

HIV Latency in CD34+ hematopoietic progenitor cells

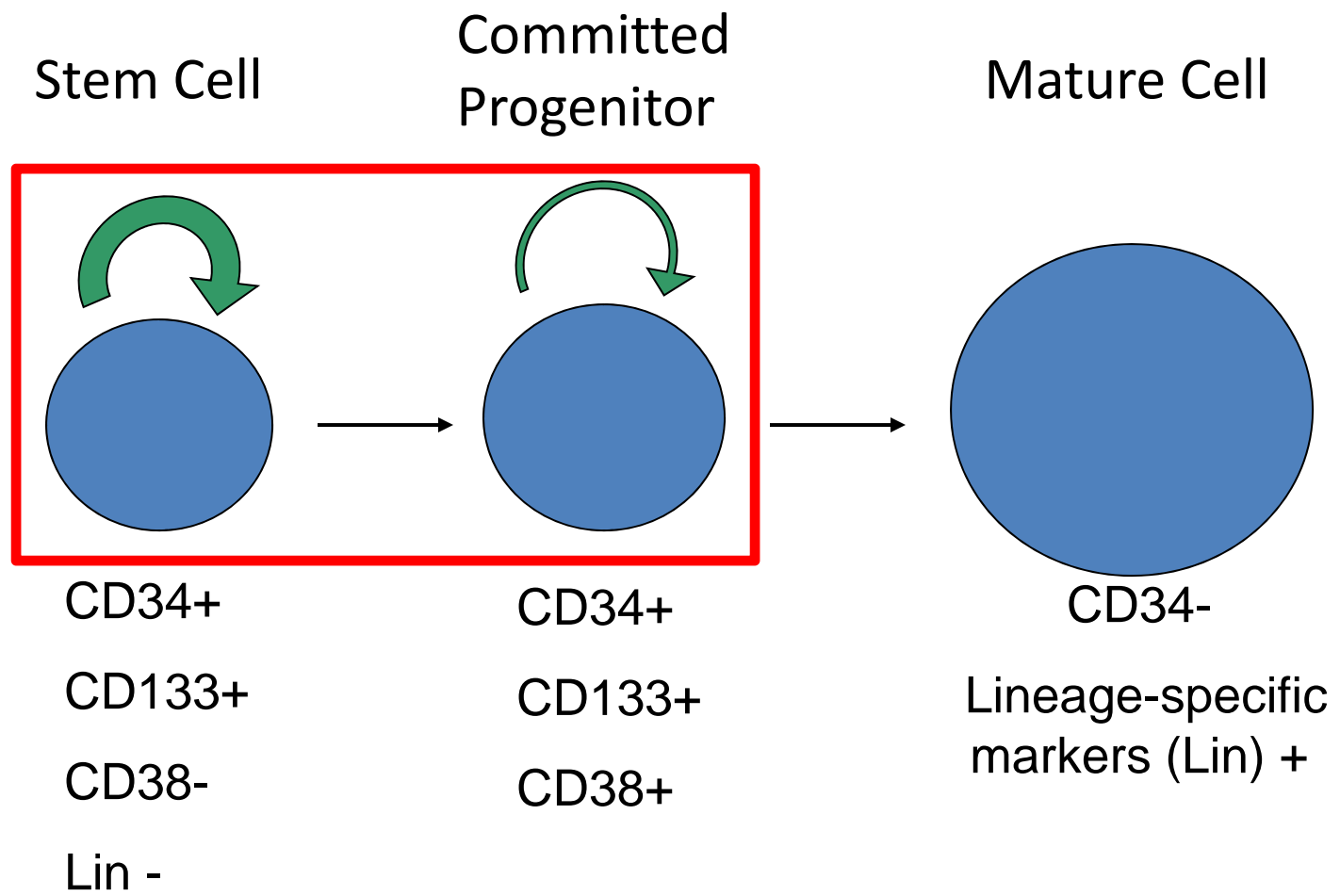
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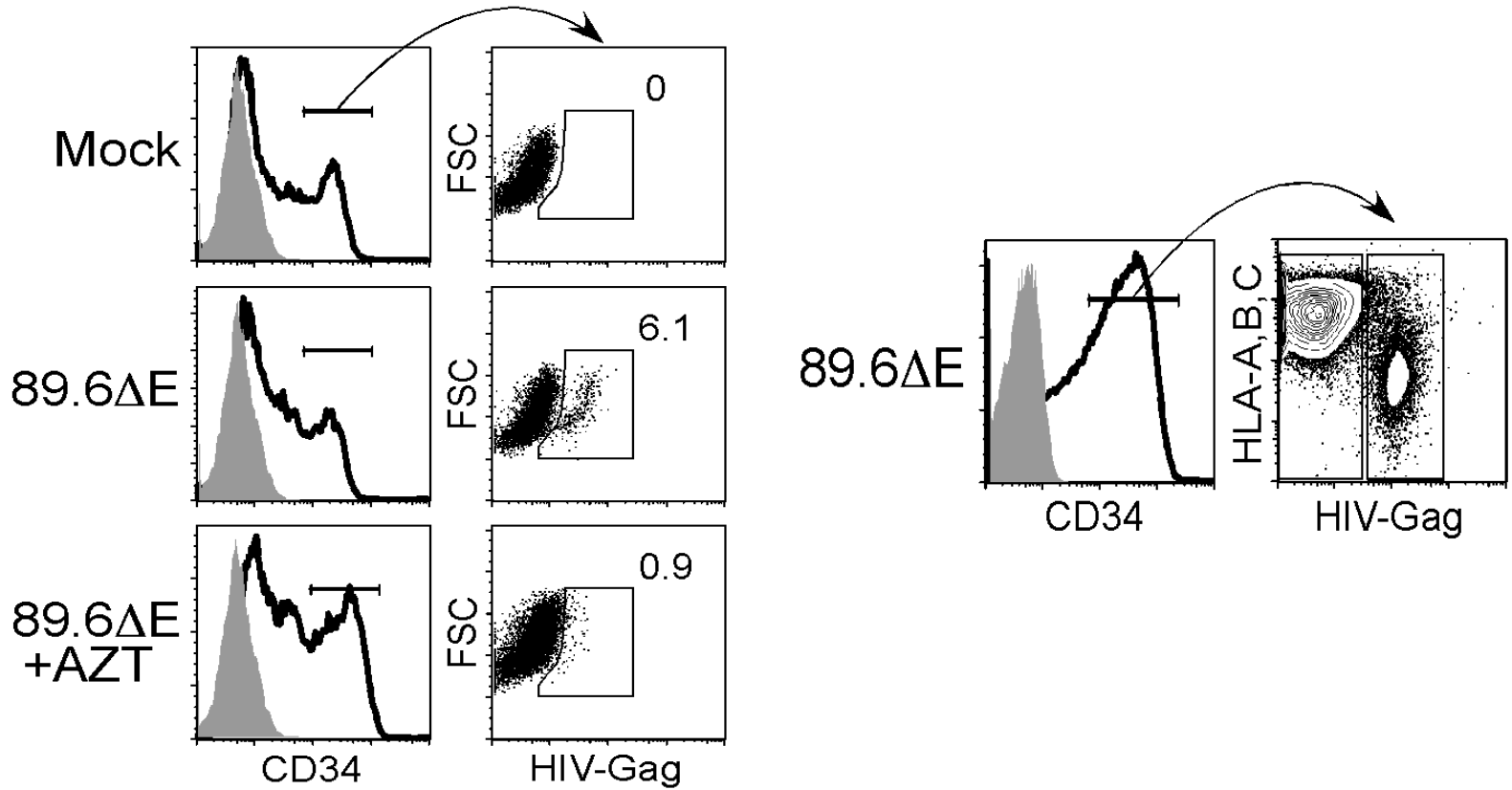
Background

- Highly active antiretroviral therapy (HAART) can reduce HIV-1 viremia below the limit of detection of standard tests.
- Despite this, residual virus is present in the blood.
- A long-lived latent reservoir for HIV-1 exists in resting memory CD4+ T cells.
- Recent evidence indicates that some residual viremia is genetically distinct from proviruses in resting CD4+ T cells or other known targets of HIV in the peripheral blood.
- A cellular source other than CD4+ T cells may contribute to residual viremia in people on HAART

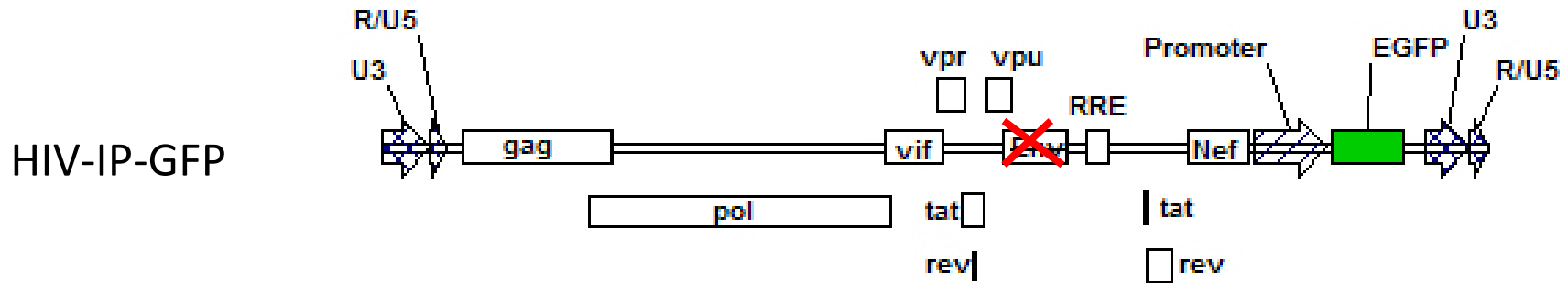
CD34+ hematopoietic progenitor cells



HIV infects CD34+ cells



Latency Reporter



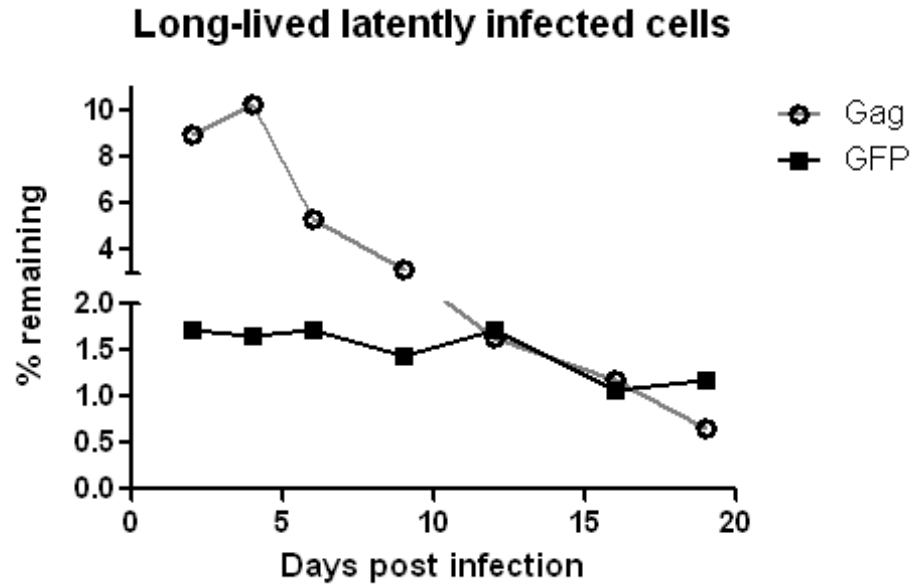
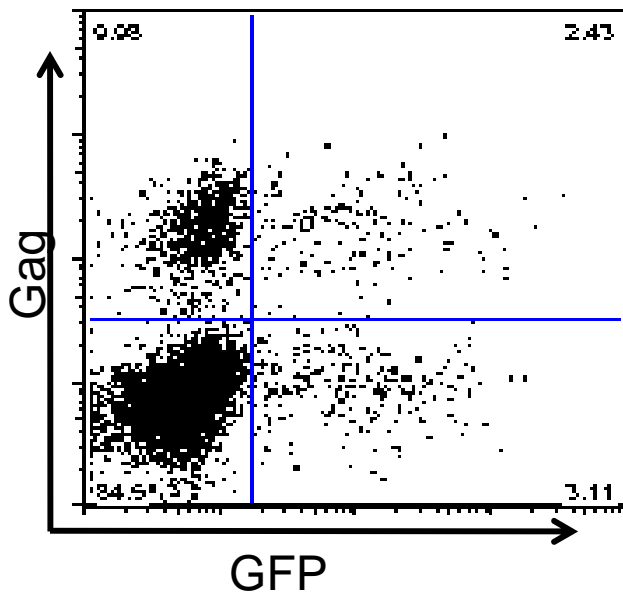
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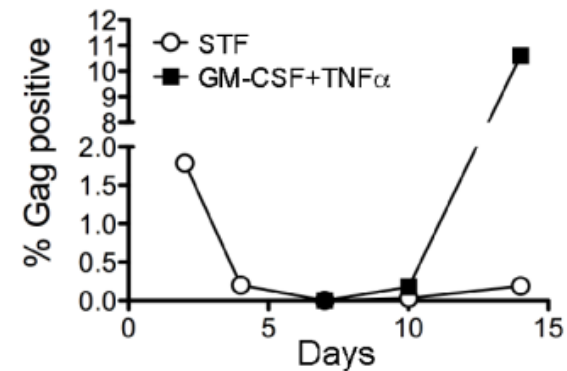
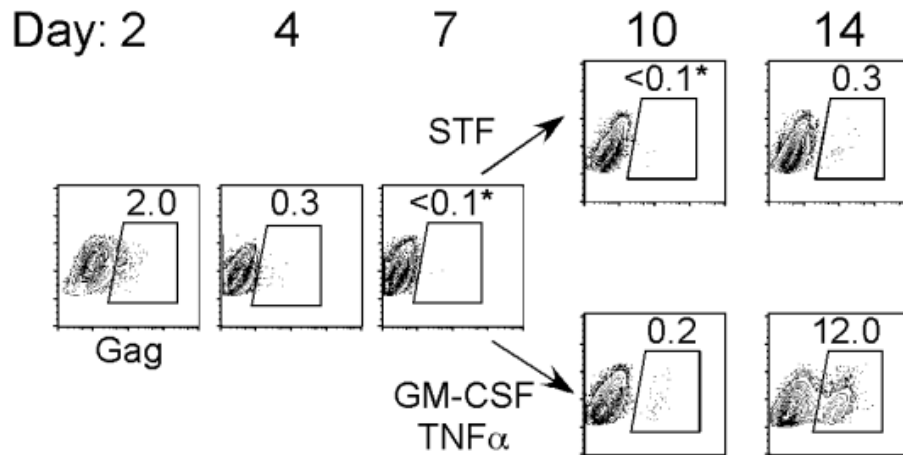
GFP driven by SFFV promoter

Can pseudotype with HIV envelope of choice

Active and Latent infection in CD34+ bone marrow progenitors

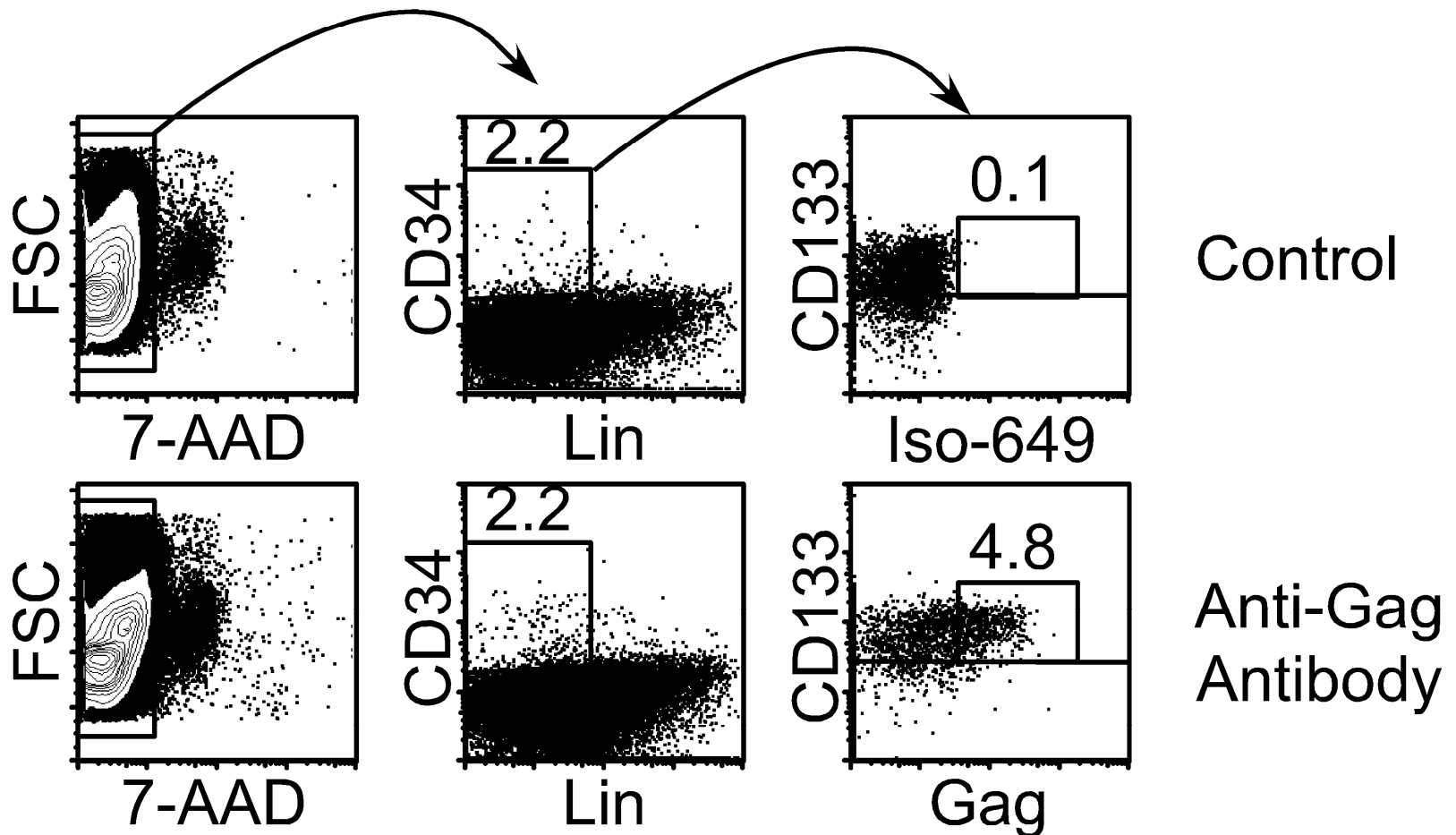


GM-CSF/TNF α stimulation induces HIV release from infected CD34+ cells

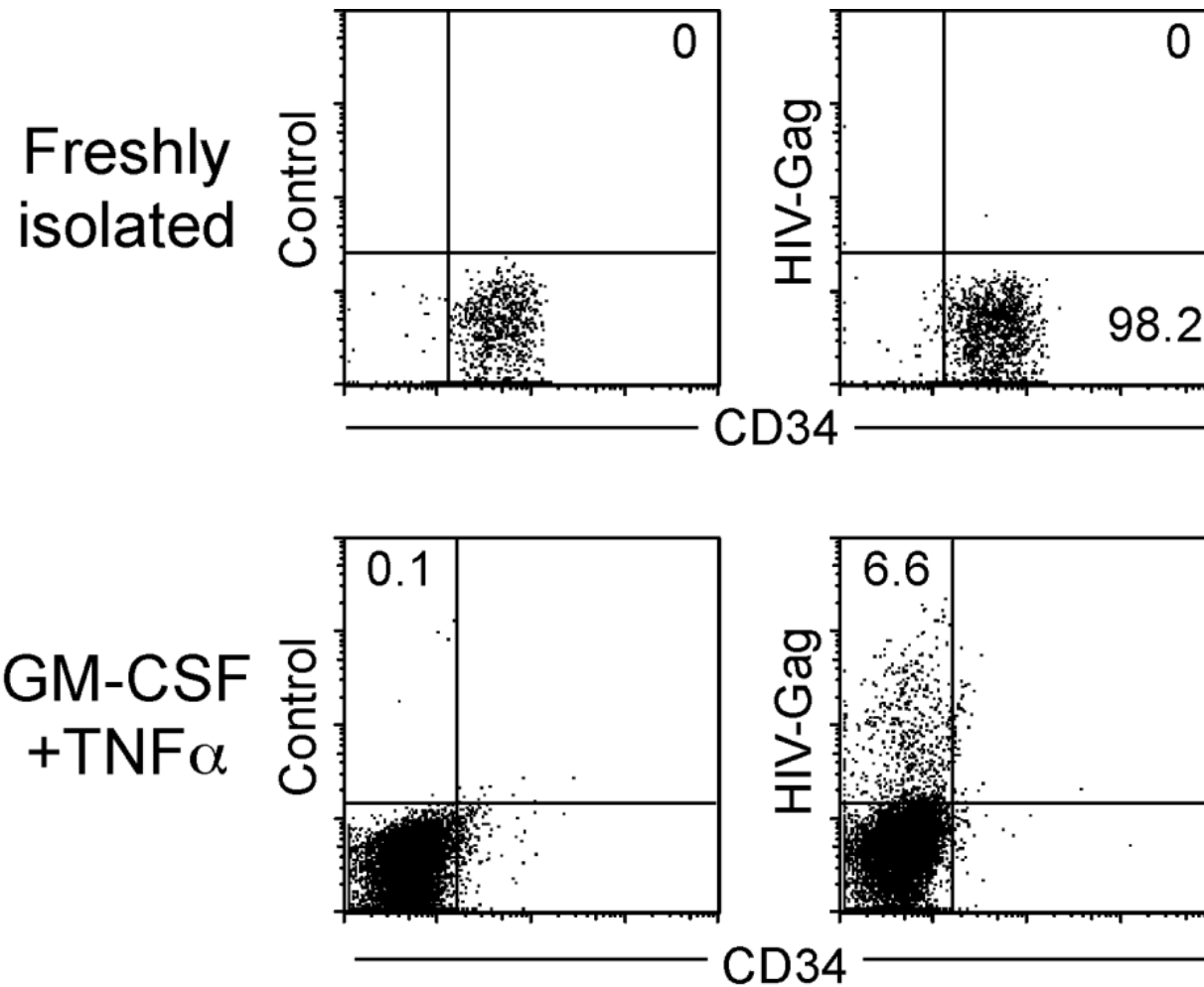


Active infection in freshly isolated CD34+bone marrow progenitors

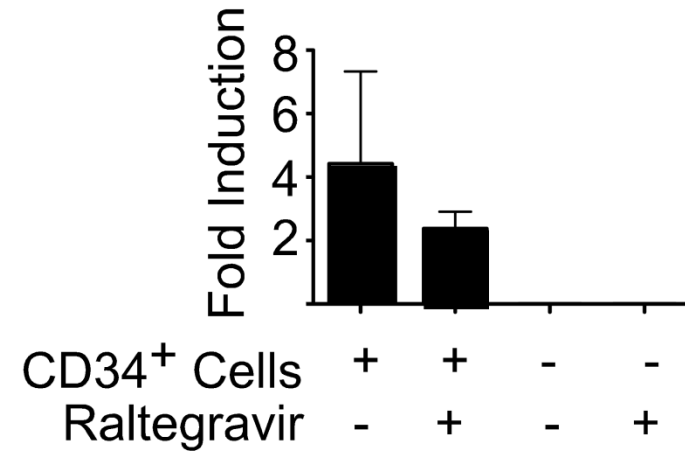
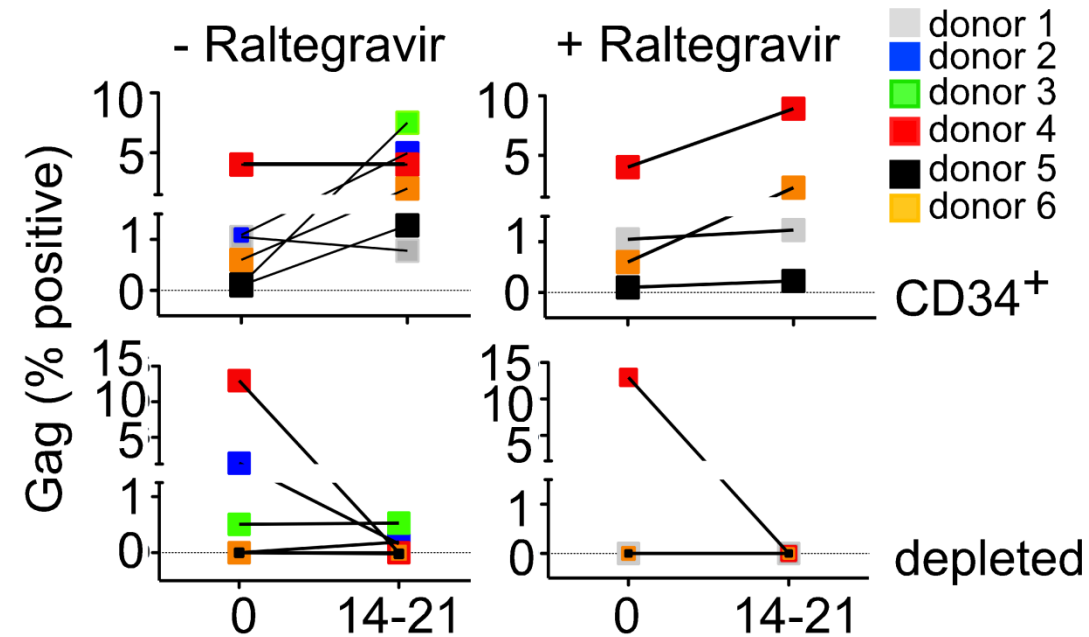
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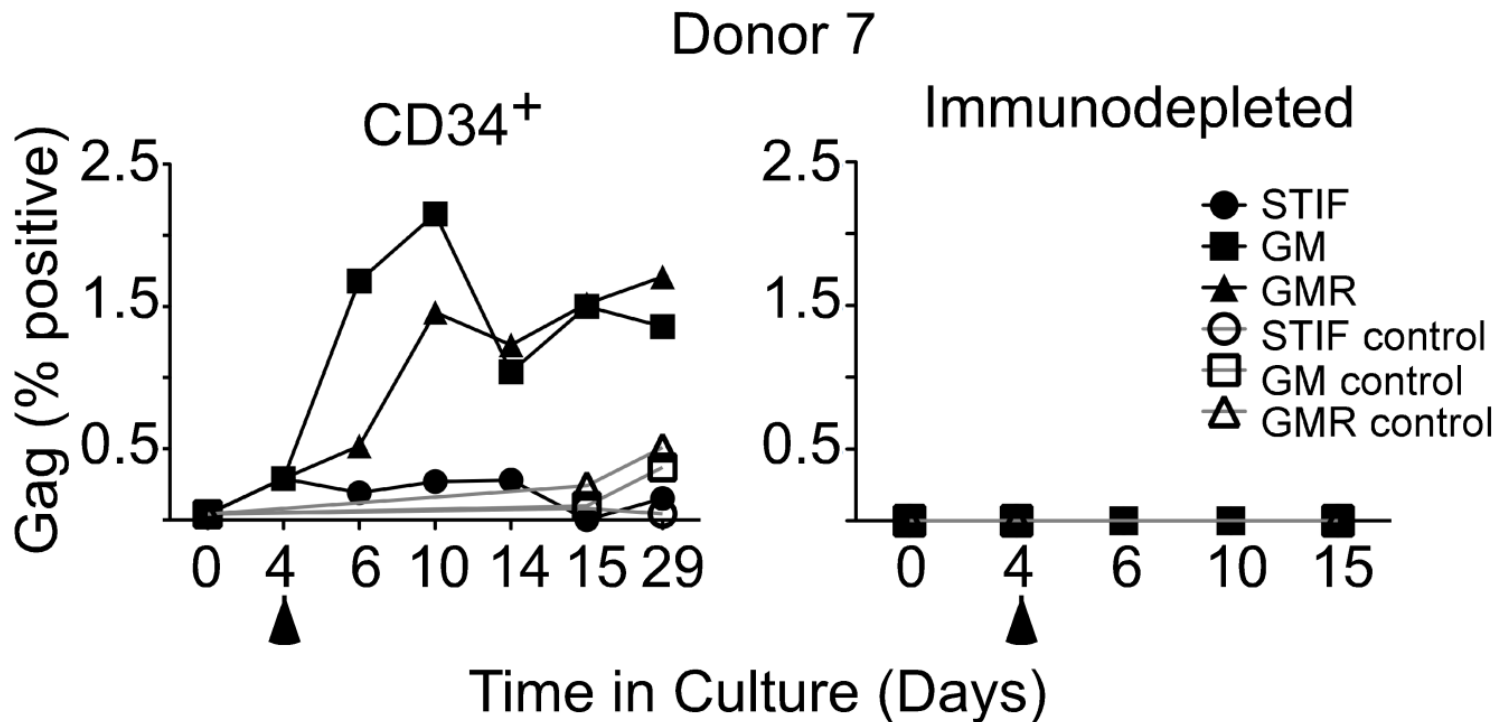
Reactivation of endogenous virus



Latency re-activation: High Viral Load donors



Latency re-activation: Donors with undetectable viral loads



Conclusions

- CD34+ hematopoietic progenitor cells are targets of HIV infection.
- HIV establishes both active and latent infection in CD34+ HPCs.
- *In vitro*, latently infected cells can be re-activated to express HIV Gag.
- Active and inducible latent infection is detectable in CD34+ cells from HIV-infected patients.

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