Viral Reservoir Characteristics in Lymphoid Tissues of HIV-1 Elite Controllers

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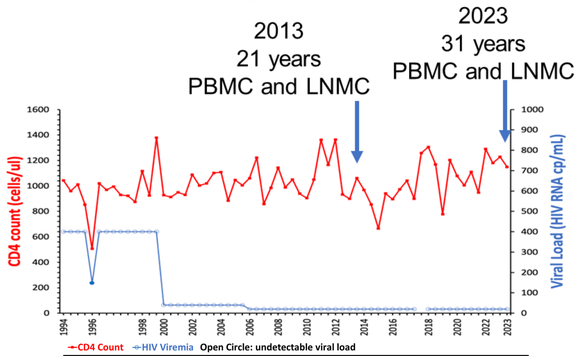
BACKGROUND

- EC maintain undetectable levels of viral replication by immune-mediated mechanisms
- Viral reservoir cells in PBMC from EC are small and frequently limited to intact proviruses integrated in heterochromatin regions, likely as a result of immune selection pressure (1)
- Viral reservoirs in lymphoid tissues from EC are less clear
- In this study, we longitudinally characterized viral reservoirs in blood and inguinal lymph node tissues from two EC

CLINICAL SUMMARY

Participant 1:

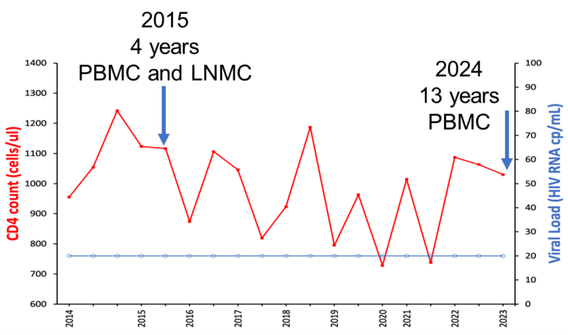
- Female, 64 years old, diagnosed 1992



HLA	A	B	C
	01:01/11:01	35:01/57:41	04:01/06:02

Participant 2:

- Female, 58 years old, diagnosed 2011



HLA	A	B	C
	02:01/30:02	15:31/57:03	16:01/18:02

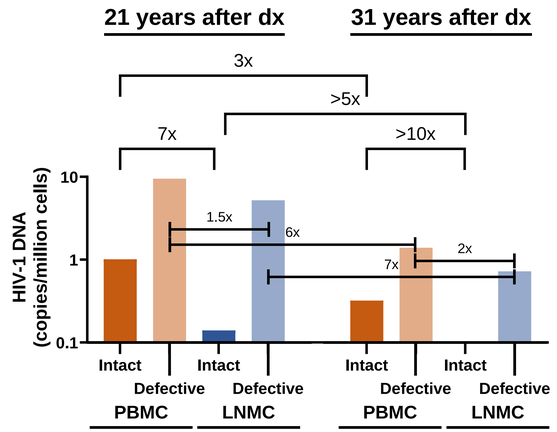
RESULTS

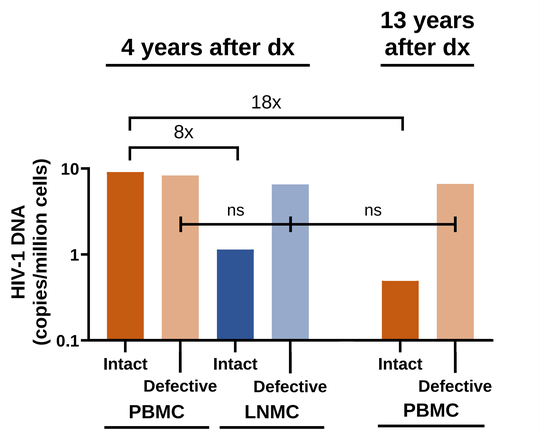
Participant 1

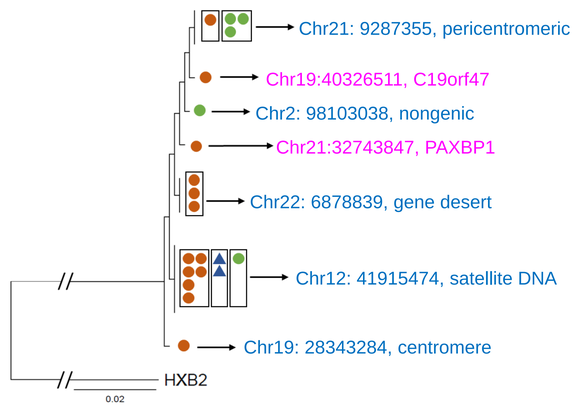
Timepoint	Sample Type	Total Cells Assayed (million)	# Intact Proviruses Detected	# Defective Proviruses Detected
21 years after dx	PBMC	13	13	109
	LNMC	14	2	73
31 years after dx	PBMC	16	5	22
	LNMC	18	0	13

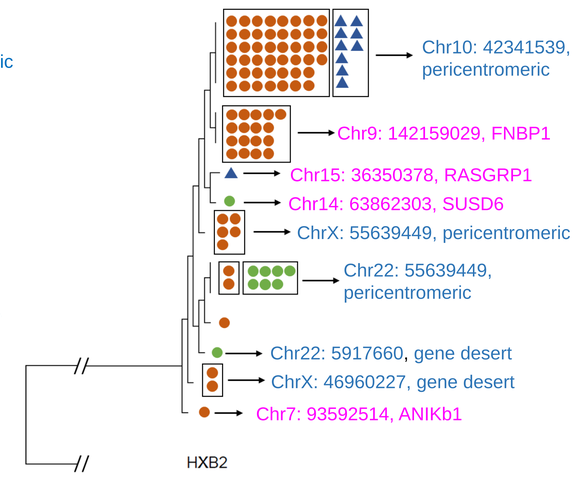
Participant 2

Timepoint	Sample Type	Total Cells Assayed (million)	# Intact Proviruses Detected	# Defective Proviruses Detected
4 years after dx	PBMC	7	67	61
	LNMC	9	10	57
13 years after dx	PBMC	18	9	123
	LNMC	NA	NA	NA









● PBMC 21 years
▲ LNMC 21 years
● PBMC 31 years
LNMC 31 years: no intact detected

Intact proviruses in genic regions
Intact proviruses in heterochromatin regions

● PBMC 4 years
▲ LNMC 4 years
● PBMC 13 years
LNMC 13 years: no sample available

METHODS

- **F**ull-**L**ength-**I**ndividual **P**roviral **Seq**uencing (FLIP-Seq)
  - Near-full-length sequencing assay to characterize the HIV reservoir in extracted DNA (2)
- **M**atched **I**ntegration Site and **P**roviral **Seq**uencing (MIP-Seq)
  - Near-full-length sequencing assay with integration site mapping of individual proviruses (3)
- **I**ntegration **S**ite **L**oop **A**mplification (ISLA) (4)
  - Integration site mapping of individual proviruses

CONCLUSIONS

The intact proviral landscape in lymph nodes is **smaller** and **less diverse** than in PBMCs

- All major intact reservoirs in LNMC are **shared** with PBMC

There is a **continuous, selective decline** of intact reservoirs across tissue types and time points

- Immune targeting of genic integration sites
- Only non-genic clones persist long-term

Future research into the immune selection forces that drive the **tissue dynamics** and **longitudinal decay** of **intact reservoirs** is needed

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