# Viral fossils reveal how our ancestors may have eliminated an ancient infection

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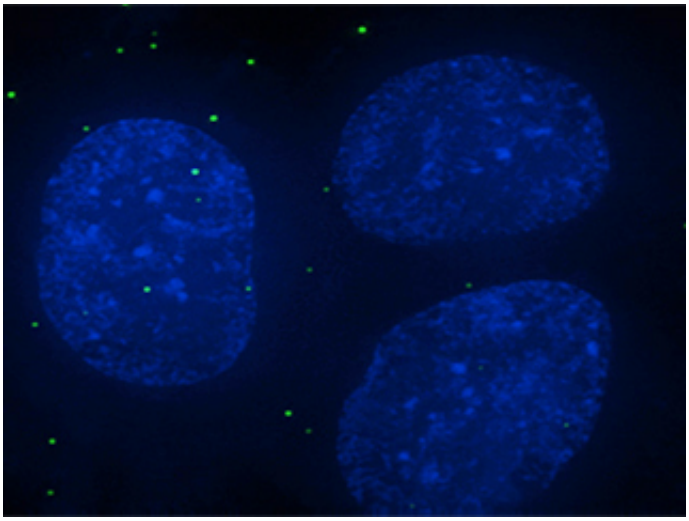

Our ancestors evolved a defense mechanism against viral protein HERT-V (green), eradicating the virus about 11 million years ago. Credit: Laboratory of Retrovirology at the Rockefeller University/eLife

Scientists have uncovered how our ancestors may have wiped out an ancient retrovirus around 11 million years ago.

Retroviruses, which include human immunodeficiency virus (HIV), are abundant in nature. Unlike other viruses, which do not usually leave a physical trace of their existence, retroviruses include a step in their life cycle where their genetic material is integrated into the genome of their host. This integration has created a genetic fossil record of extinct

retroviruses that is preserved in the genomes of modern organisms.

Writing in the journal *eLife*, researchers from the Rockefeller University and the Howard Hughes Medical Institute (HHMI), US, set out to discover how extinct viral lineages could have been eliminated. To do this, they analysed retroviral fossils left by human endogenous retrovirus T (HERV-T), which replicated in our primate ancestors for approximately 25 million years before it was eradicated about 11 million years ago.

Working with Robert Gifford from the University of Glasgow, the team first compiled a near-complete catalog of HERV-T fossils in old-world monkey and ape genomes. They then reconstructed the HERV-T retrovirus' outer envelope protein - a type of protein that allows a virus particle to bind to cells and begin the viral replication cycle.

"Our analyses first suggested that HERV-T likely used a cell-surface protein called MCT-1 to bind to cells and infect ancient old-world primates," says first author Daniel Blanco-Melo, who carried out the study at the Rockefeller University but is now a postdoctoral researcher at the Icahn School of Medicine at Mount Sinai, New York.

"Next, we identified one particular fossilised HERV-T gene in the human genome that encodes an unexpectedly well-preserved envelope protein. This gene was absent in non-hominid primate genomes, but was integrated into an ancestral hominid genome around 13 to 19 million years ago. We believe its function may have been switched around this time so that it could block infection by causing MCT-1 depletion from cell surfaces."

Taken together, these findings suggest a scenario in which HERV-T began to infiltrate primate germlines (series of cells that are seen as continuing through successive generations of an organism) using MCT-1

as a receptor. Ancestral hominids later evolved a defence mechanism whereby they switched a HERV-T gene to serve as an antiviral gene against itself.

"Broadly speaking, this study shows how analysing viral fossils can provide a wealth of insight into events that occurred in the distant past," says senior author Paul Bieniasz, HHMI Investigator and Professor of Retrovirology at the Rockefeller University. "In particular, it represents an example of how viruses themselves can provide the genetic material that animals use to combat them, sometimes leading to their own extinction."

**More information:** Daniel Blanco-Melo et al, Co-option of an endogenous retrovirus envelope for host defense in hominid ancestors, *eLife* (2017). DOI: 10.7554/eLife.22519

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