a selective advantage, perhaps protecting them from future infections by viruses from those families. The study shows that integration of the ancient viral sequences was probably mediated by movable elements, LINEs, which are abundant in mammalian genomes.

"In a way, one might even think of these integrations as genomic vaccinations," says Skalka.

Demonstrating conclusively that the viral sequences have some biological function will take additional work. However, the team has noted that expression of some of these viral open reading frames has been detected in human tissues, which supports the possibility that they are biologically active in host species.

More information: Belyi VA, Levine AJ, Skalka AM (2010) Unexpected Inheritance: Multiple Integrations of Ancient Bornavirus and Ebolavirus/Marburgvirus Sequences in Vertebrate Genomes. PLoS Pathog 6(7): e1001030. <u>doi:10.1371/journal.ppat.1001030</u>



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