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Towards an HIV Cure
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Pathways to an HIV cure, 28 July 2022

Broadly neutralizing antibodies and the HIV reservoir

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Conflict of interest disclosure

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No relevant financial relationships to disclose.

Community Slide

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What key question was asked?

Can broadly neutralizing antibody (bNAb) therapy impact the HIV reservoir?

What was the key finding / take-home message?

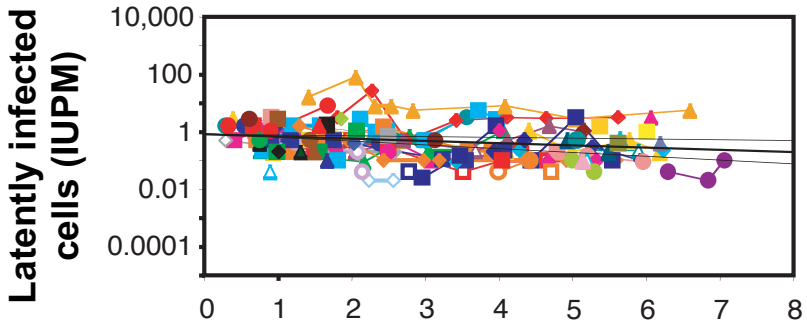
Changes in the size and composition of the intact proviral reservoir after bNAb therapy.

How is this important for an HIV cure?

Goal of HIV-1 cure research is to reduce or silence the reservoir.

Reservoir
Half-Life

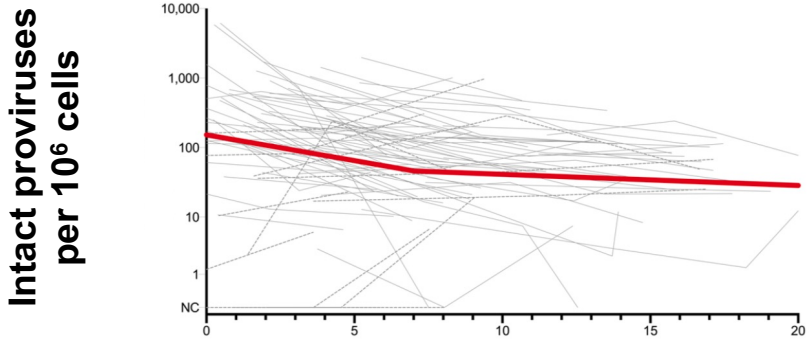
QVOA



$T_{1/2}$= 3.7 years

Siliciano et al – Nature Medicine 2013

IPDA

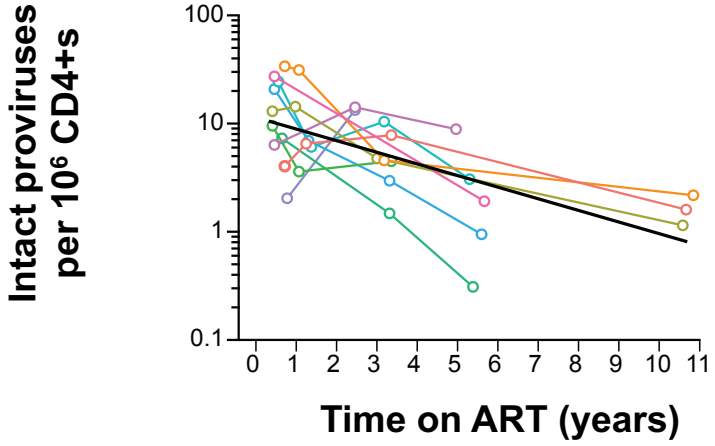


$T_{1/2}$= 4 years (0-7 years)

$T_{1/2}$= 18.7 years (>7 years)

Peluso et al – JCI Insight 2020

Q4PCR



$T_{1/2}$= 4.9 years

Cho et al – PNAS 2022

bNAbs
Mechanism

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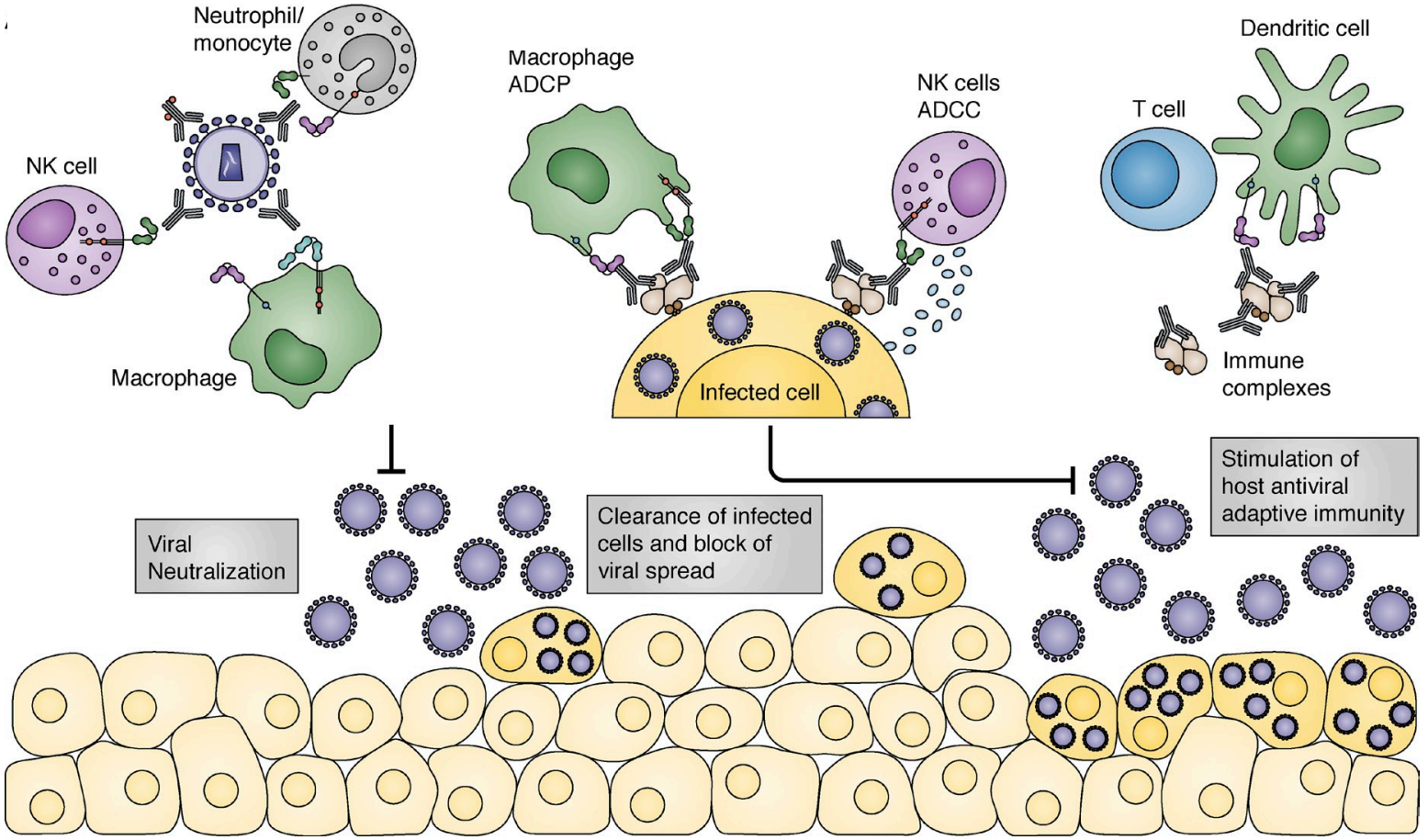
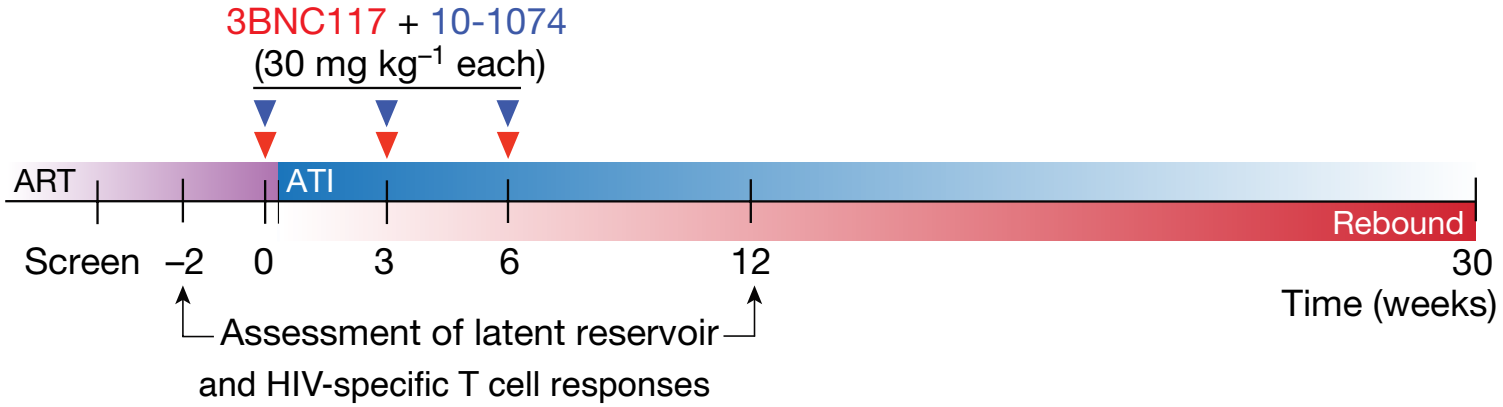


Bournazos et al – JEM 2013

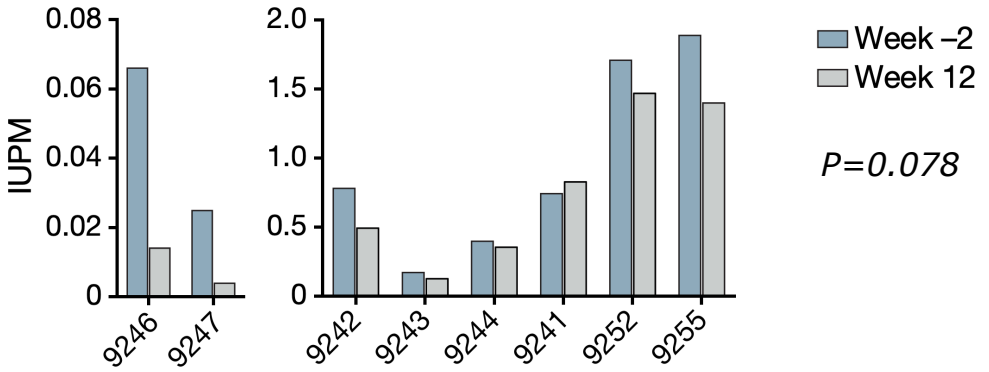
1. **Broadly neutralizing antibodies mediate effector functions**

2. **Therapy** with **bNabs** potentially eliminates infected CD4+ T cells and **reduces HIV-1 latent reservoir** in people living with HIV



3BNC117 + 10-1074

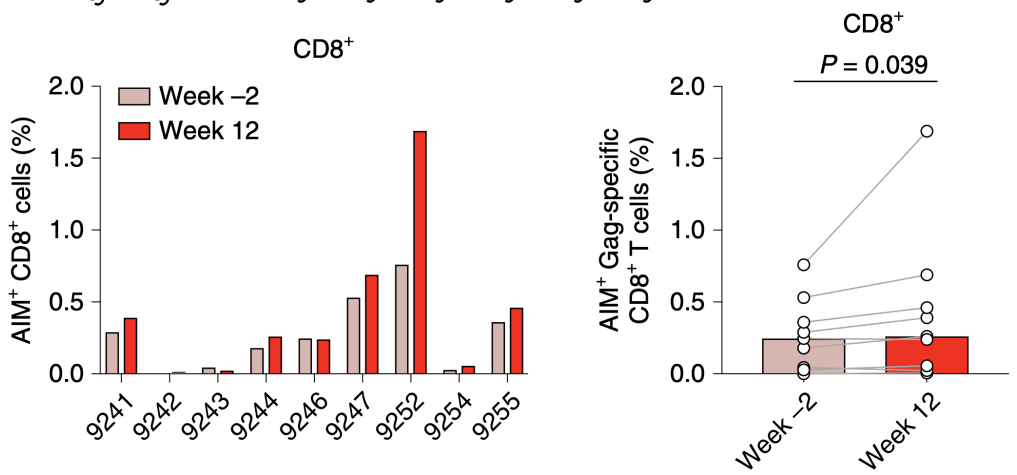
Q²VOA



IUPM reduction, not significant

Mendoza et al – Nature 2018

AIM assay



Increased HIV-specific T cell immunity

Niessl et al – Nature Medicine 2020

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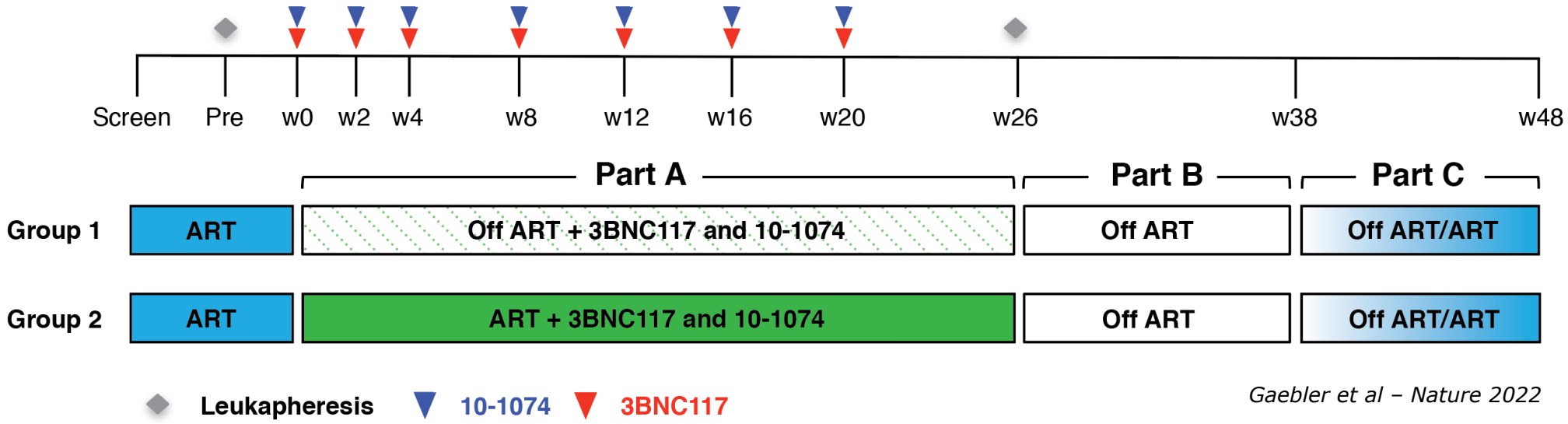
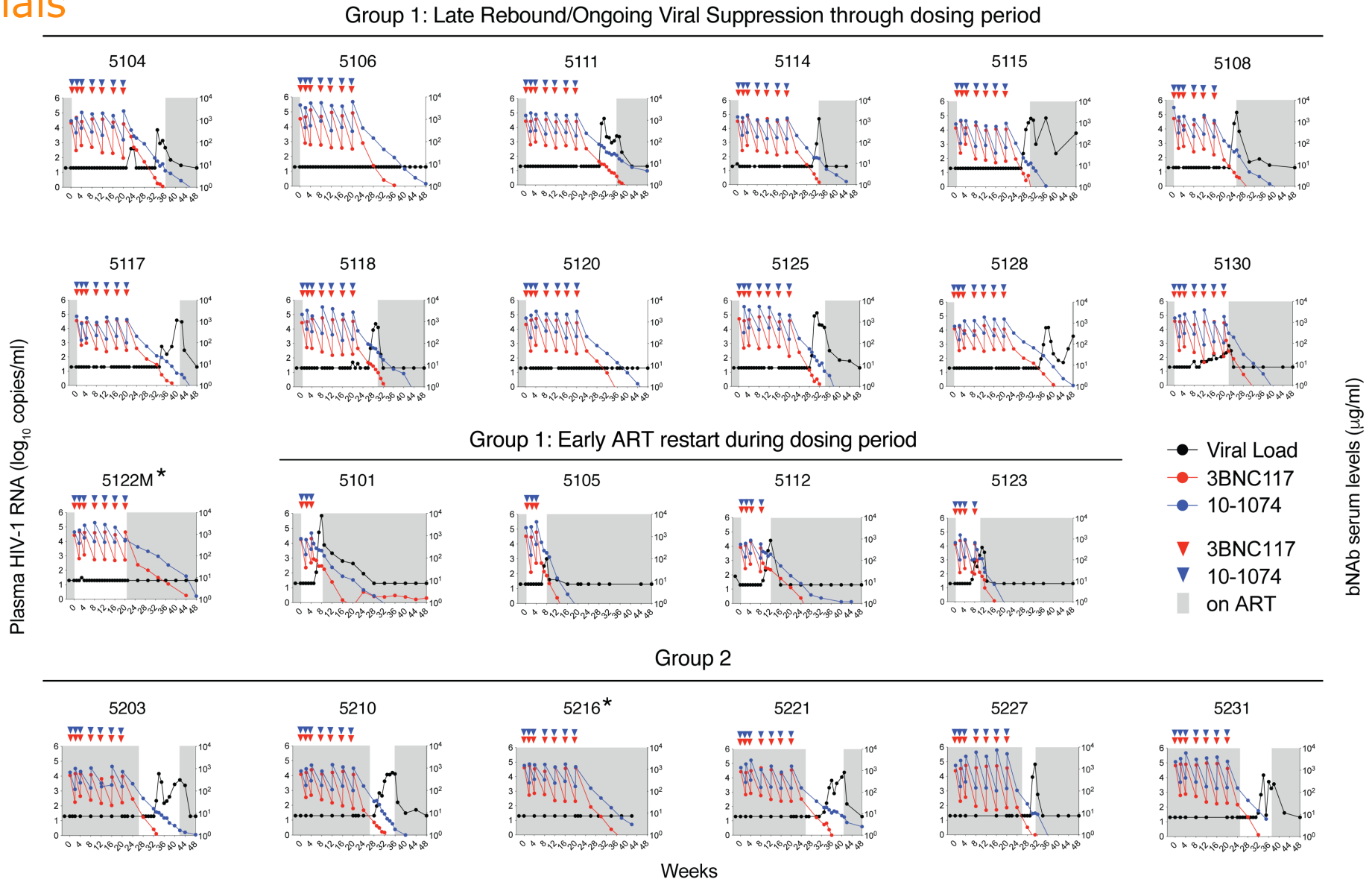
3BNC117 + 10-1074



Gaebler et al – Nature 2022


Group 1: Late Rebound/Ongoing Viral Suppression through dosing period
5104
5106
5111
5114
5115
5108
5117
5118
5120
5125
5128
5130
Group 1: Early ART restart during dosing period
5122M*
5101
5105
5112
5123
Group 2
5203
5210
5216*
5221
5227
5231
Plasma HIV-1 RNA (log10 copies/ml)
bNAb serum levels (μg/ml)
Viral Load
3BNC117
10-1074
3BNC117
10-1074
on ART
Weeks

Reservoir
Q4PCR

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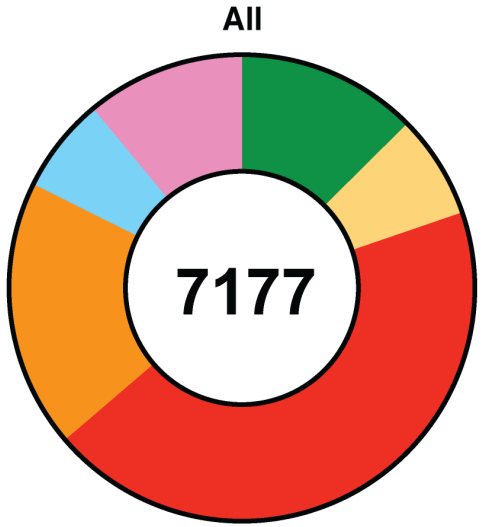

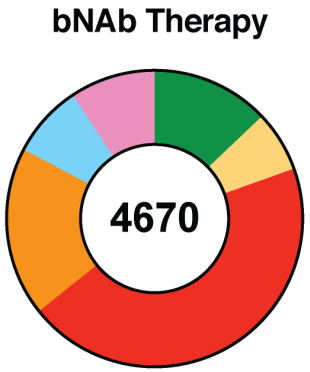

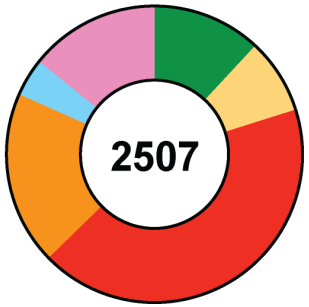

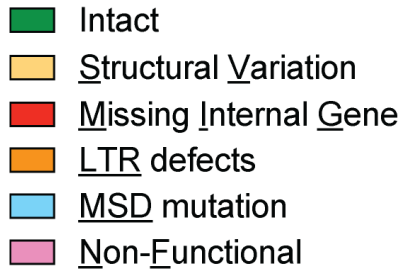

Sequences recovered

902 intact (12.6%) proviruses

6275 defective (87.4%) proviruses

Reservoir Quantification

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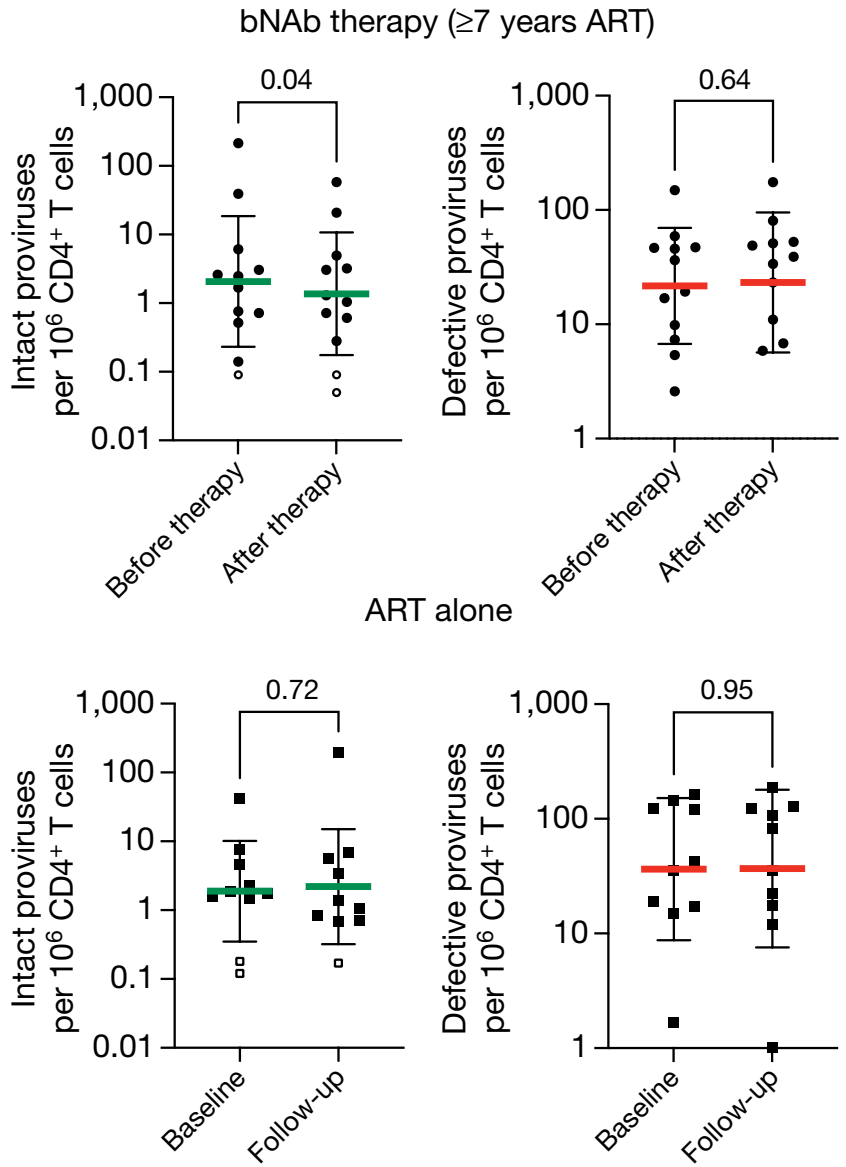
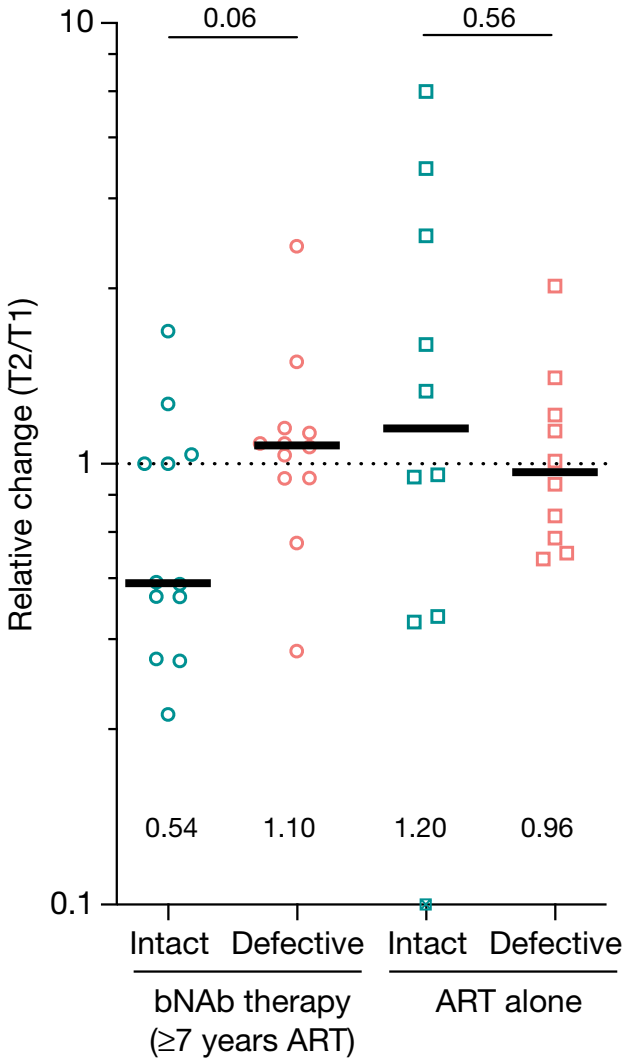
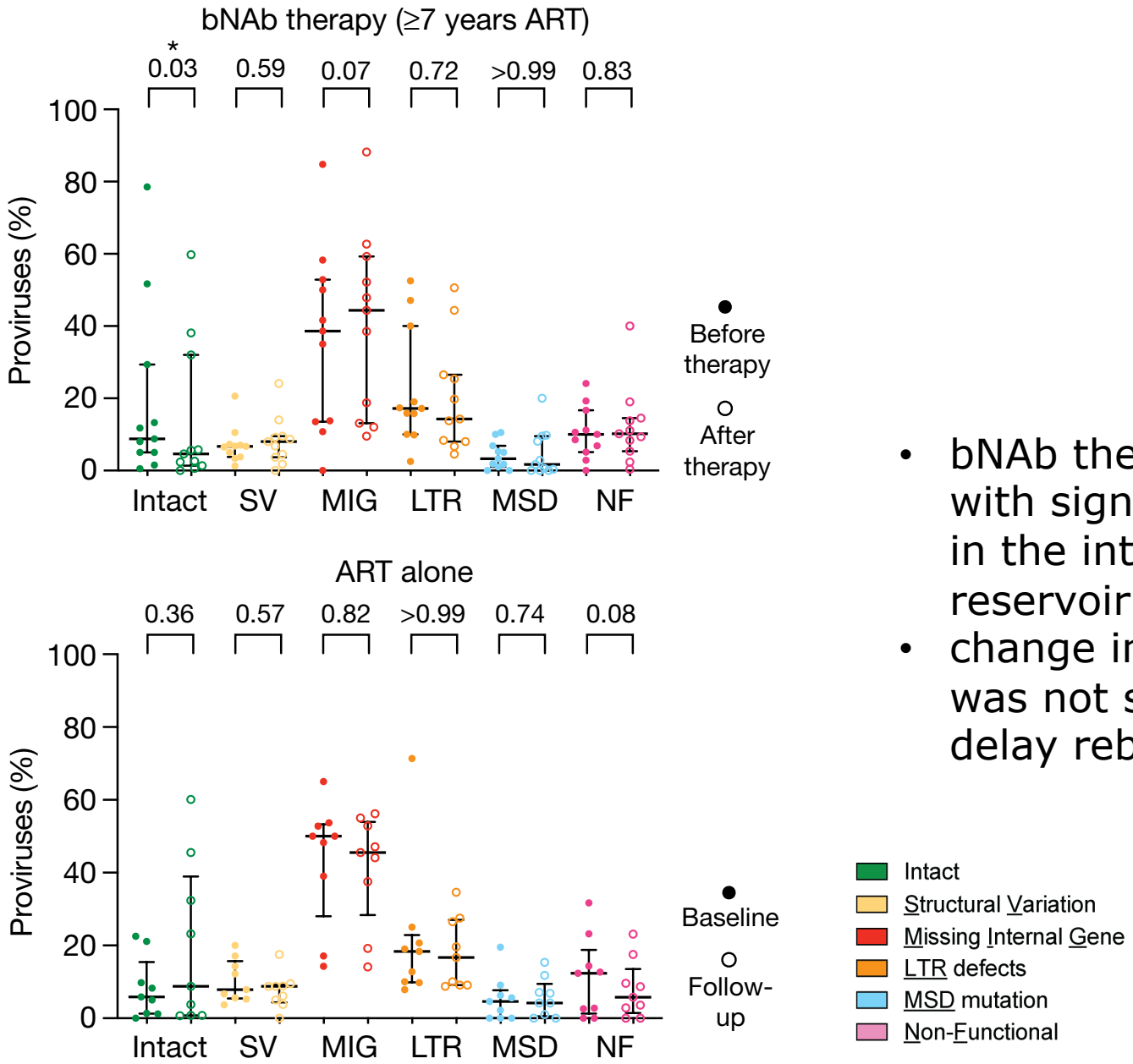


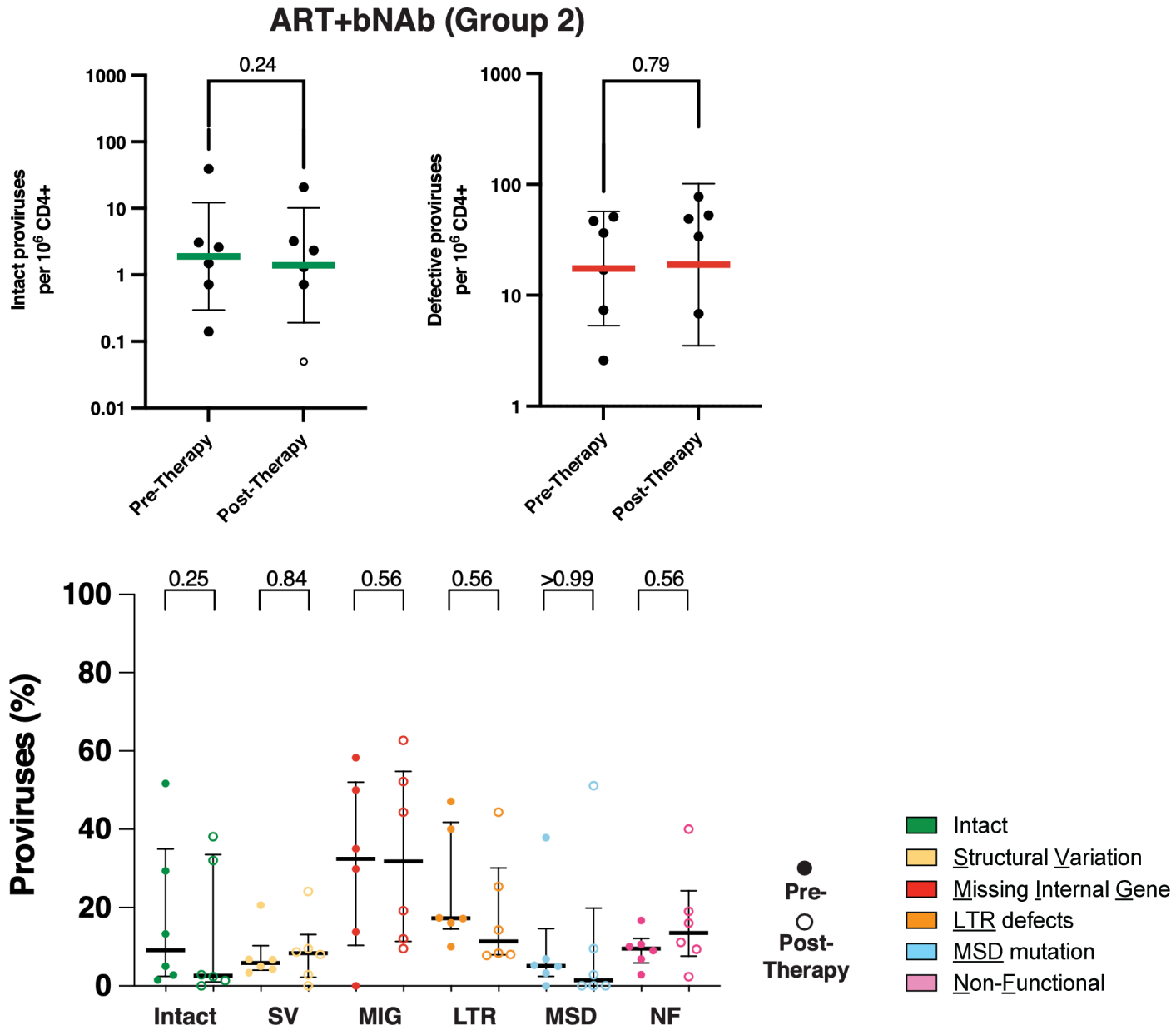


Reservoir
Composition



- bNAb therapy associated with significant decrease in the intact proviral reservoir
- change in reservoir size was not sufficient to delay rebound

Reservoir
Group 2 (ART+bNAb)



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Conclusions

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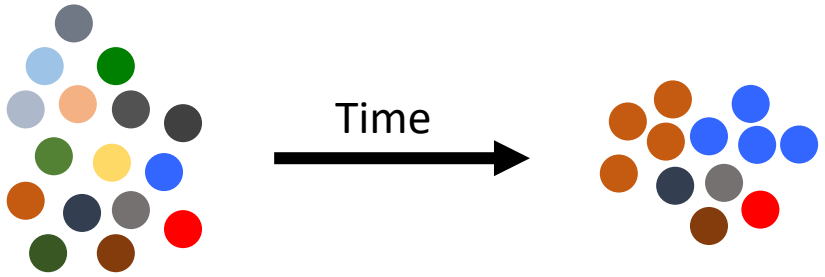
→ Immunotherapy with 3BNC117 and 10-1074 was associated with significant decrease in the intact proviral reservoir without measurable effect on the defective reservoir



Hypothesis:
Antibody therapies might **interfere** with **clonal expansion** and **reservoir maintenance** by **targeting** dividing **cells** that **express viral proteins directly** or by **enhancing** CD8+ **T cell immunity**

→ However, magnitude of the change in reservoir size after bNAb therapy was not sufficient to delay rebound.

Outlook:
Longer, and **larger studies** to **determine immunological mechanisms** as well as a **precise half-life** of the **intact reservoir** during **antibody therapy**

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CFAR Einstein-Rockefeller-CUNY Center for AIDS Research

BEAT-HIV DELANEY COLLABORATORY

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