RESTRICTION OF LENTIVIRAL CAPSIDS BY PRIMATE TRIM34

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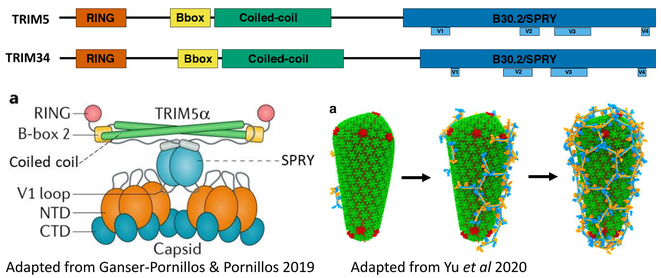
Joy Twentyman [1, 2], Abby L. Felton [2], Michael Emerman [2,3], Molly OhAinle [4]

[1] Department of Global Health, University of Washington, Seattle, WA, USA, [2] Division of Human Biology, Fred Hutchinson Cancer Research Center, Seattle, WA, USA,
[3] Division of Basic Sciences, Fred Hutchinson Cancer Research Center, Seattle, WA, USA, [4] Department of Molecular and Cell Biology, University of California–Berkeley, Berkeley, CA, USA

TRIM34 is broadly conserved across primates as a TRIM5α-dependent lentiviral restriction factor.

BACKGROUND

- Host factors and pathogens are in evolutionary conflict
- Restriction factors can inhibit cross-species transmission of lentiviruses
- TRIM34 is a paralog of TRIM5α
- TRIMs restrict lentiviruses by multimerizing onto CA



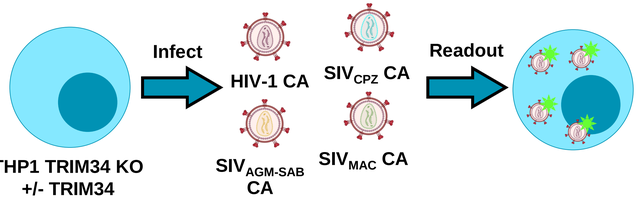
Adapted from Ganser-Pornillos & Pornillos 2019 — Adapted from Yu *et al* 2020

- TRIM34 identified as a restriction factor of HIV-1 N74D
- TRIM34 requires TRIM5α to restrict HIV-1 N74D
- TRIM34 and TRIM5α colocalize
- TRIM34 also restricts $SIV_{AGM-TAN}$ and SIV_{MAC}

METHODS

EXPERIMENTAL METHODS

- Inducible TRIM34 overexpression in THP-1 TRIM34 KO
- Infect with fluorescent reporter viruses expressing chimeric gag/pol containing different CA proteins
- Readout = flow cytometry



STATISTICAL METHODS

Figures 1, 3, 4: Welch's 1-tailed t-test
Figure 2: Kruskal-Wallis 1-way ANOVA with Dunn's correction for multiple comparisons

ns = nonsignificant
* $p \leq 0.05$
** $p \leq 0.01$
*** $p \leq 0.001$

RESULTS

Figure 1. Diverse primate TRIM34 alleles restrict $SIV_{AGM-TAN}$, $SIV_{AGM-SAB}$, and SIV_{MAC} CA in the presence of endogenous TRIM5α

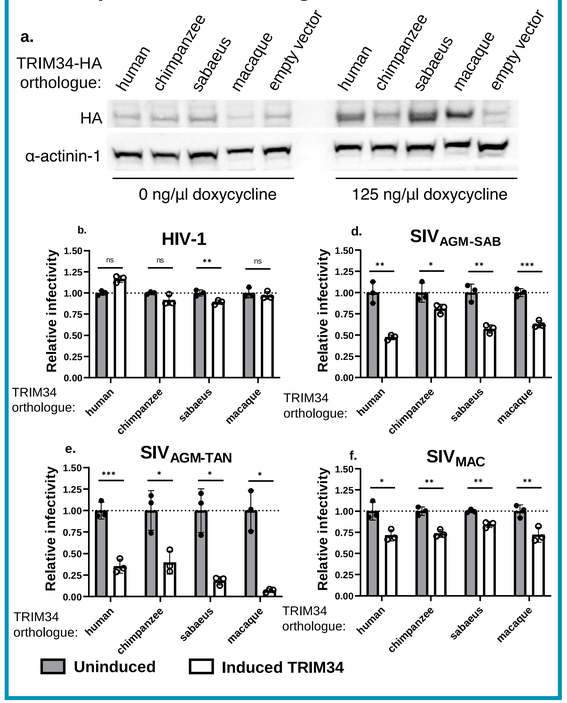


Figure 2. TRIM34 requires TRIM5α to restrict $SIV_{AGM-SAB}$

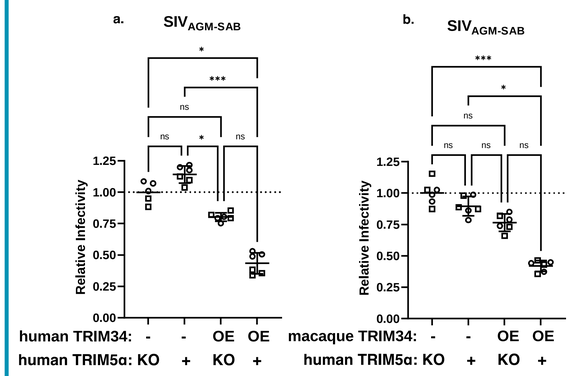


Figure 3. TRIM5α v1 loop is required for TRIM34-mediated restriction of $SIV_{AGM-SAB}$

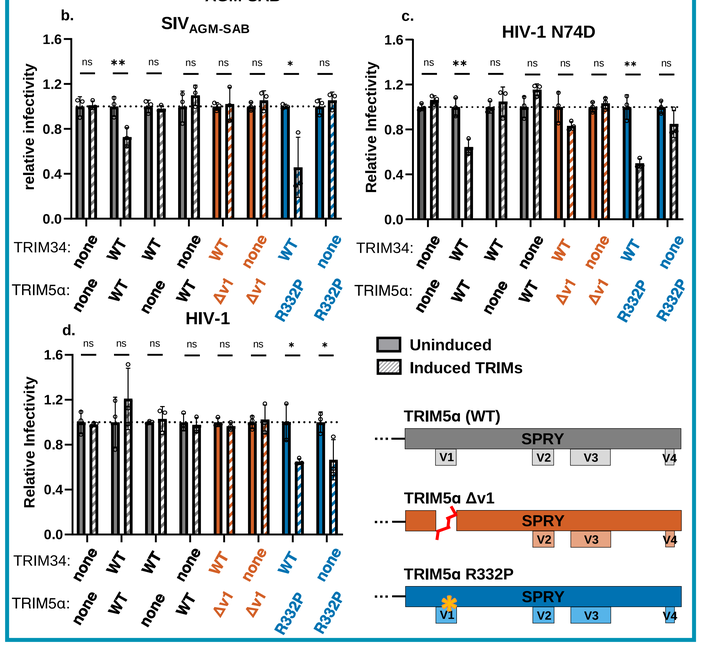
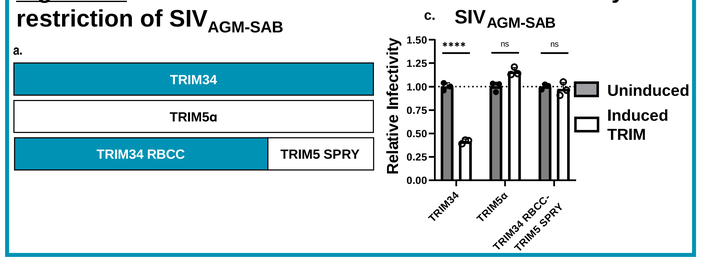


Figure 4. TRIM34 SPRY domain is necessary for restriction of $SIV_{AGM-SAB}$



CONCLUSIONS

- **Diverse primate TRIM34 orthologues have been broadly conserved as lentiviral restriction factors**
- **Restriction by TRIM34 requires TRIM5a**
- **TRIM5a v1 loop is required for TRIM34-mediated restriction**
- **Together, TRIM34 and TRIM5a can restrict capsids that neither can restrict individually**

SELECTED REFERENCES

Ganser-Pornillos & Pornillos. Restriction of HIV-1 and other retroviruses by TRIM5. Nat Rev Microbiol (2019).
Ohainle et al. A virus-packageable CRISPR screen identifies host factors mediating interferon inhibition of HIV. Elife (2018).
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SUPPORT

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