Restriction of Primate Lentiviruses by TRIM34 & TRIM5α

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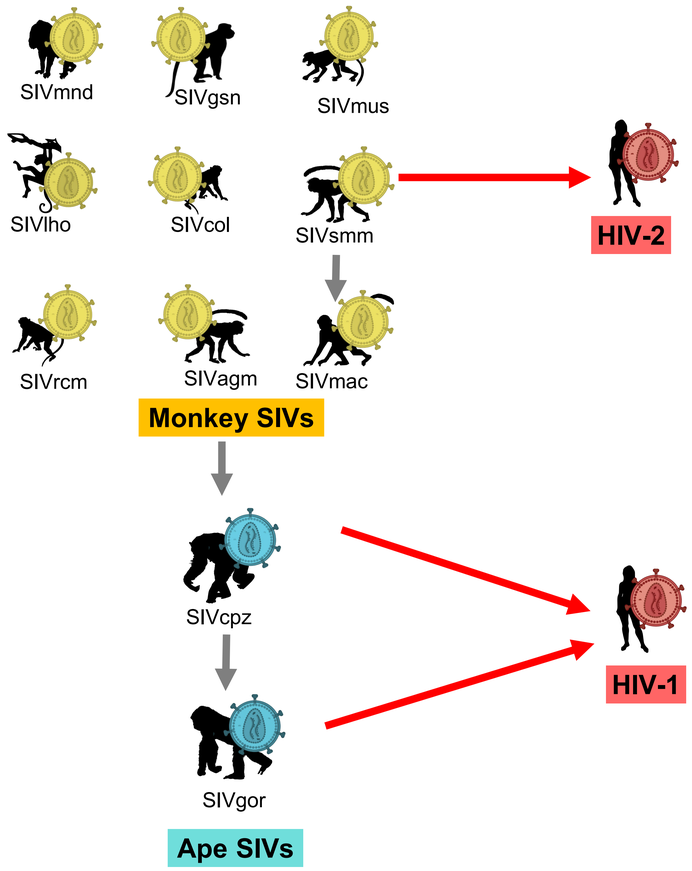
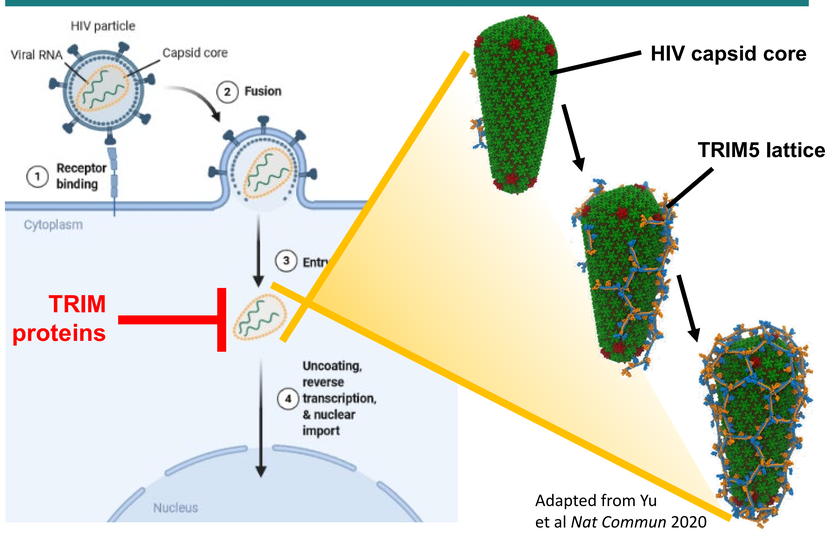
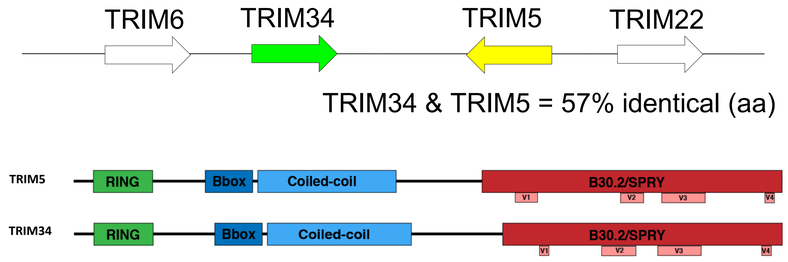
HIV arose through cross-species transmissions of ape SIVs



TRIM proteins restrict lentiviral infection by multimerizing onto viral capsid

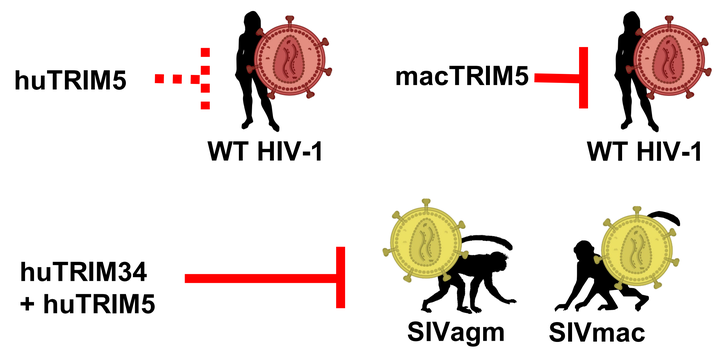


TRIM34 & TRIM5α are paralogs with shared evolutionary history



- Restriction by TRIM34 depends on the presence of TRIM5α.
- TRIM5α has evolved rapidly under positive selection, suggesting direct interaction with viral substrate.
- TRIM34 and TRIM5α have both maintained residues thought to be important for multimerization.

TRIM34 & TRIM5α-mediated restriction differs by species



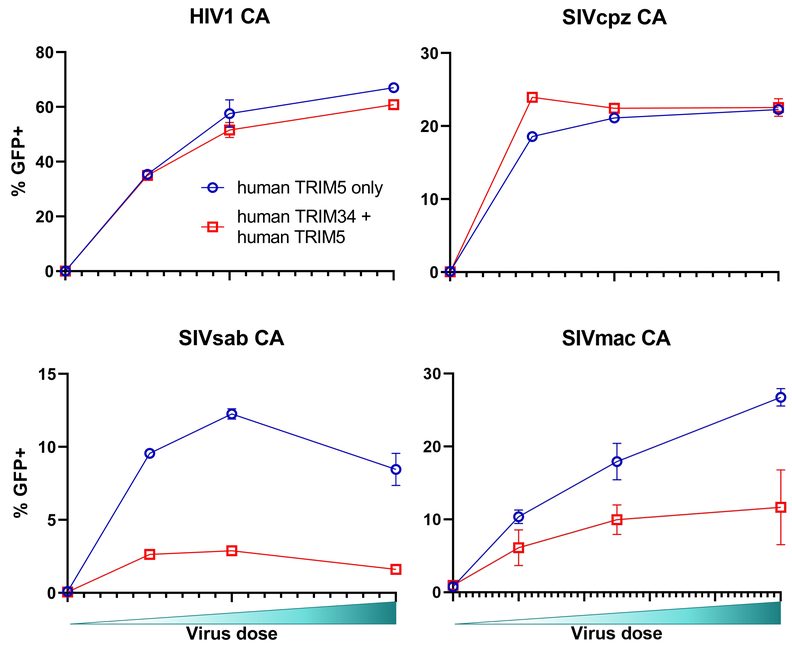
Hypotheses & experimental strategy

Hypothesis: TRIM34 and TRIM5α interact at the viral capsid to restrict HIV.

Hypothesis: TRIM5α determines specificity of TRIM34-mediated restriction, and TRIM34 may alter this specificity

Co-express TRIM34 & TRIM5α orthologues (same or different species) → Challenge with SIV or HIV capsids (matched or unmatched to TRIMs) → Map restriction to specific domains or residues

Results: SIVsab and SIVmac are restricted by TRIM34 in the presence of human TRIM5α



Work in progress & future directions

Is TRIM5 required for TRIM34-mediated restriction of SIVsab and SIVmac CA?
→ If so, do TRIM5 orthologues from any species work or only certain ones?

What is unique about SIVsab and SIVmac that makes them susceptible to restriction by TRIM34?

Significance

- Define species-specific differences in TRIM34 and TRIM5α orthologues that affect cross-species transmission of SIVs.
- Understand how TRIM34 and TRIM5α influenced SIV adaptation to new host species.

Selected References

Ganser-Pornillos, B. K. & Pornillos, O. Restriction of HIV-1 and other retroviruses by TRIM5. *Nat. Rev. Microbiol.* **17**, 546–556 (2019).

Ohainle, M. *et al.* A virus-packageable CRISPR screen identifies host factors mediating interferon inhibition of HIV. *Elife* **7**, 1–32 (2018).

Ohainle, M. *et al*. TRIM34 acts with TRIM5α to restrict HIV-1 and SIV capsids. *PLOS Pathog.* (2020).