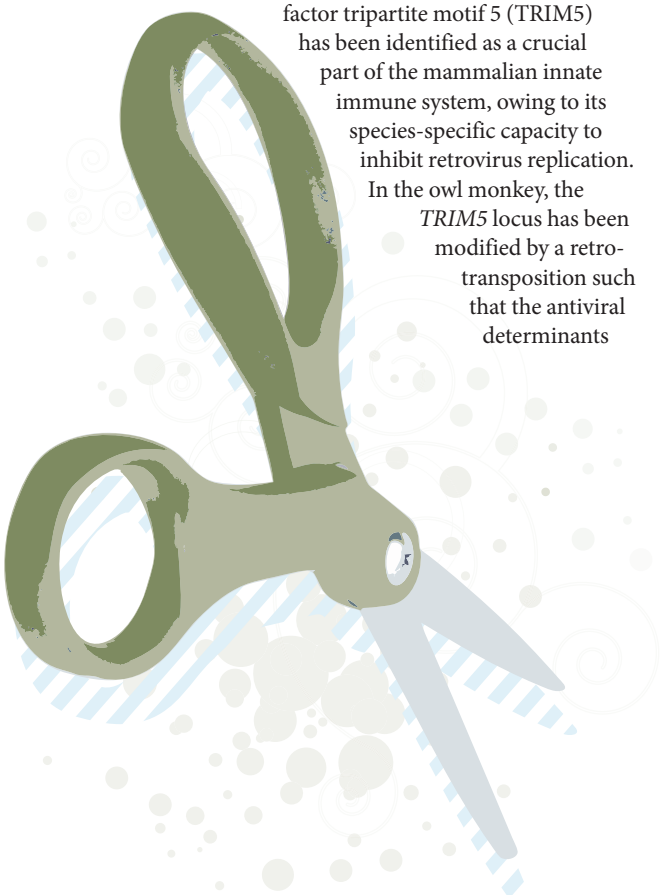
EVOLUTION

# Monkey genomes get TRIMmed

An evolutionary event at the *TRIM5* locus of the owl monkey genome that led to the expression of the fusion protein TRIMCyp had been heralded as a remarkable, but anomalous, occurrence. Now, three groups, reporting in *Proceedings of the National Academy of Sciences*, have detected an identical CypA insertion at the TRIM5 locus of three macaque species. These insertions are, however, at different locations compared with that of the owl monkey, and thus are important examples of convergent evolution in divergent species.



The anti-retroviral restriction factor tripartite motif 5 (TRIM5) has been identified as a crucial part of the mammalian innate immune system, owing to its species-specific capacity to inhibit retrovirus replication. In the owl monkey, the *TRIM5* locus has been modified by a retrotransposition such that the antiviral determinants in the B30.2 domain of TRIM5 have been replaced by cyclophilin A (CypA). Because a subset of lentiviruses recruit CypA to their capsids during infection, TRIMCyp from owl monkeys can block the transmission of these viruses. Until now, however, the expression of TRIMCyp was thought to be unique to owl monkeys.

Wilson *et al.* discovered a *TRIM5* allele, which they named *Mamu7*, in the genomes of rhesus macaques while sequencing for genetic polymorphisms. Similarly, Bieniasz, Hatziioannou and colleagues identified the TRIMCyp fusion protein in pigtailed macaques after investigating unusual patterns of retroviral-infection sensitivity. Both groups amplified and sequenced their respective TRIMCyp-encoding sequences and found them to be distinct from owl monkey TRIMCyp-encoding sequences, which was indicative of independent evolution.

Both research groups then assessed the inhibitory effects of their newly discovered TRIMCyp-like molecules on the infection of various lentiviruses, and detected lentivirus-specific interactions. Both found that TRIMCyp can restrict the infection of multiple lentiviruses, including HIV-2 and feline immunodeficiency virus. However, in contrast to owl monkey TRIMCyp, HIV-1 infection was not inhibited by TRIMCyp in either investigation. This led both groups to suggest that TRIMCyp proteins have distinct specificities for viruses from different simian immunodeficiency virus lineages. Bieniasz, Hatziioannou and colleagues found that a single amino-acid mutation that was acquired during or after CypA transposition is the cause of this lentivirus specificity.

Intriguingly, a third group, Brennan *et al.*, have also detected TRIMCyp in pigtailed macaques and cynomolgus macaques. It would be an astonishing coincidence if the same two genes had fused randomly more than once during primate evolution. The authors of these studies suggest that the strong evolutionary pressure that has been applied by immunodeficiency viruses has led to this striking example of convergent evolution.

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**ORIGINAL RESEARCH PAPERS** Wilson, S. J. *et al.* Independent evolution of an antiviral TRIMCyp in rhesus macaques. *Proc. Natl Acad. Sci. USA* 19 Feb 2008 (doi:10.1073/pnas.0709003105) | Virgen, C. A., Kratovac, Z., Bieniasz, P. D. & Hatziioannou, T. Independent genesis of chimeric TRIM5-cyclophilin proteins in two primate species. *Proc. Natl Acad. Sci. USA* 19 Feb 2008 (doi:10.1073/pnas.0709258105) | Brennan, G., Kozyrev, Y. & Hu, S. L. TRIMCyp expression in old world primates *Macaca nemestrina* and *Macaca fascicularis*. *Proc. Natl Acad. Sci. USA* 19 Feb 2008 (doi: 10.1073/pnas.0709511105)