

Transmitted/Founder Virus-Like Variants are Archived in the Reservoir

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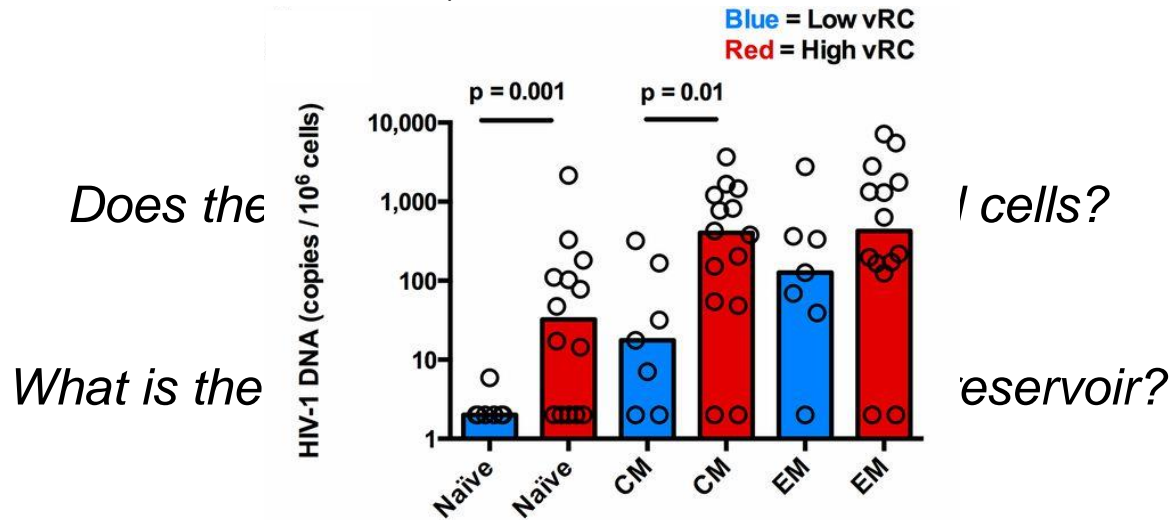
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Transmitted/Founder Virus (TFV) and Early Infection Events

- In a rhesus macaque model, reservoir seeding occurs as early as three days following SIV infection (Whitney et al. *Nature* 2014)
- TFV replication impacts HIV DNA burden in naïve and central memory CD4+ T cells (Claiborne et al. *PNAS* 2015)



Study Group and Sampling Strategy



- 13 recently infected individuals (7 men, 6 women)
- Subtype C infections
- All remained ART-naïve for >2 yrs from the estimated date of infection (EDI)
- All volunteers subsequently on ART with viral load <100 copies/mL



HIV Infection
(seroconversion)



- Near full-length genome amplification
- Single genome amplification (SGA)
- Sequencing with Pacific Biosciences (Dilernia et al. *NAR* 2015)

ART Initiation

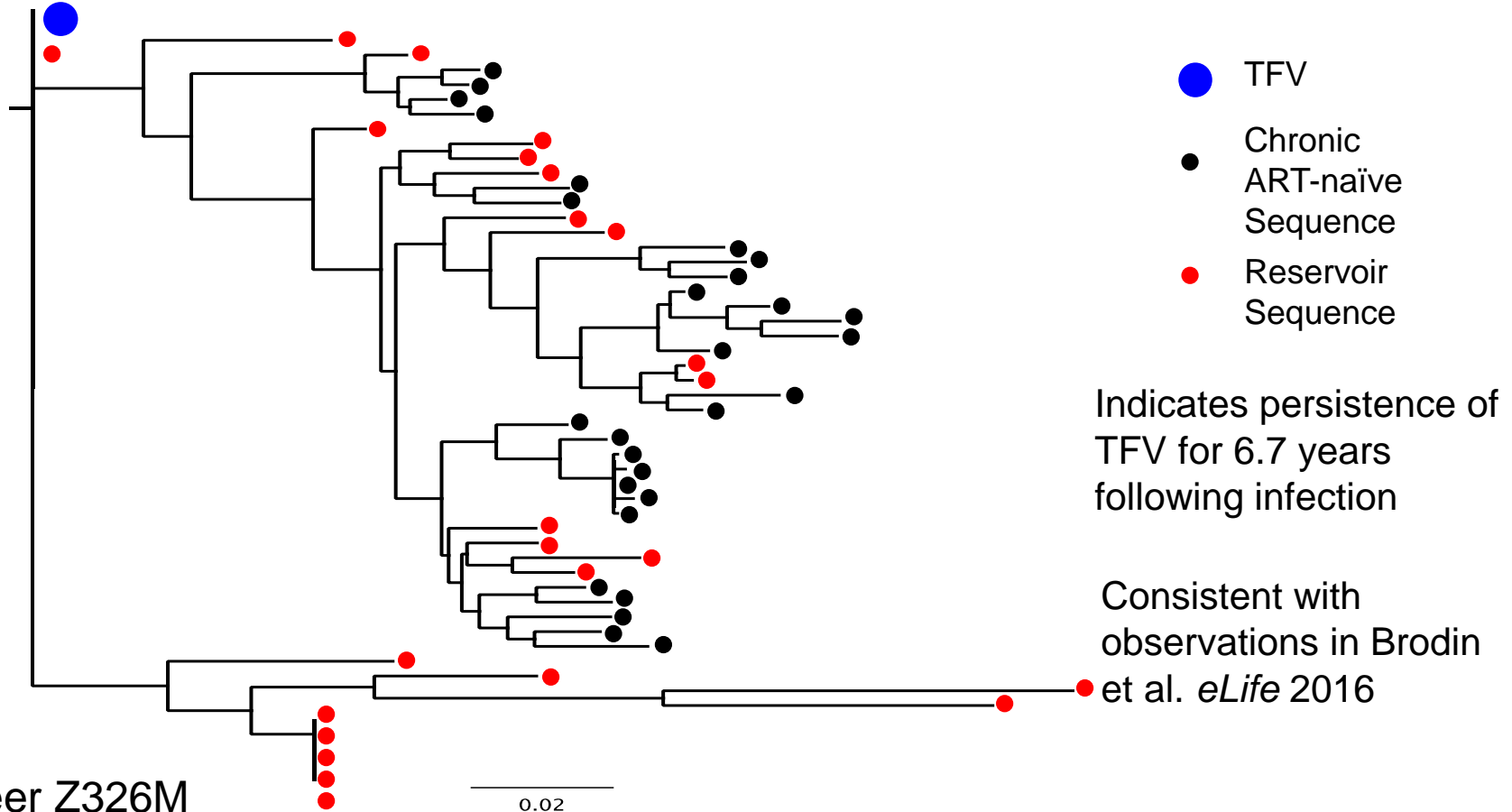


- *env* gene amplification with SGA (chronic)

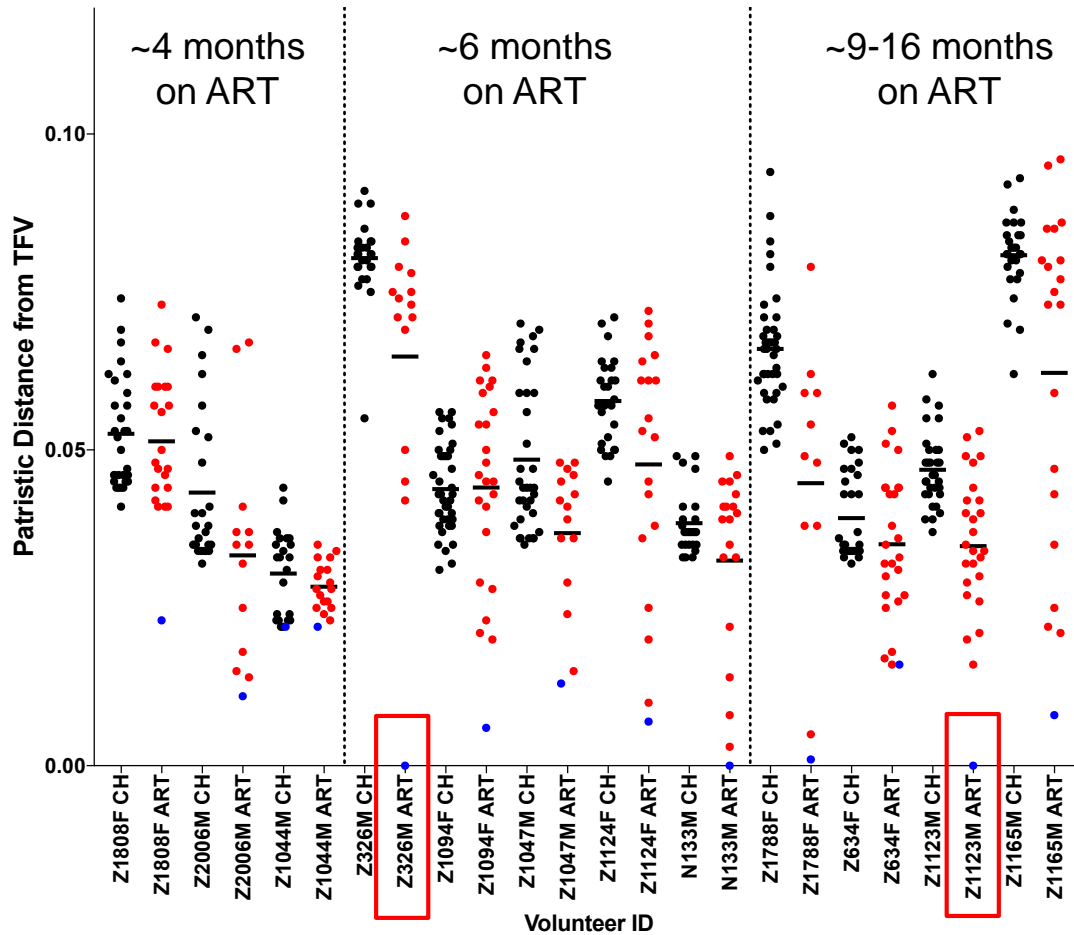


- *env* gene amplification with SGA (reservoir)

TF or TFV-like Variants Archived in the Reservoir

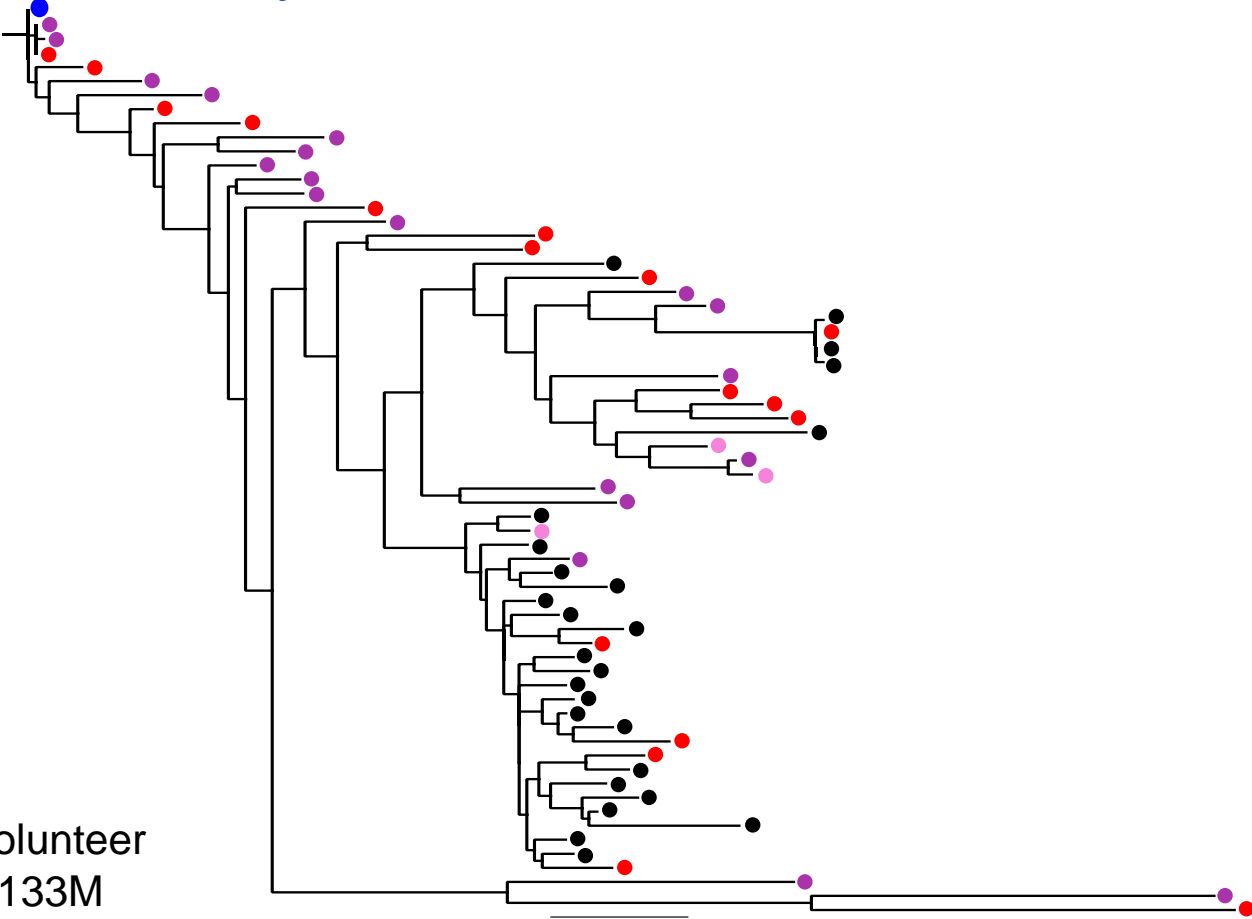


TF or TFV-like Variants Archived in the Reservoir



- Two individuals with TFV in reservoir
- The closest relative of the TFV is from the reservoir in 10 of 11 single variant infections

Early Viral Variants Maintained with Continued Treatment



TFV

Chronic Infection
(2.77 yrs from EDI)

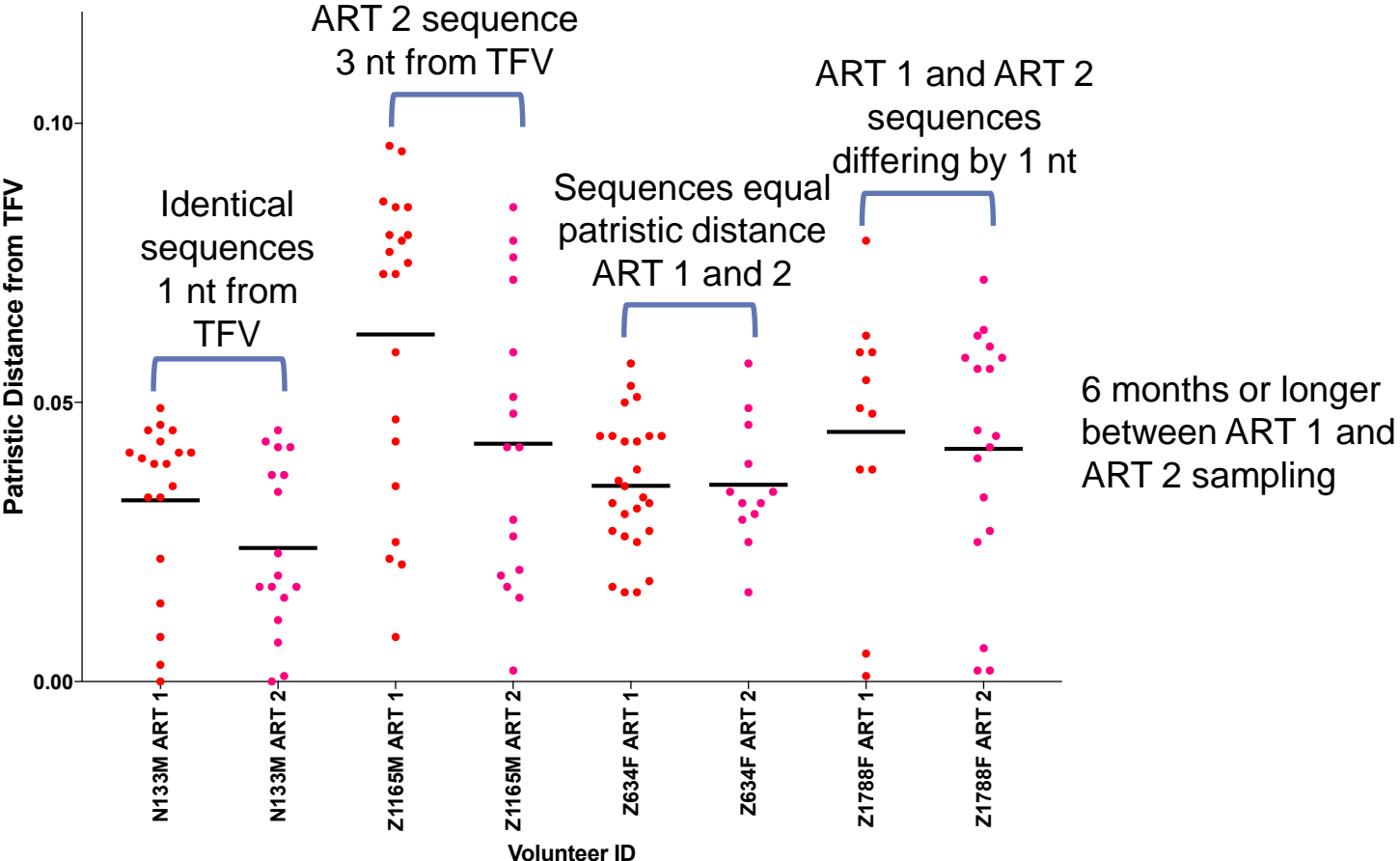
Reservoir 1
(0.56 yrs on ART, 3.43 yrs from EDI)

Reservoir 2
(1.27 yrs on ART, 4.14 yrs from EDI)

Volunteer
N133M

0.01

Early Viral Variants Maintained with Continued Treatment



Conclusions

- Reservoir is seeded throughout infection
 - TFV or TFV-like variants in reservoir indicate very early seeding and viral persistence
 - Proviral variants most closely related to chronic infection variants indicate continued seeding during ART-naïve infection
- Continued time on treatment does not abrogate persistence of early infection variants in the reservoir, and the contribution of these early sequences to the reservoir may be enriched on longer treatment

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Multivariant Infection

MJ4 (lab strain)

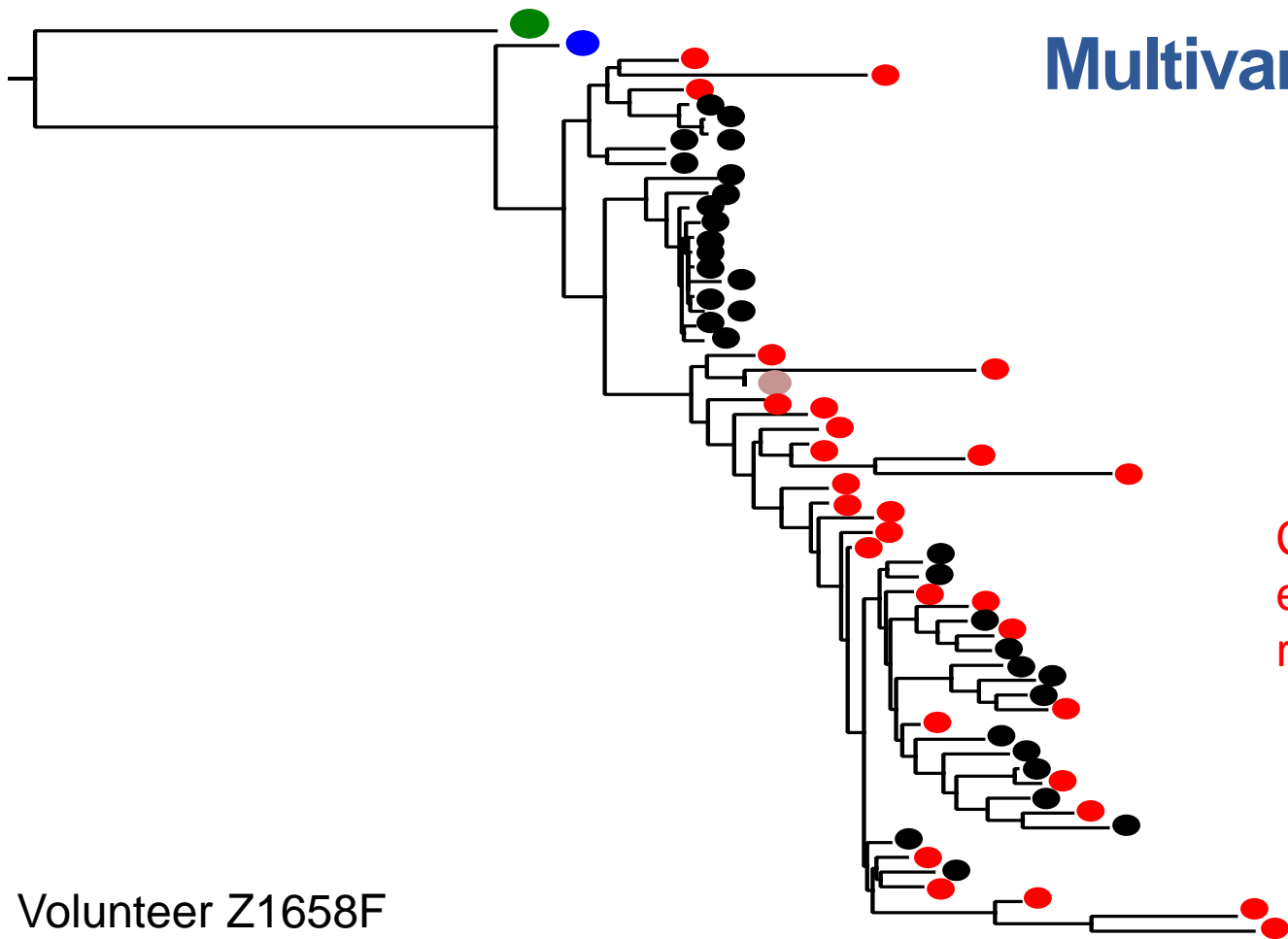
TFV A

TFV B

Chronic Infection

Reservoir

Close relatives to
either TFV in the
reservoir



Volunteer Z1658F

0.04