

DECEMBER 13-16, 2022 www.hiv-persistence.com



Investigating the Role of Naïve CD4+ T-cells as a CTL Resistant Sanctuary for Intact HIV Proviruses

Jared Weiler Jones Lab

HIV Persistence During Therapy 2022 NIAID Young Investigator Session



EDITION



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Background

- We have previously published <u>indirect</u> evidence that cells harboring the HIV-1 reservoir are resistant to killing by CTL (Huang et al. JCI 2018, Ren and Huang et al. JCI 2020)
- Reservoir cells transcribing HIV RNA over express CTL resistance factors (Collora et al. Immunity 2022)
- Hypothesis: If we broadly direct CTL killing against total CD4 cells, reservoir harboring cells will be enriched amongst survivors [Direct evidence of CTL resistance]

Direct Assessment of CTL Resistance in *ex vivo* CD4⁺ T Cells with Intact Proviruses





MIAMIUSA

n = 6, 2-way ANOVA



n = 6, 2-way ANOVA

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MIAMIUSA

n = 6, 2-way ANOVA



n = 6, 2-way ANOVA

Naïve CD4⁺ T cells exhibit resistance to killing by CTL



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Memory

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n = 8, Paired T-test

Naïve CD4⁺ T cells harbor a greater proportion of intact proviruses than memory CD4⁺ T cells



Naïve gated on CD45RA⁺, CCR7⁺, CD27⁺, CD95⁻

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Direct Assessment of CTL Resistance in *ex vivo* CD4⁺ T Cells with Intact Proviruses



Within naïve CD4⁺ T cells, survival advantage of reservoir harboring cells is heterogeneous across donors



Within naïve CD4⁺ T cells, survival advantage of reservoir harboring cells is heterogeneous across donors



Within naïve CD4⁺ T cells, survival advantage of reservoir harboring cells is heterogeneous across donors



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COMMUNITY SUMMARY

Key question

• Are HIV reservoirs resistant to CTL killing?

Key findings

- Some types of cells harboring the HIV reservoir are resistant to elimination
- These cells that are resistant to elimination generally have a greater proportion of replication competent HIV
- Heterogeneity exists between donors and their ability to eliminate these HIV harboring cells

Next steps

• To look at this CTL resistance in more donors and figure out how to induce susceptibility to eliminination in these resistant cells

Acknowledgments

Jones Lab Brad Jones

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Twitter @AwesomeJonesLab @Reachforthecure

Flow cytometry core

Paul Byrne Jason McCormick Tomas Baumgartner

Collaborators

Kiera Clayton Guinevere Lee Robert Furler Tae-Wook Chun

