# TRIM5-mediated retrovirus restriction is modulated by type I interferon

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Since the identification in 2004 of the interferon-stimulated gene (ISG) tripartite motif-containing protein 5 α (TRIM5α) from rhesus macaques as a restriction factor preventing HIV-1 infection in these monkeys, the antiretroviral activity of several primate TRIM5α orthologs against HIV-1 has been described, establishing the model that TRIM5α inhibits retroviral infection in a species-specific manner, preventing host cell infection by retroviruses from different species through fragmentation of incoming viral capsids and the activation of innate immune pathways. However, the long held dogma that retroviruses have evolved to evade the TRIM5α ortholog present in species to which they are endemic has recently changed by the identification of human TRIM5α as a major determinant in the Type 1 IFN-induced suppression of HIV-1 replication, presumably contributing to the immune control of HIV-1 in infected humans.

Given that IFN levels are elevated during natural retrovirus infection and that IFN treatment enables human TRIM5α restriction of HIV-1, we evaluated the IFN-induced restriction of distinct retroviruses in presence of TRIM5α orthologues from different primate species. To this end, we ectopically expressed different TRIM5α orthologues in human U87 cells where endogenous TRIM5α and MX2 expression had been ablated using CRISPR–Cas9 genome editing, and then challenged with a wide range of GFP-encoding retrovirus-based vectors in the presence or absence of IFN. This approach reveals that IFN treatment changes the patterns of TRIM5α-mediated retrovirus restriction, suggesting that the role of TRIM5α in retrovirus infection should be re-examined under conditions that more closely mimic those encountered during natural virus infection.