Effect of HIV-1 Infection and Virus Production on CD4+ T Cell Proliferation

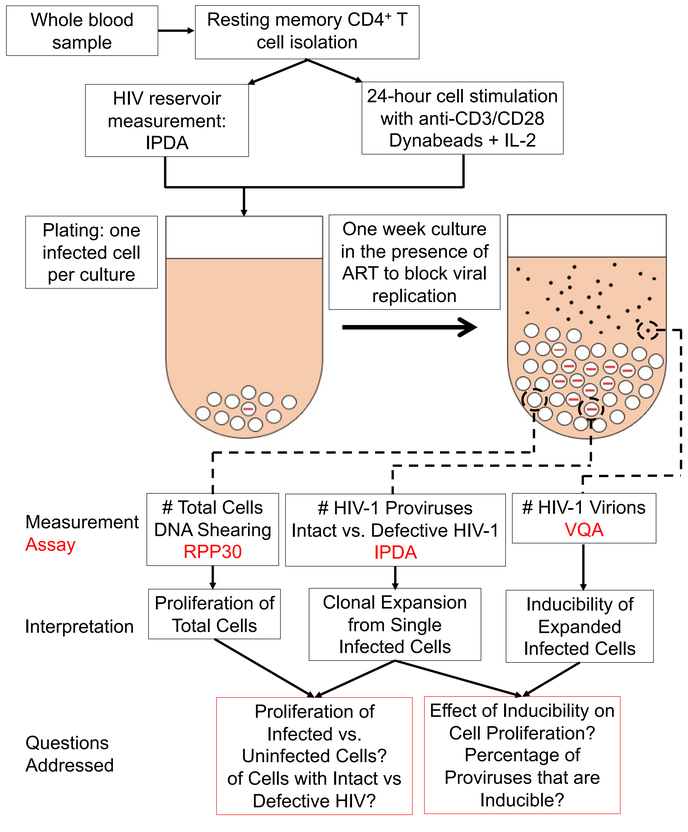
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BACKGROUND

- In persons living with HIV-1 on long-term ART, the majority of latently-infected CD4+ T cells with a replication-competent provirus are part of clonal populations. Proliferation is a major mechanism of persistence of the HIV-1 latent reservoir.
- Induction of latent HIV-1 proviruses is stochastic. Subsequent transcription and expression of HIV-1 proteins can be cytotoxic. Although the same stimuli can induce both viral gene expression and cell proliferation, the relationship between these cell fates remains unclear.
- The goal of this study was to determine the effects of HIV-1 infection, virion production, and HIV-1 integration site on CD4+ T cell proliferation following cellular activation.

METHODS



ACKNOWLEDGEMENTS

Study Participants

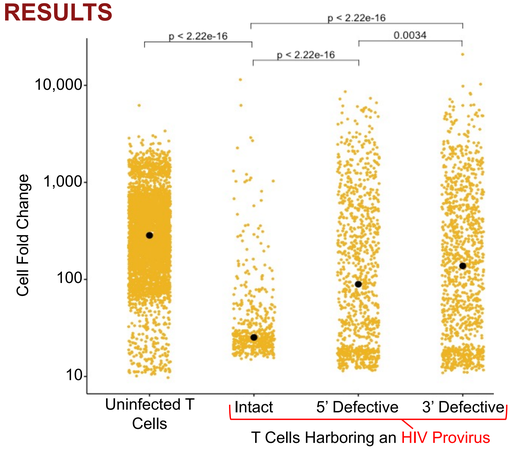
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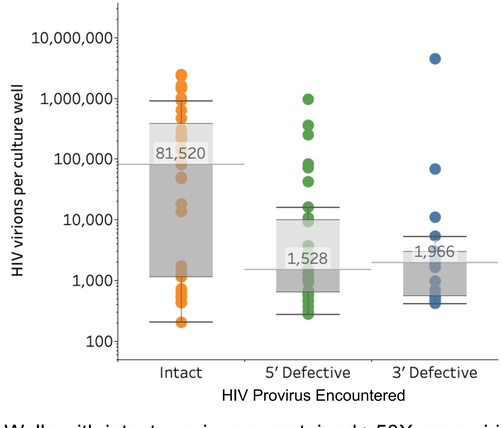
BEAT-HIV DELANEY COLLABORATORY

CD4+ T cells carrying an intact HIV-1 provirus have a reduced proliferative response to TCR stimulation which is independent of immune pressure.

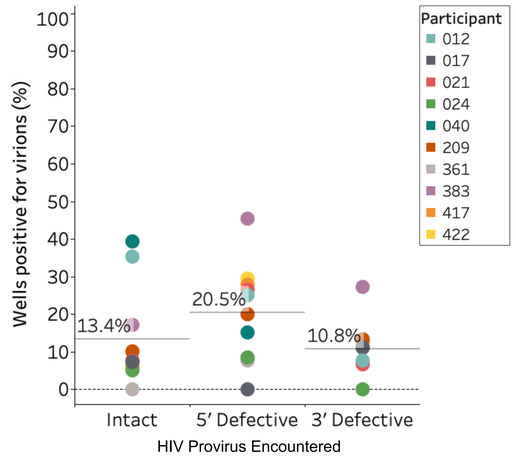
RESULTS



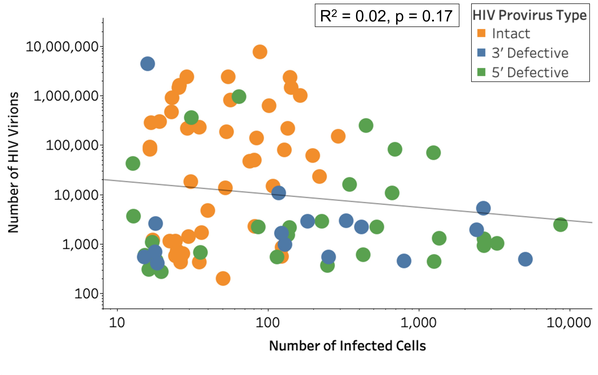
Following TCR stimulation, the number of progeny CD4+ T cells with an intact HIV-1 provirus generated from a single cell was 22.5% that of CD4+ T cells harboring a defective provirus and 8.9% that of uninfected CD4+ T cells.



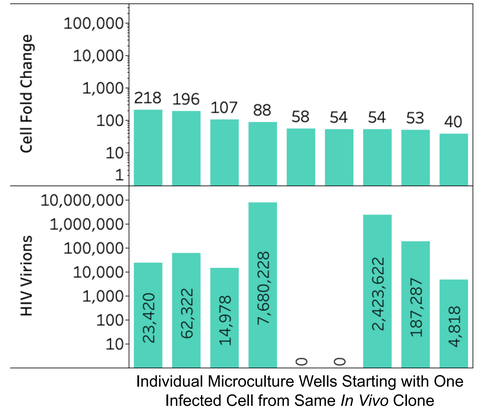
Wells with intact proviruses contained >50X more virions per well compared to wells with defective proviruses.



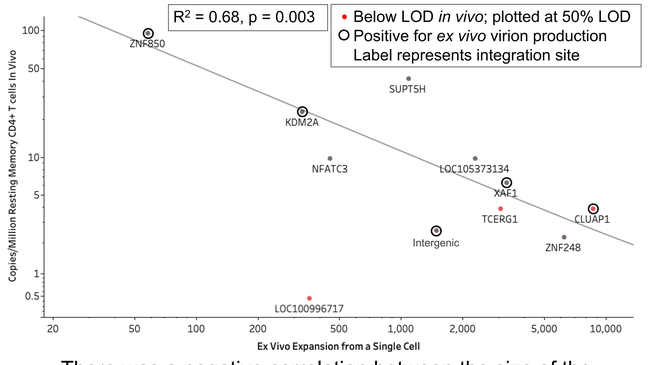
Wells with intact and defective proviruses were just as likely to contain virions, but >80% of wells had no virion production.



There was no correlation between virion production and cell proliferation. However, cells with intact proviruses tended to produce more virus, while cells with defective proviruses generally proliferated better.



Individual daughter cells belonging to the same *in vivo* clone produced virions *ex vivo*, but some divided without producing virions.



There was a negative correlation between the size of the infected cell clone *in vivo* and the amount of *ex vivo* expansion by a single infected cell from that clone.

CONCLUSIONS

- Latently-infected T cells expanded suboptimally *ex vivo.*
- Clinically, anti-proliferative agents are unlikely to be useful, as they may have a greater effect on normal T cell responses than on infected cell proliferation.
- Virion production was associated with but did not fully explain restricted infected cell proliferation.
- Cells from the same *in vivo* clone that received the same stimulation displayed varied inducibility.

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