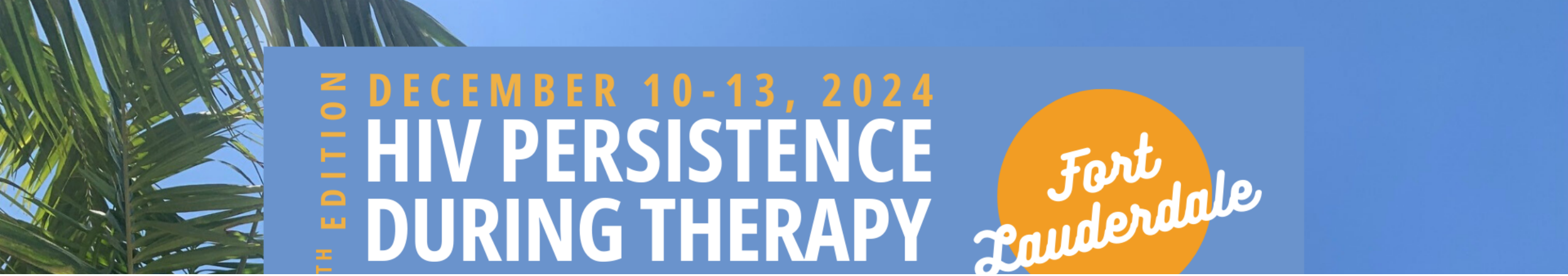
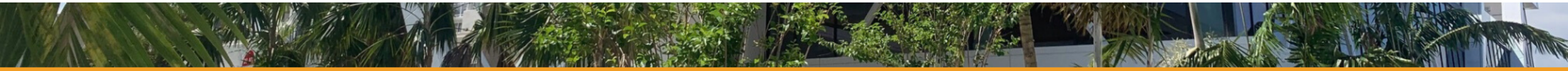


HIV infection induces T cell quiescence, leading to proviral latency

Saba Valadkhan

Associate Professor

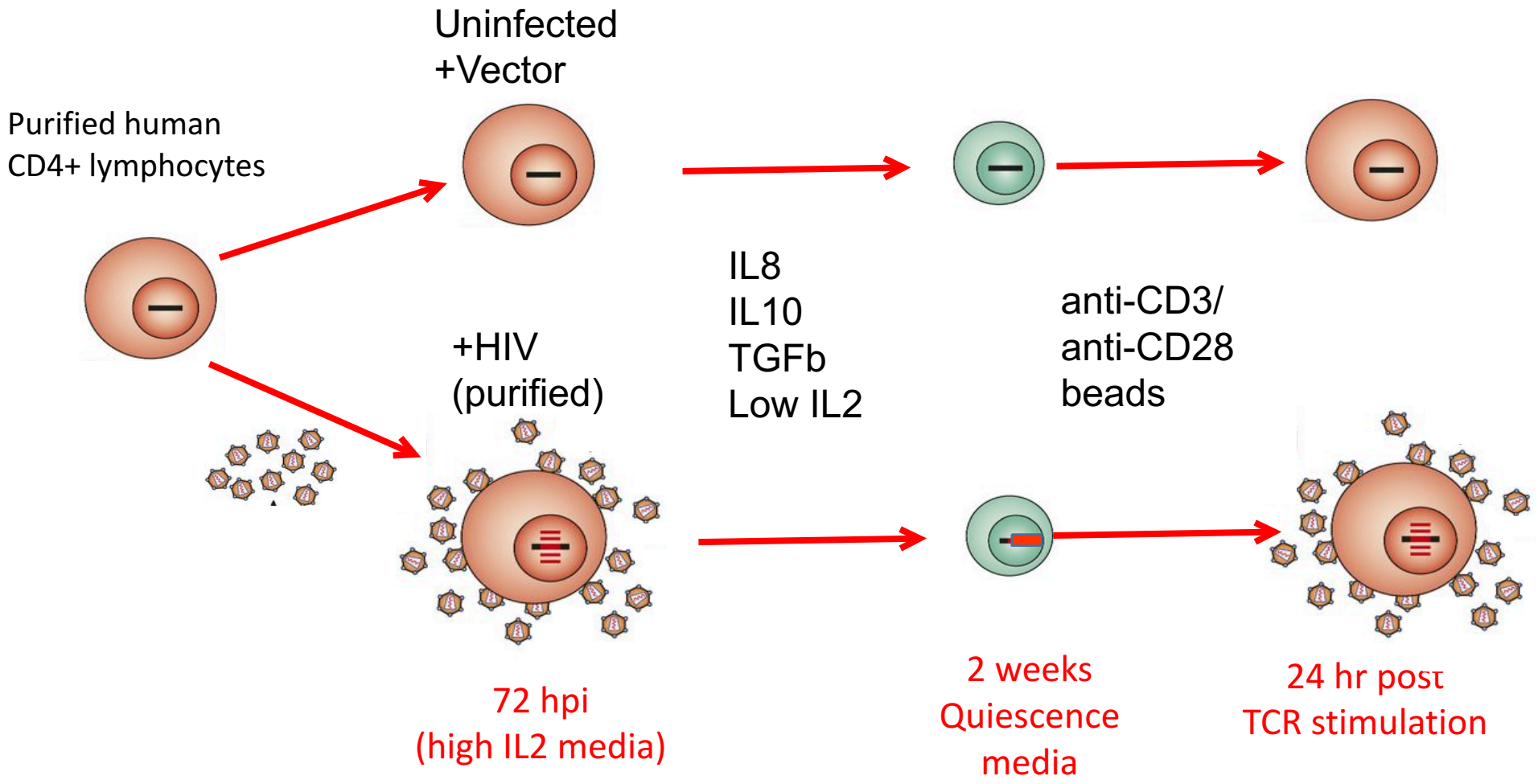
Case Western Reserve University School of Medicine



CONFLICTS OF INTEREST

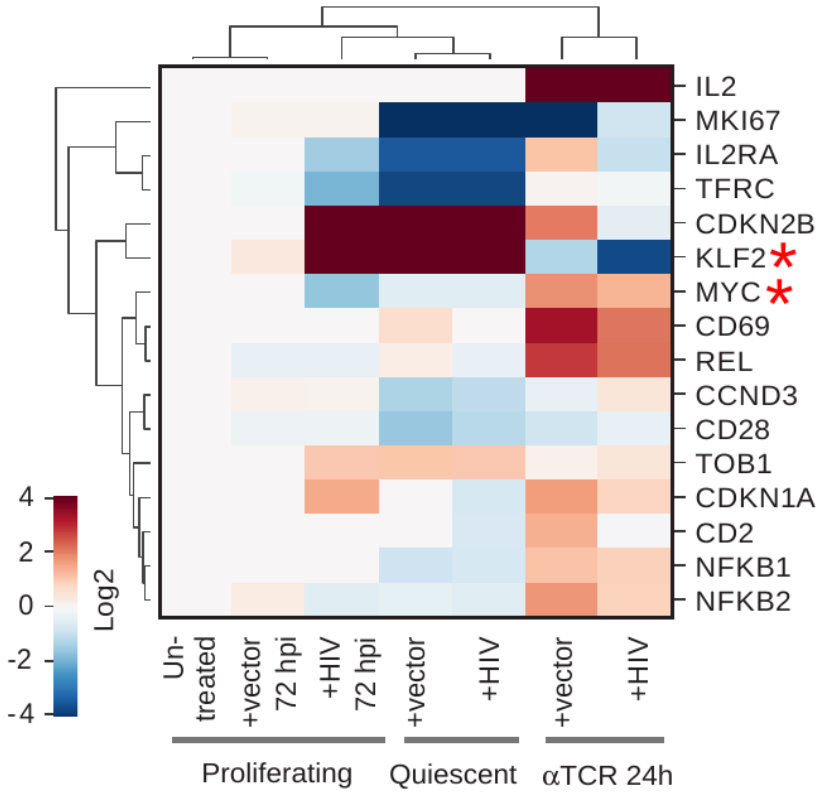
None

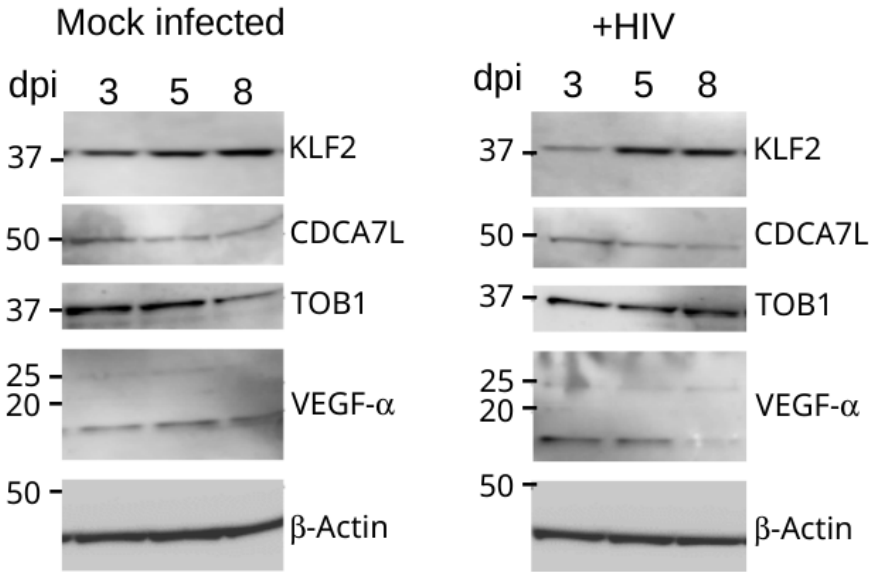
Transcriptome analysis of pure populations of HIV infected (& vector/mock infected) human primary CD4+ lymphocytes



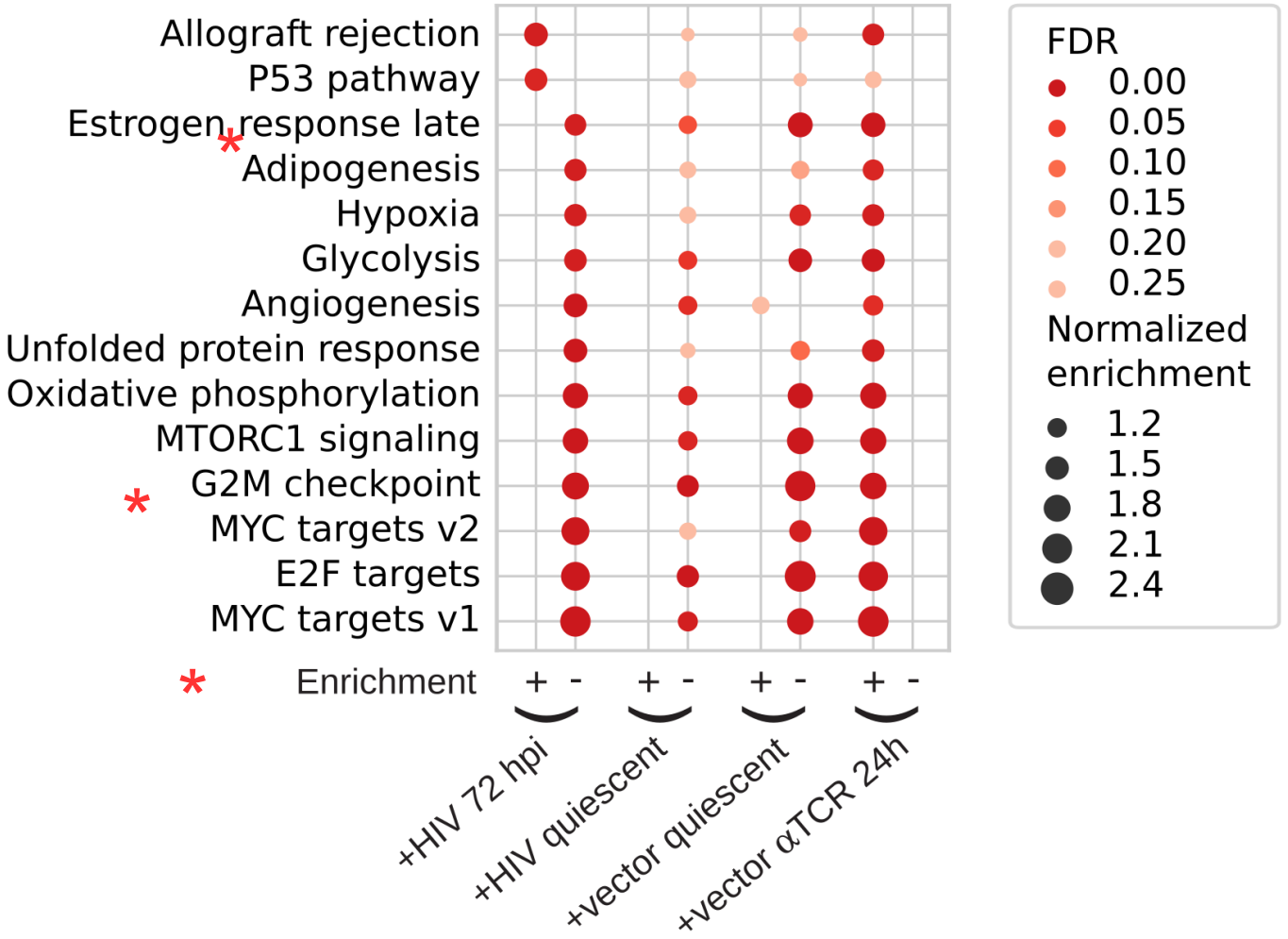
The HIV construct used is a single round NL4-3 derivative virus (Dobrowolski et al. 2019)

Early after infection, HIV infected cells show strong downregulation of key proliferation markers

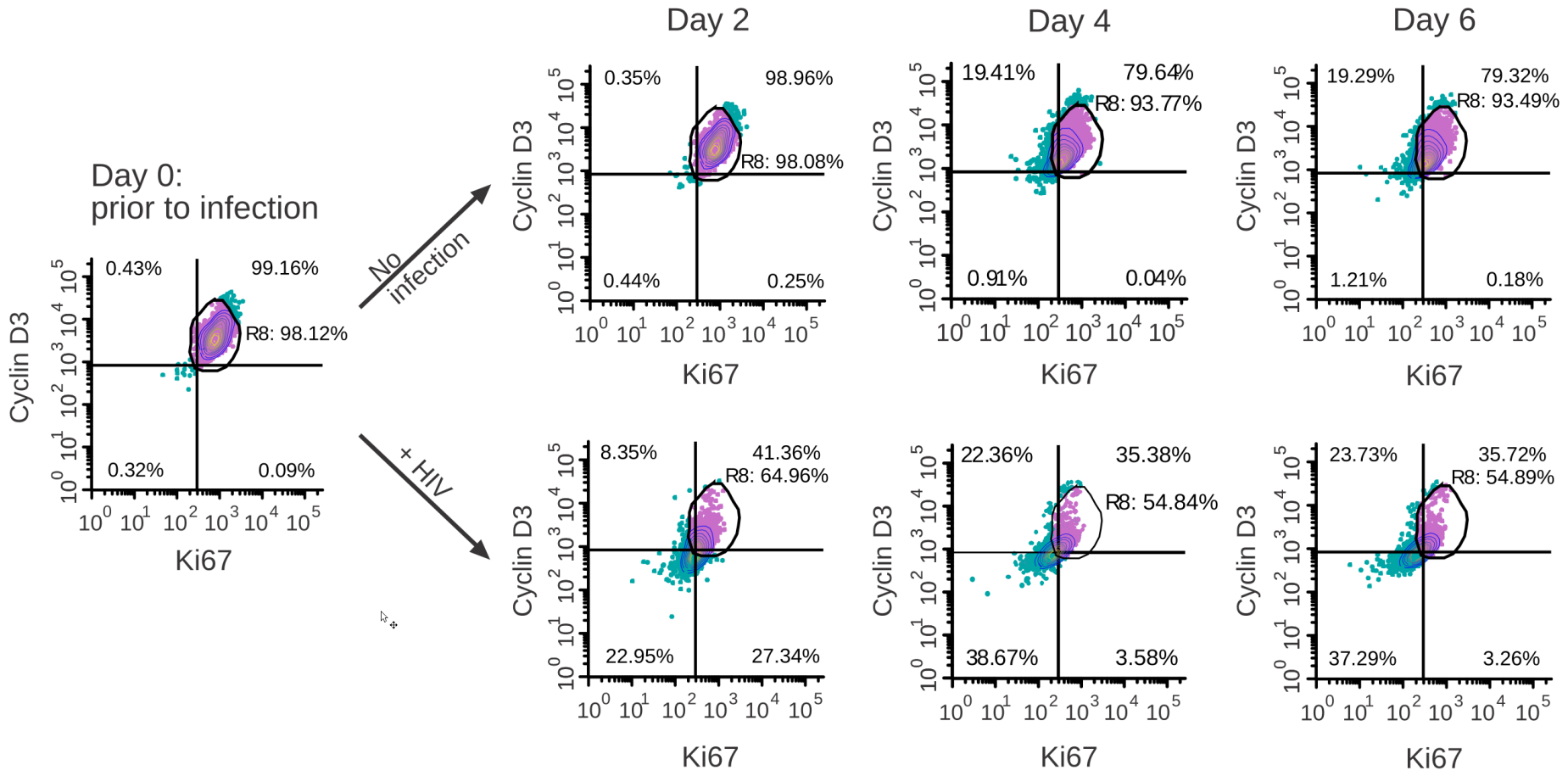




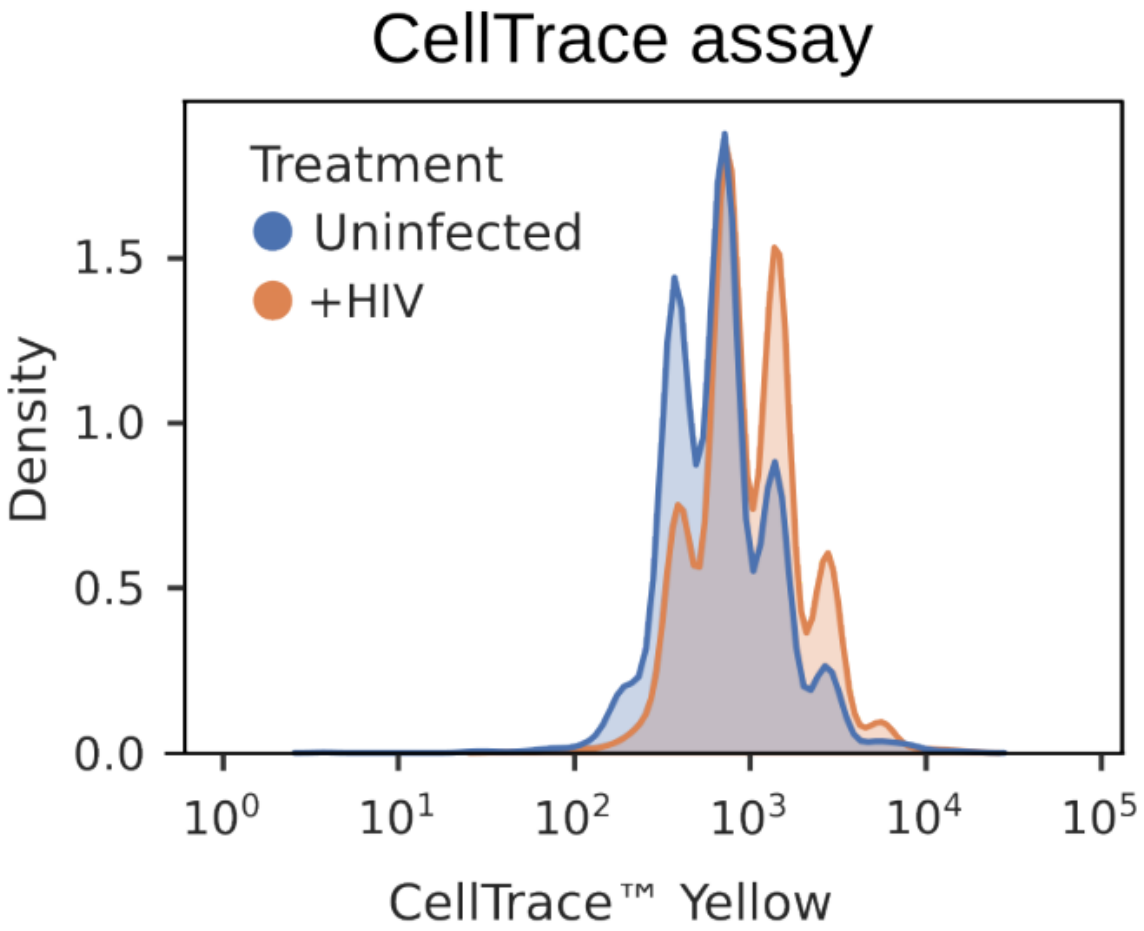
HIV infection leads to downregulation of multiple proliferative pathways



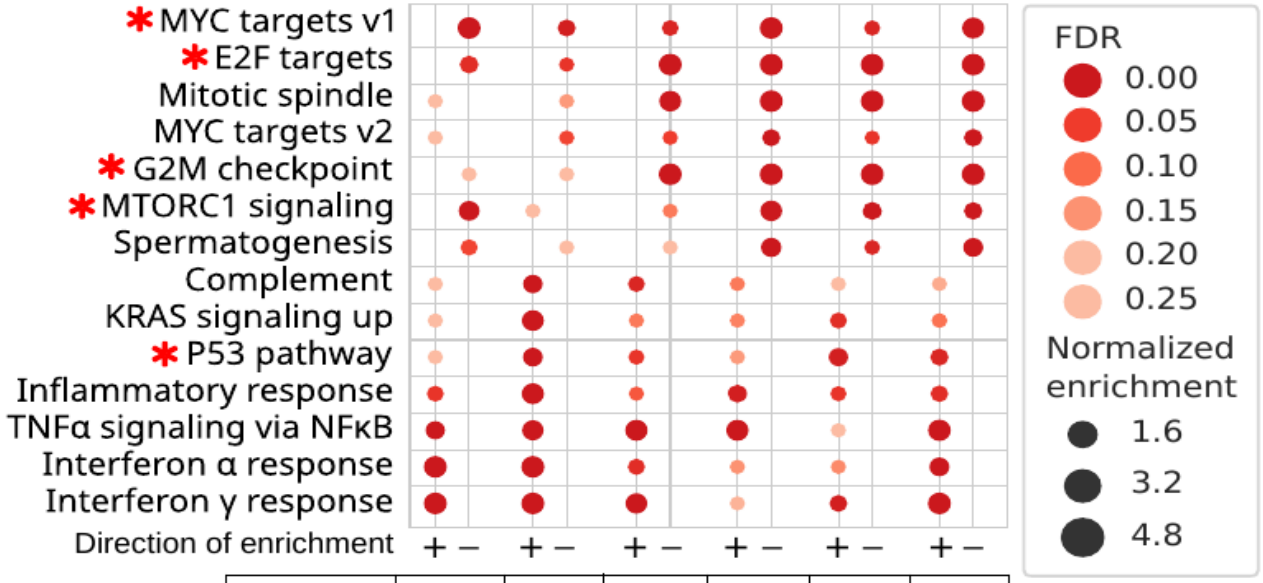
Flow cytometry studies confirm the HIV-induced quiescence phenotype



CellTrace assays confirm the strong slowdown of cellular proliferation after HIV infection



HIV-induced quiescence phenotype is observed in multiple independent studies

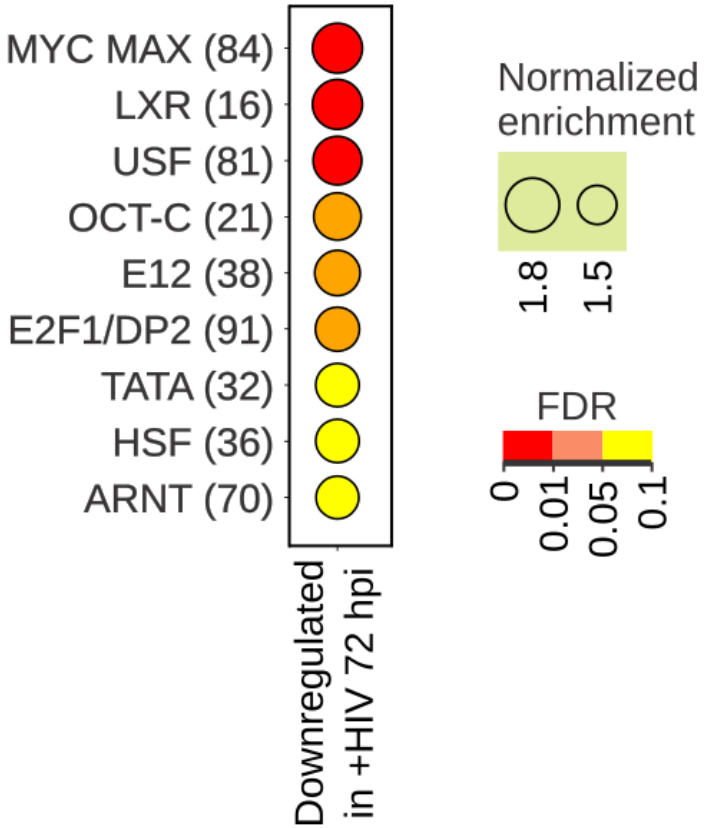


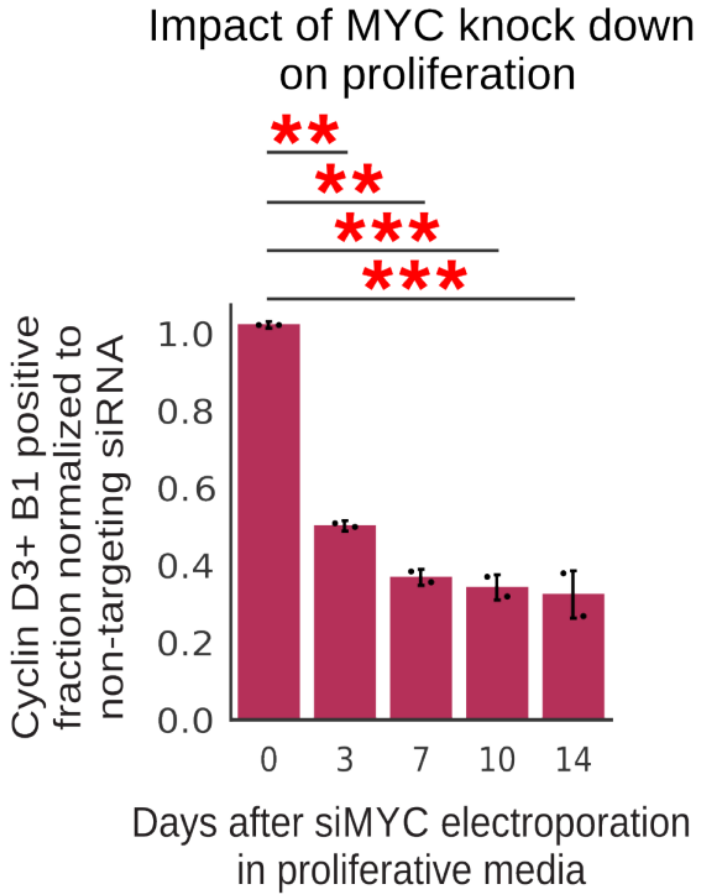
HIV strain	NL4-3	IIIB	Ba-L	CH007	CH106	REJO
hpi	72	48	48	48	48	48
CD4 subset	Mixed	Purified memory cells				
Accession	GSE 127468	GSE166375				

Infected with replication competent viruses

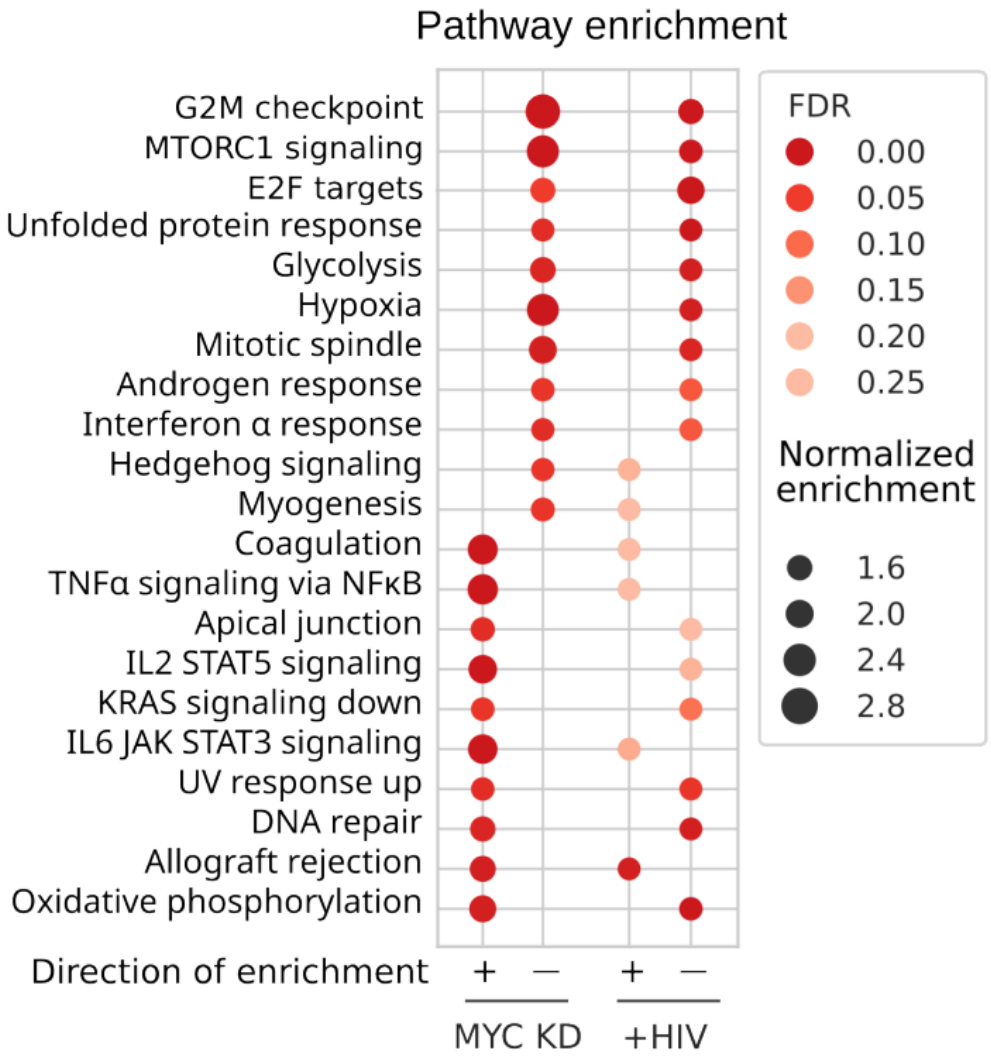
Both lab strains and primary isolates

MYC targets are strongly downregulated after HIV infection

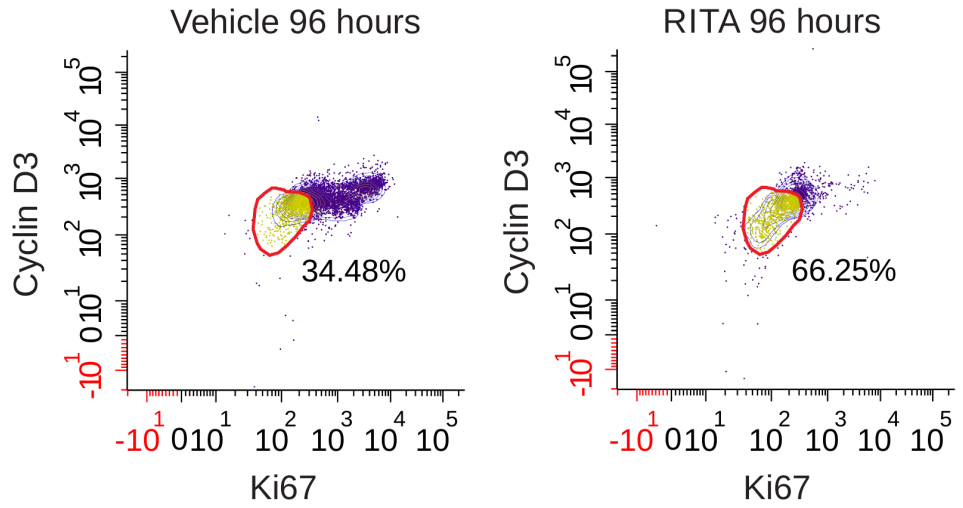


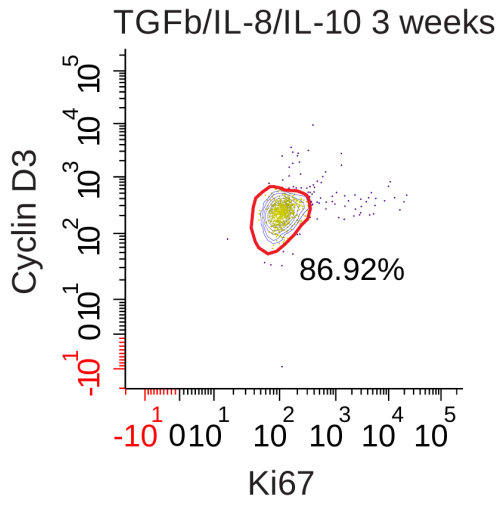


Knock down of MYC largely recapitulates the HIV-induced transcriptomic pattern of quiescence

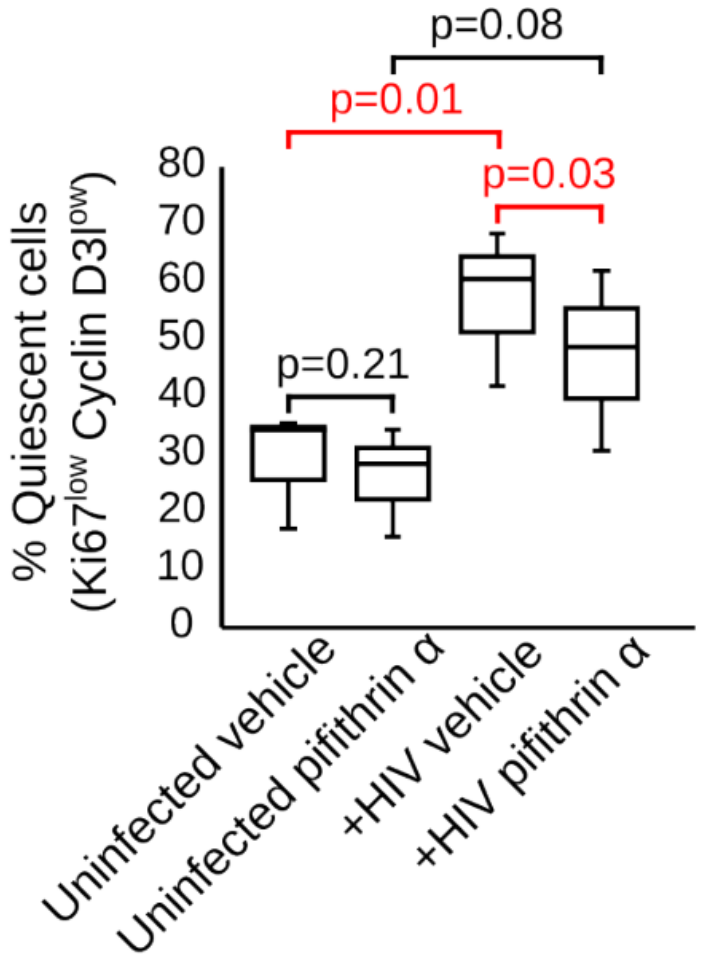


Activation of p53 pathway using RITA results in loss of proliferative markers in primary human CD4+ T cells

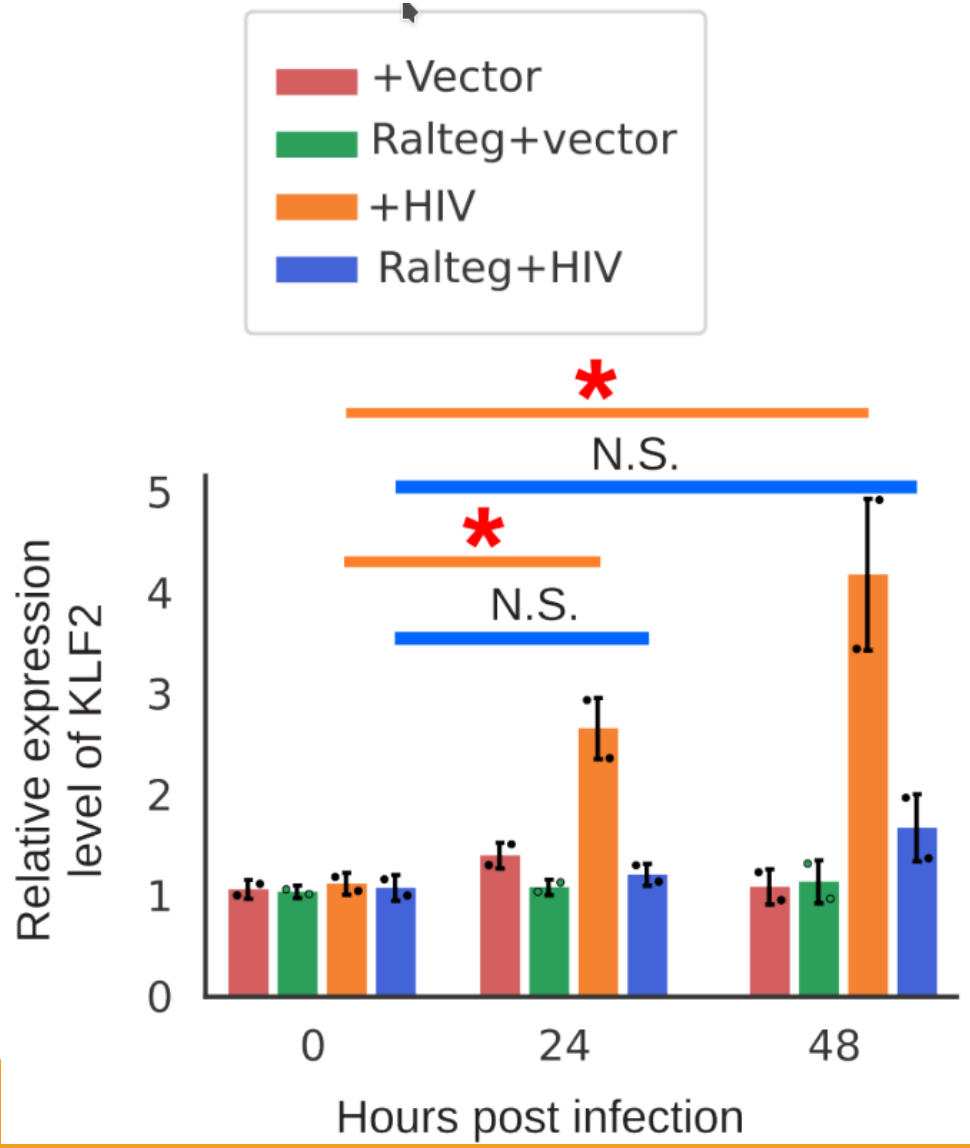




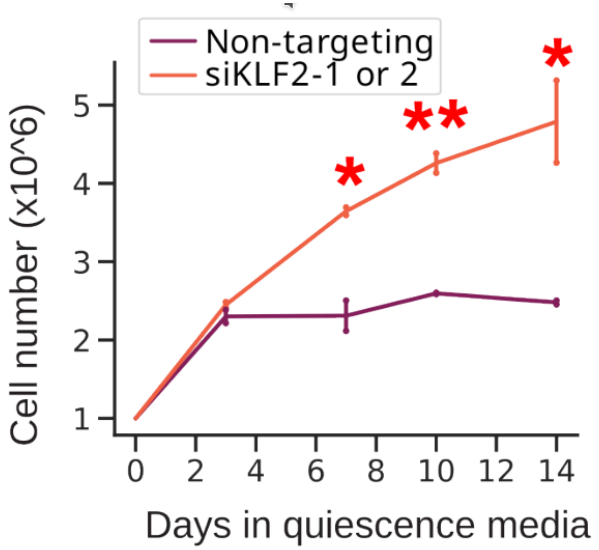
Inhibition of p53 pathway partially inhibits the HIV-induced quiescence phenotype

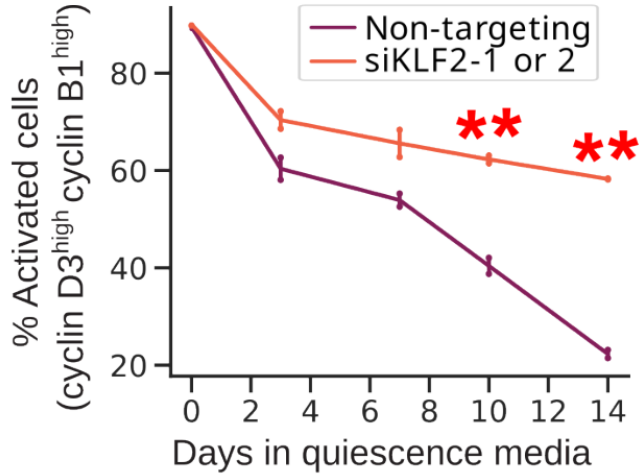


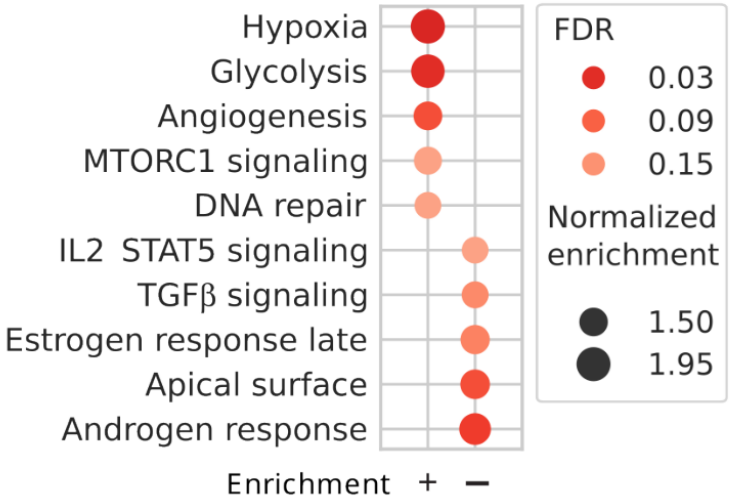
KLF2 is strongly induced after HIV infection in a manner dependent on HIV integration



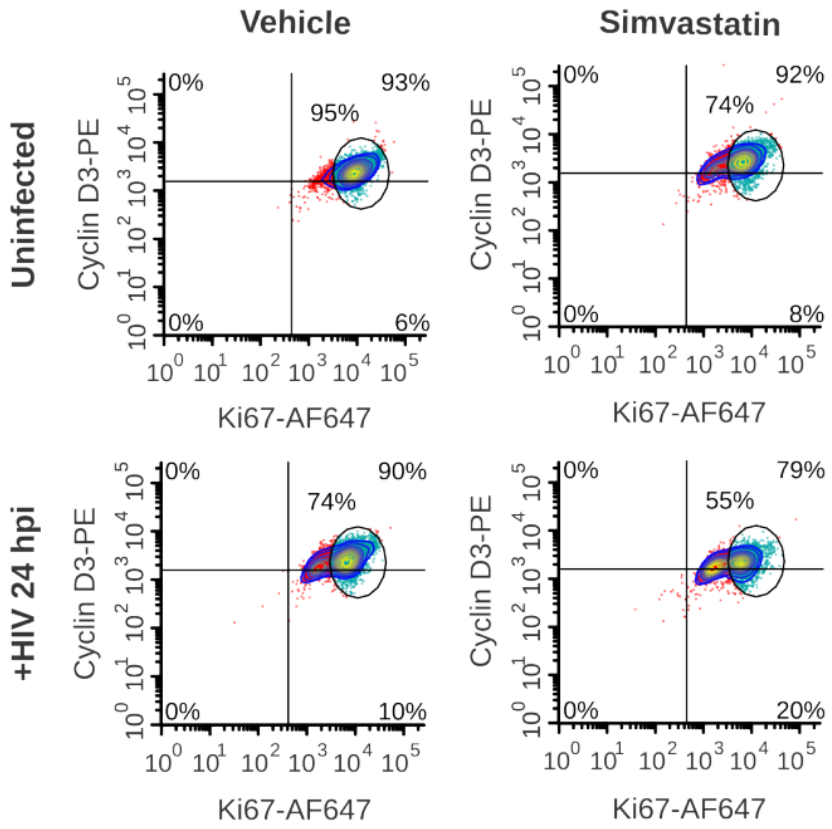
KLF2 knock down blocks entry into quiescence

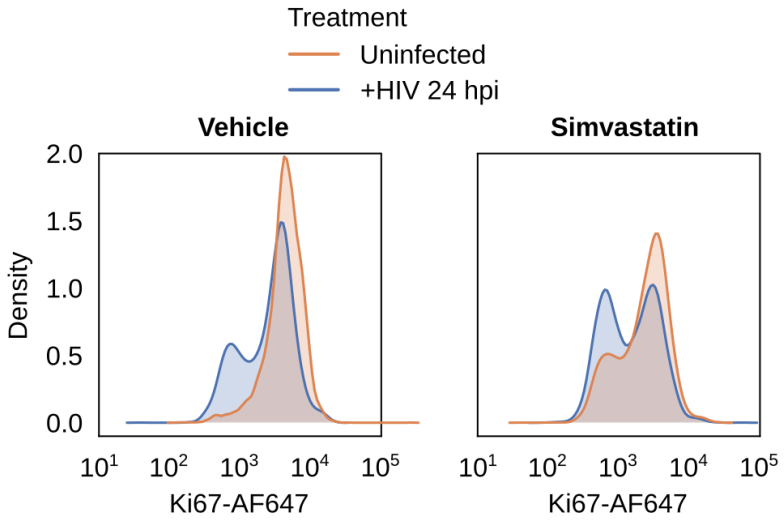




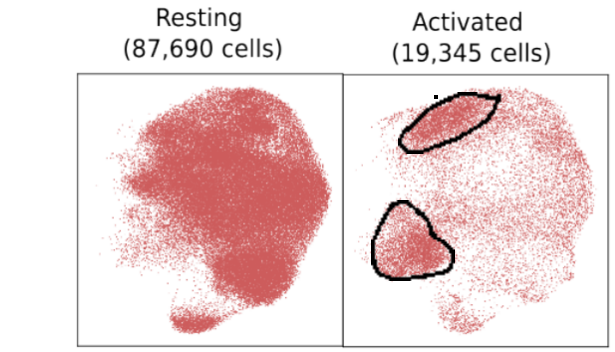


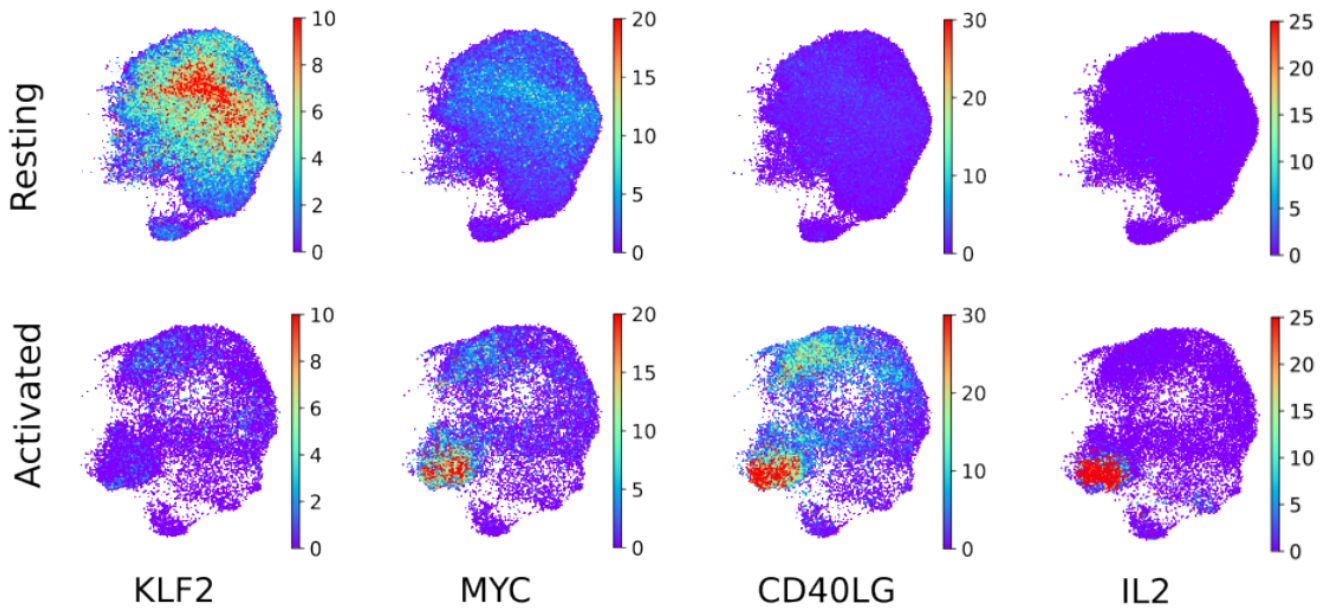
KLF2 induction accelerates entry into quiescence

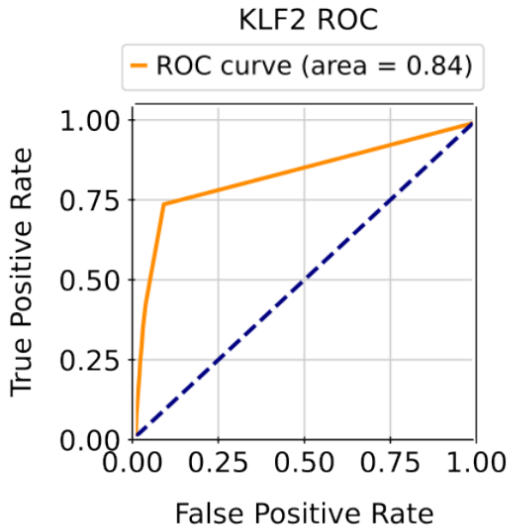




KLF2 expression is a strong predictor of CD4+ T cell resting state

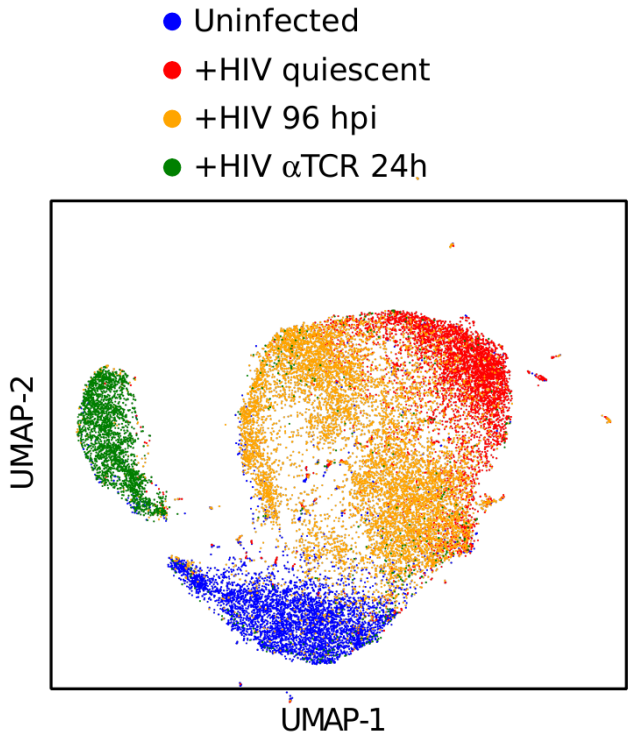


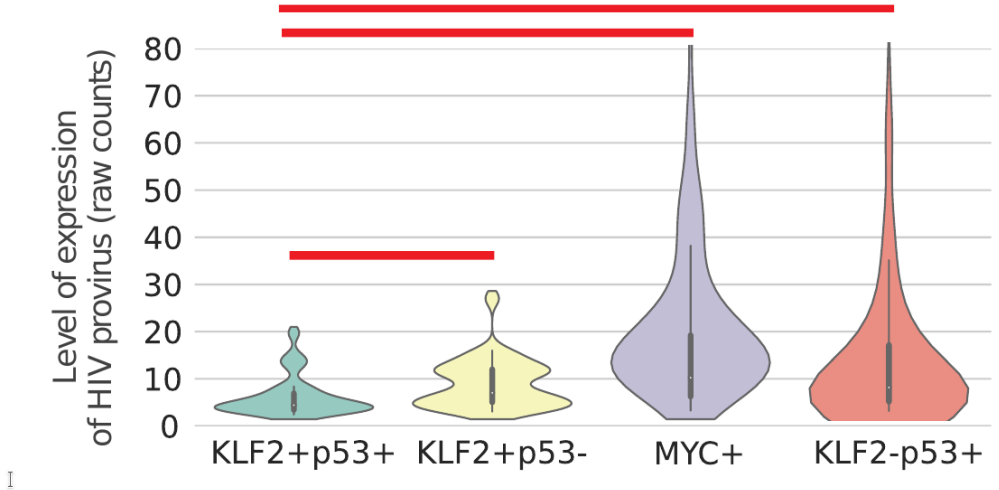


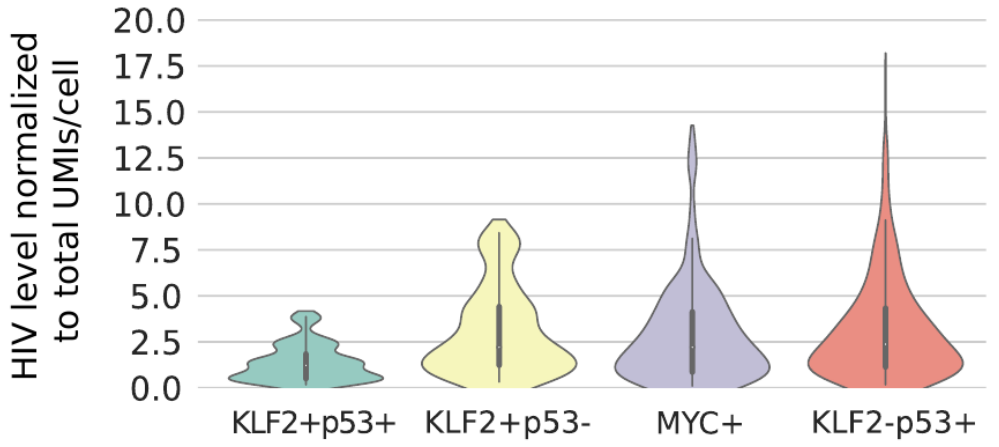


SABES cohort of PWH
(Lama et al., 2018,
Collora et al. , 2022)

Dual activation of p53 and KLF2 pathways leads to proviral transcriptional silencing







Collaboration with K. Leskov

Summary

HIV infection leads to the induction of a quiescent state in CD4+ T cells, including loss of proliferative markers, shut down of metabolic pathways and slow down of proliferation

This HIV-induced quiescence is observed with diverse HIV constructs including primary isolates in addition to lab strains

HIV infection leads to the induction of two strong anti-proliferative pathways, KLF2 and p53, leading to downregulation of MYC and induction of a quiescent state

HIV infected cells that show the signature of expression of KLF2 and p53 have a very low proviral transcription level, suggesting that the HIV-induced quiescence state can lead to proviral latency

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