

Towards
an HIV Cure
IAS

New strategies in HIV Cure

Block, Lock, & Excise



HIV Obstruction by Programmed Epigenetics

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**Weill Cornell
Medicine**


AIDS 2022

Affiliated Independent Event



Affiliated Independent Event

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Conflict of interest disclosure

Received Consulting fees/honoraria from Abbvie and ViiV Healthcare

Ownership Interest (stocks, stock options, or other ownership interest excluding diversified mutual funds) with Cytodyn and service on the board directors and will not be discussing the off-label or investigational use of products.

No research support is received.



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- BLOCK** Inhibiting HIV transcription
- LOCK** Keeping the virus blocked without therapy
- EXCISE** Inactivating proviral DNA in the genome

*Using epigenomic and genomic approaches to
permanently inactivate HIV*



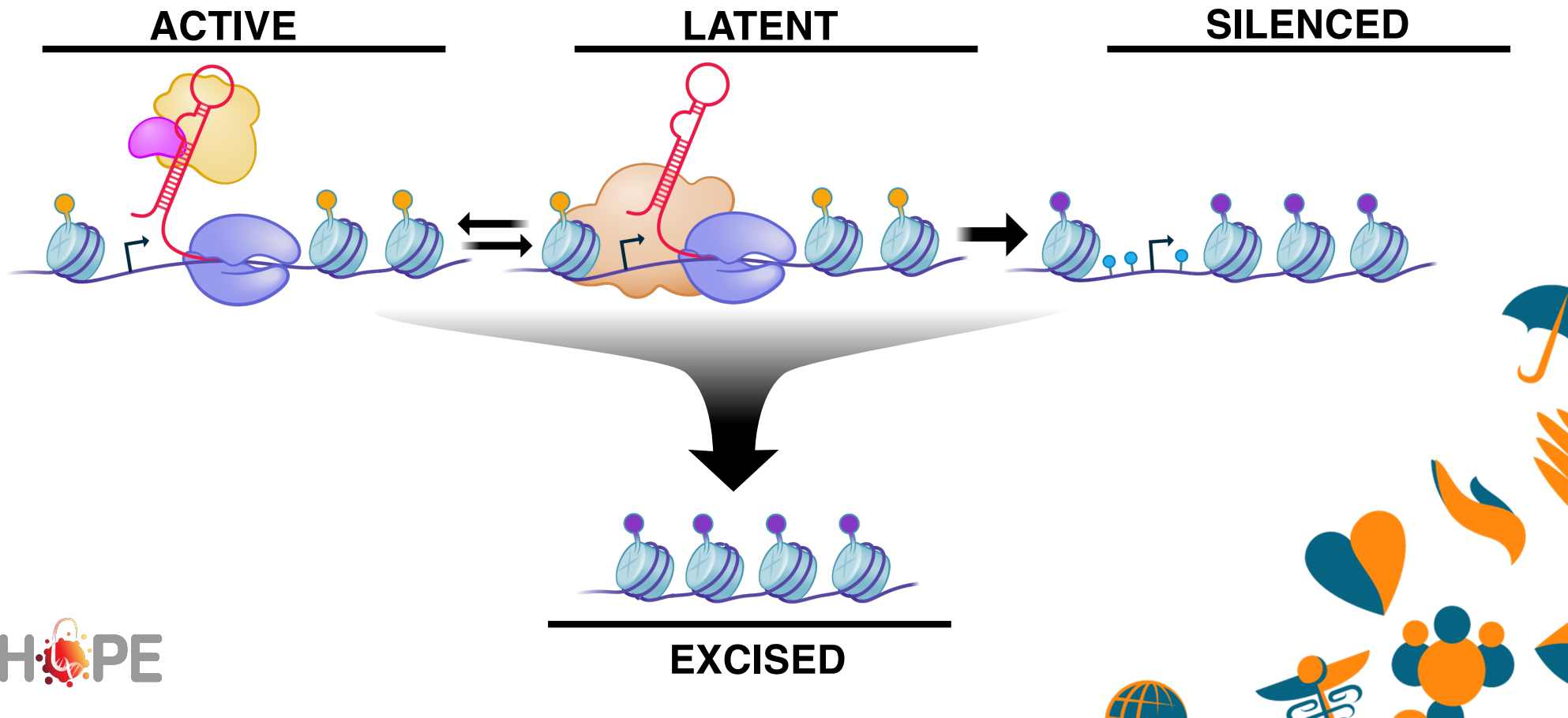
HOPE

Accelerating HIV's natural path to an endogenous retrovirus



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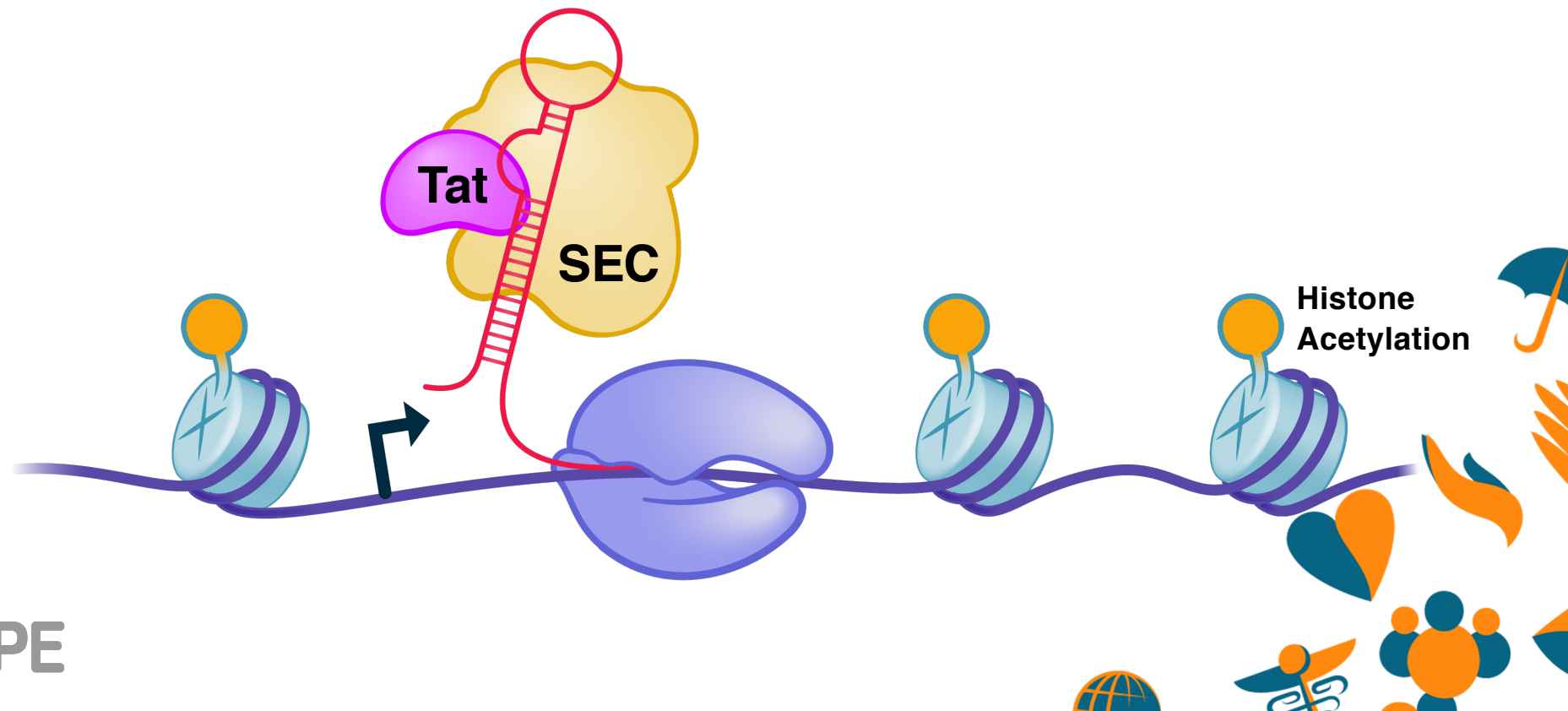


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ACTIVE

Ac

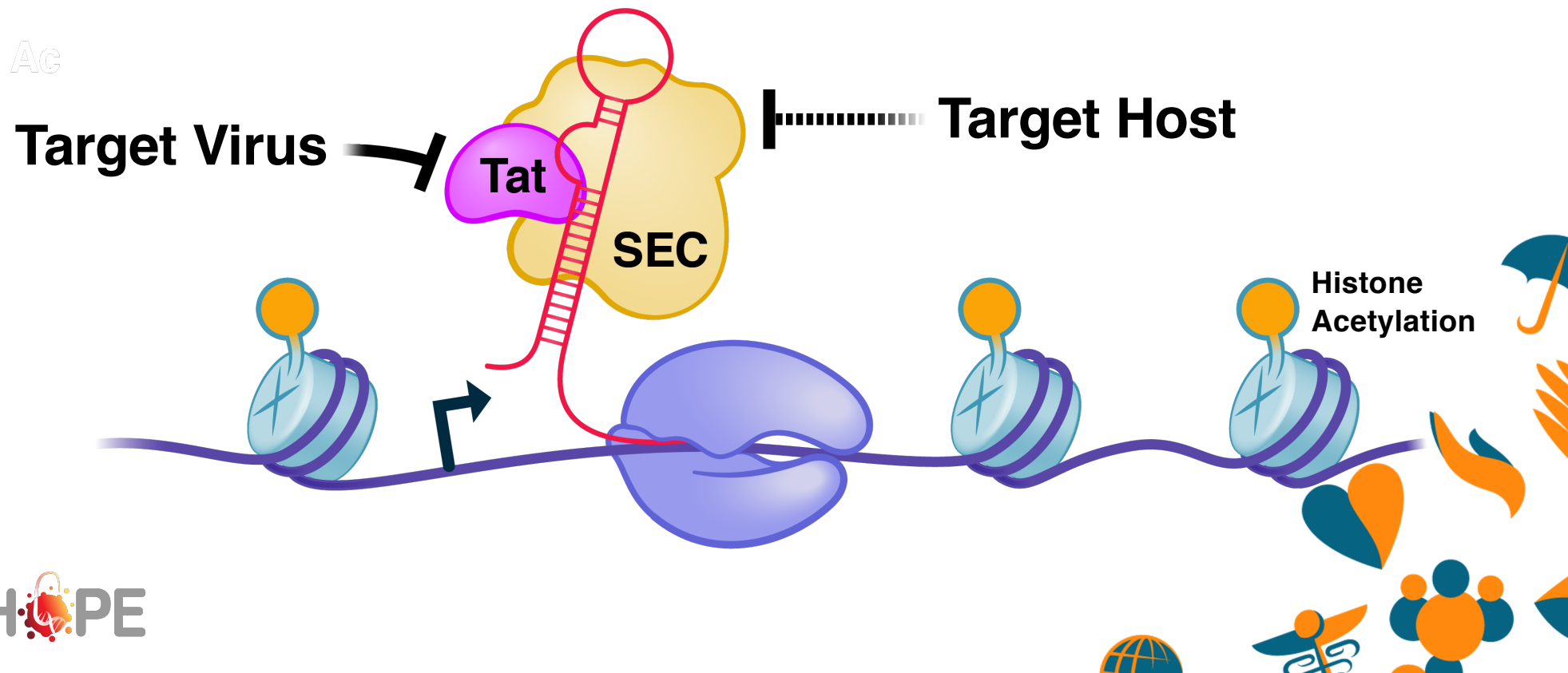


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ACTIVE

Ac



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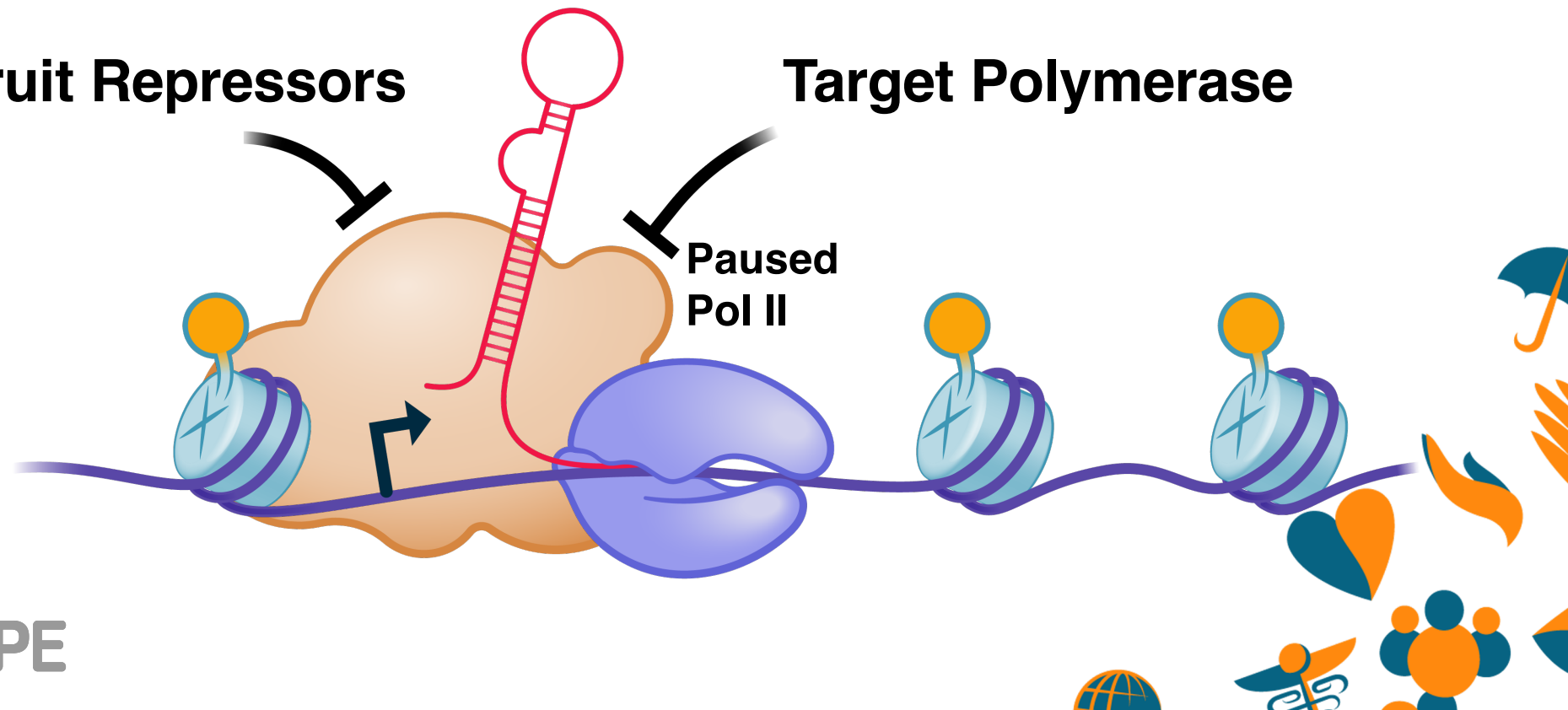
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LATENT

Recruit Repressors

Target Polymerase

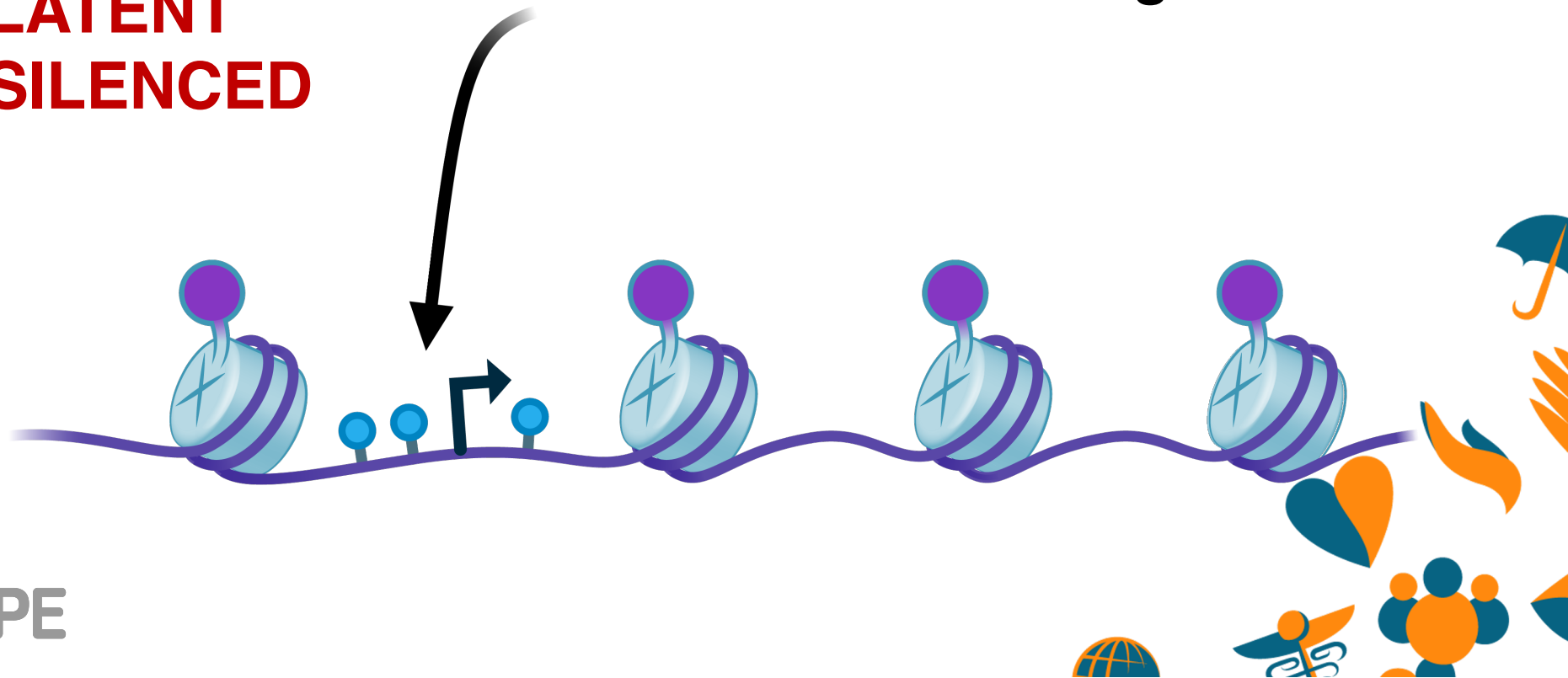


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ACTIVE
LATENT
SILENCED

Remove or alter HIV genome



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EXCISED



RF1: Define HIV silencing by targeting host and viral factors

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Co-Directors



Valente



Greene

Members



Feschotte



Kumar



Murthy



Ndhlovu



Nixon



Roan



Ott



Verdin

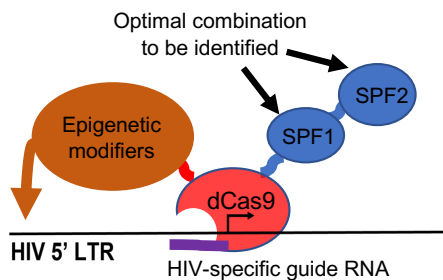


RF1 Hypothesis:

HIV transcription and chromatin structure offer unique targets for silencing

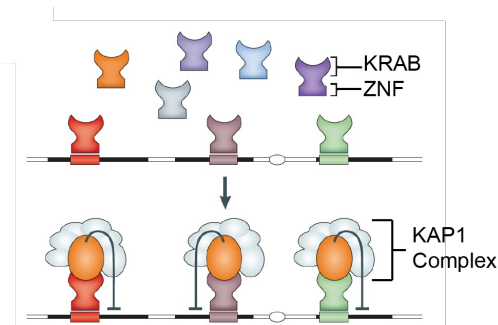
Goal 1

Identify **host regulators** of HIV proviral silencing



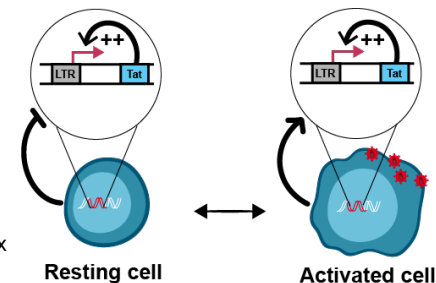
Goal 2

Learn from **endogenous retroviruses** how to silence HIV



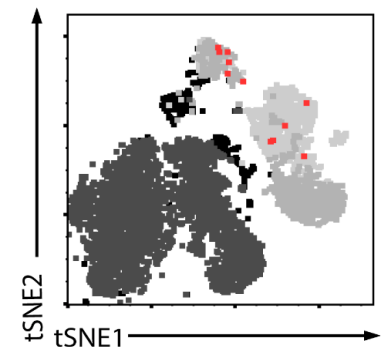
Goal 3

Define role of **Tat** in HIV silencing



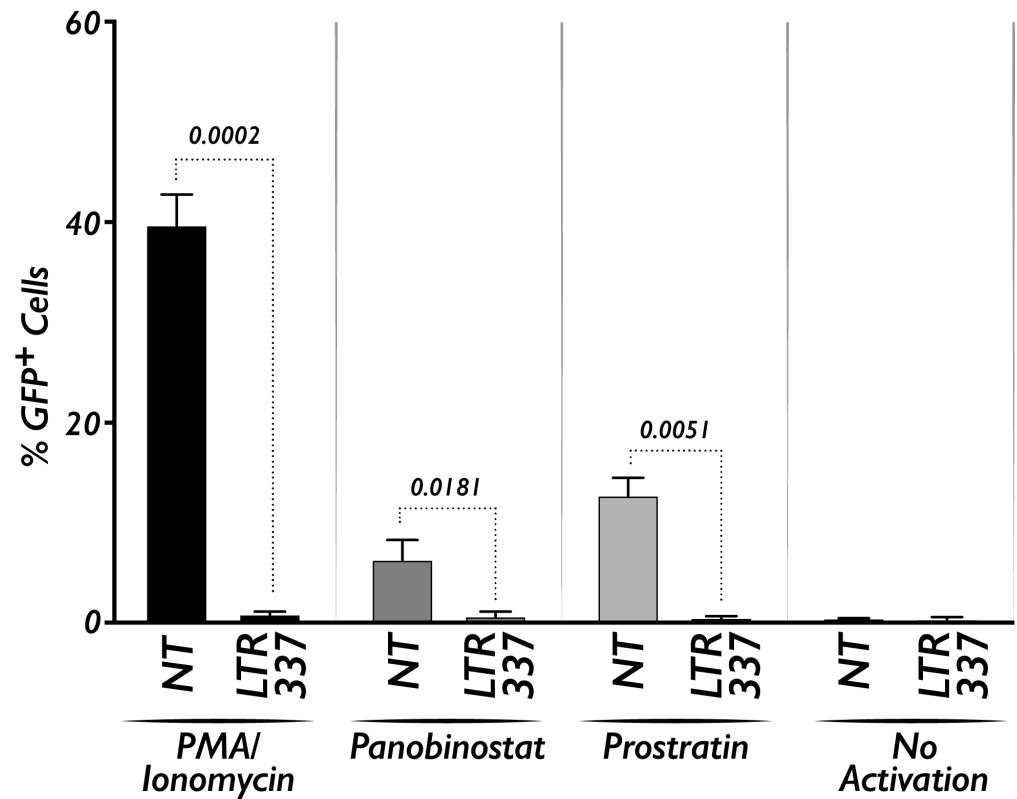
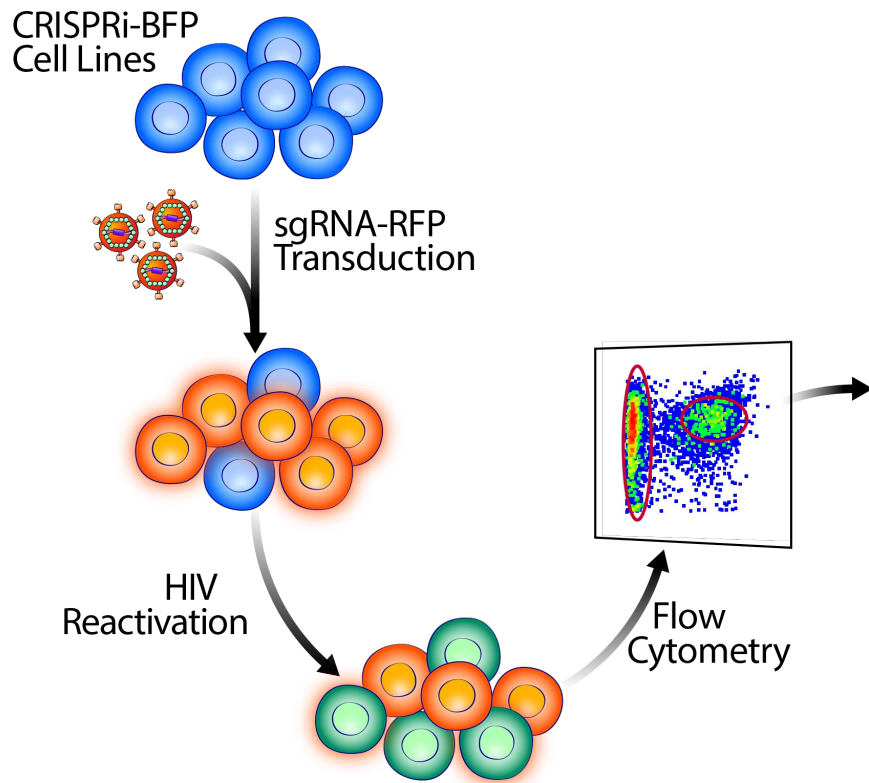
Goal 4

Characterize **-omics** of HIV silencing



CRISPRi efficiently blocks HIV transcription

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Warner Greene

RF2: Develop next-generation HIV silencing approaches

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Co-Directors



Ndhlovu



Roan

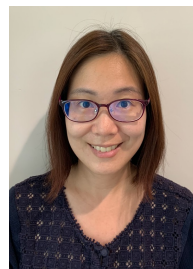
Members



Ake



Feschotte



Hsu



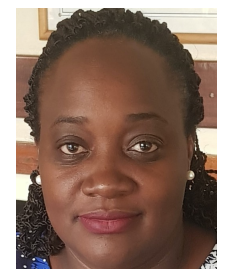
Kallas



Kibuuka



Kumar



Mwesigwa



Agan



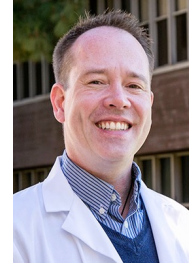
Nath



Nixon



Ott



Smith



Valente



Verdin



Weibel



RF2 Hypothesis:

Viral rebound is suppressed with silencing-promoting agents (SPA) after ART is stopped

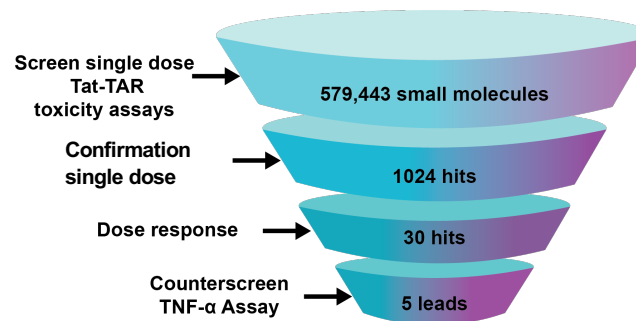
Goal 1

Determine *in vivo* effects of candidate SPAs



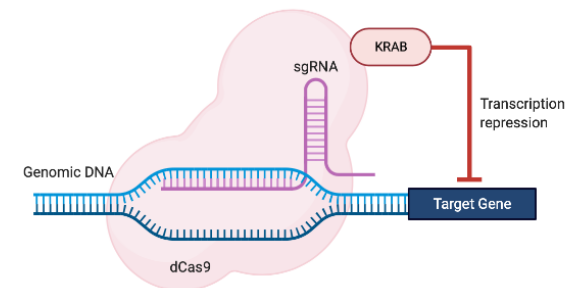
Goal 2

Develop novel SPAs



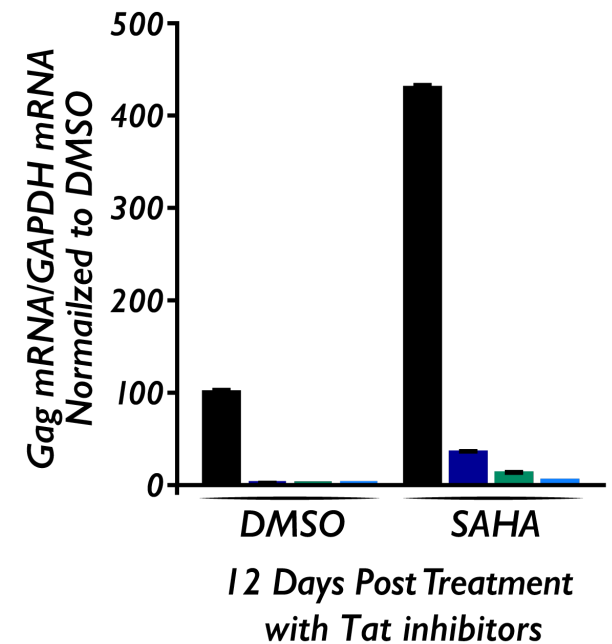
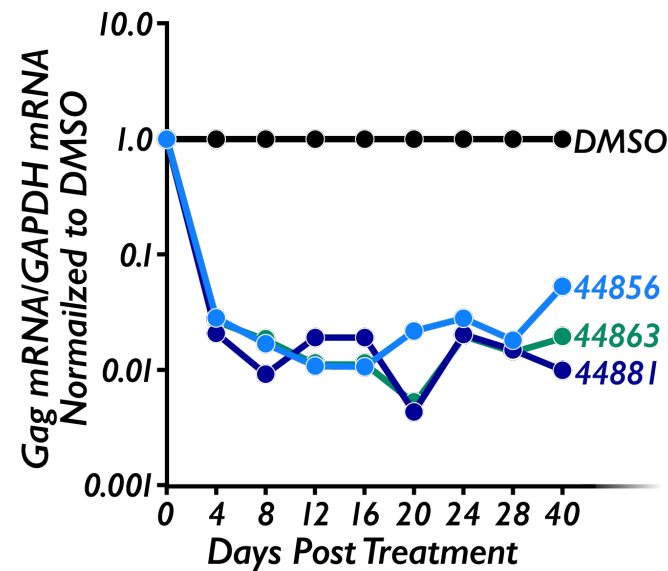
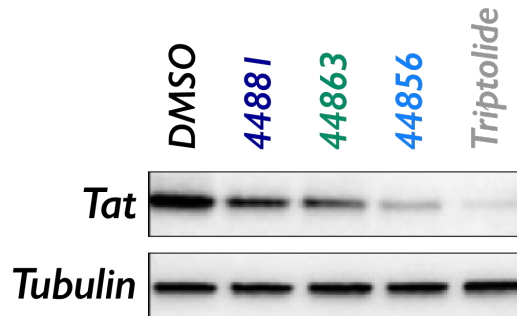
Goal 3

Apply **sequence-specific** SPAs *in vivo*



Tat inhibitors silence HIV transcription

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Susana Valente

RF3: Disable the HIV provirus by targeted genome engineering

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Co-Directors



Kumar



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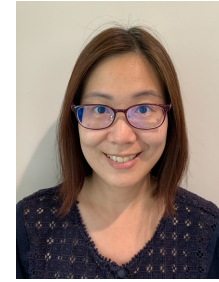
Chemnitz



Feschotte



Greene



Hsu



Hauber



Lange



Murthy



Ndhlovu



Nixon



Valente

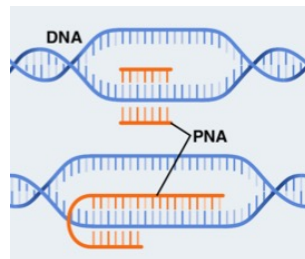
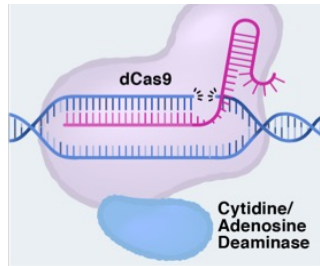
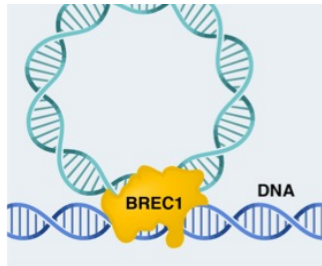


RF3 Hypothesis:

In vivo delivery of genome-engineering therapeutics permanently inactivates HIV without genotoxicity

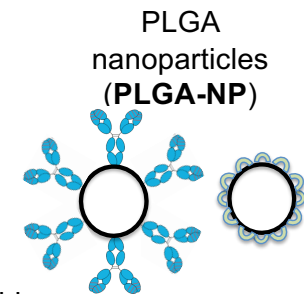
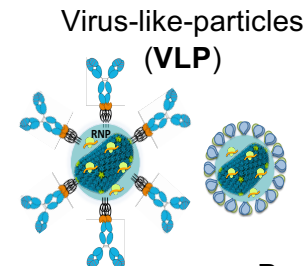
Goal 1

Develop **double strand break-free** genome engineering method

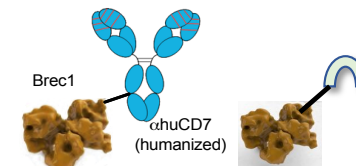


Goal 2

Establish *in vivo* delivery platforms

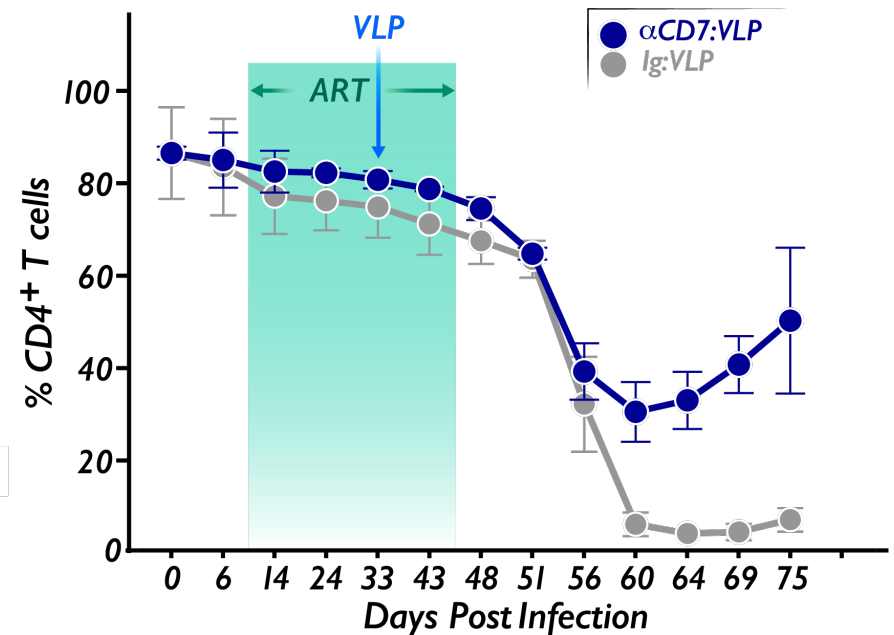
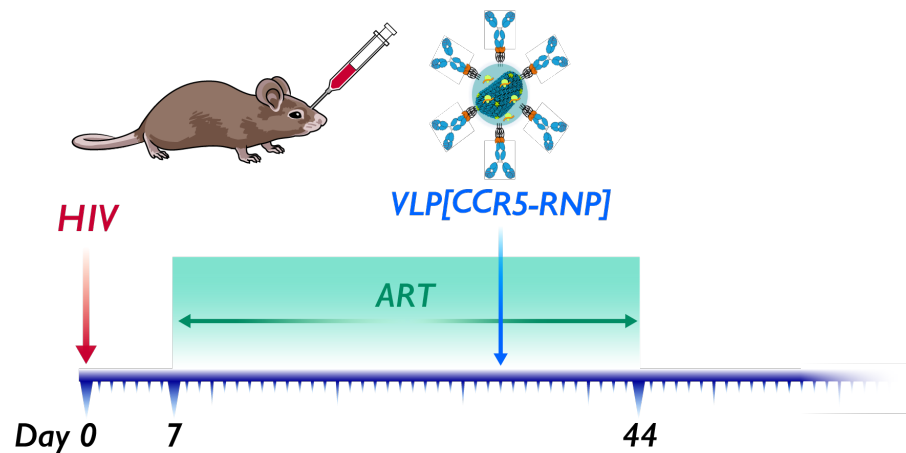


Protein/Peptide conjugates



In vivo delivery of α CD7 VLPs targets CD4 T cells in mice

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CAIR: Community Arts Integrated Research

Researchers and community **working together**.

Teaching-learning model '*through the arts*' and '*with the arts*' to understand complex HIV CURE research concepts and for researchers to better understand what it is like living with the infection.



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Defechereux

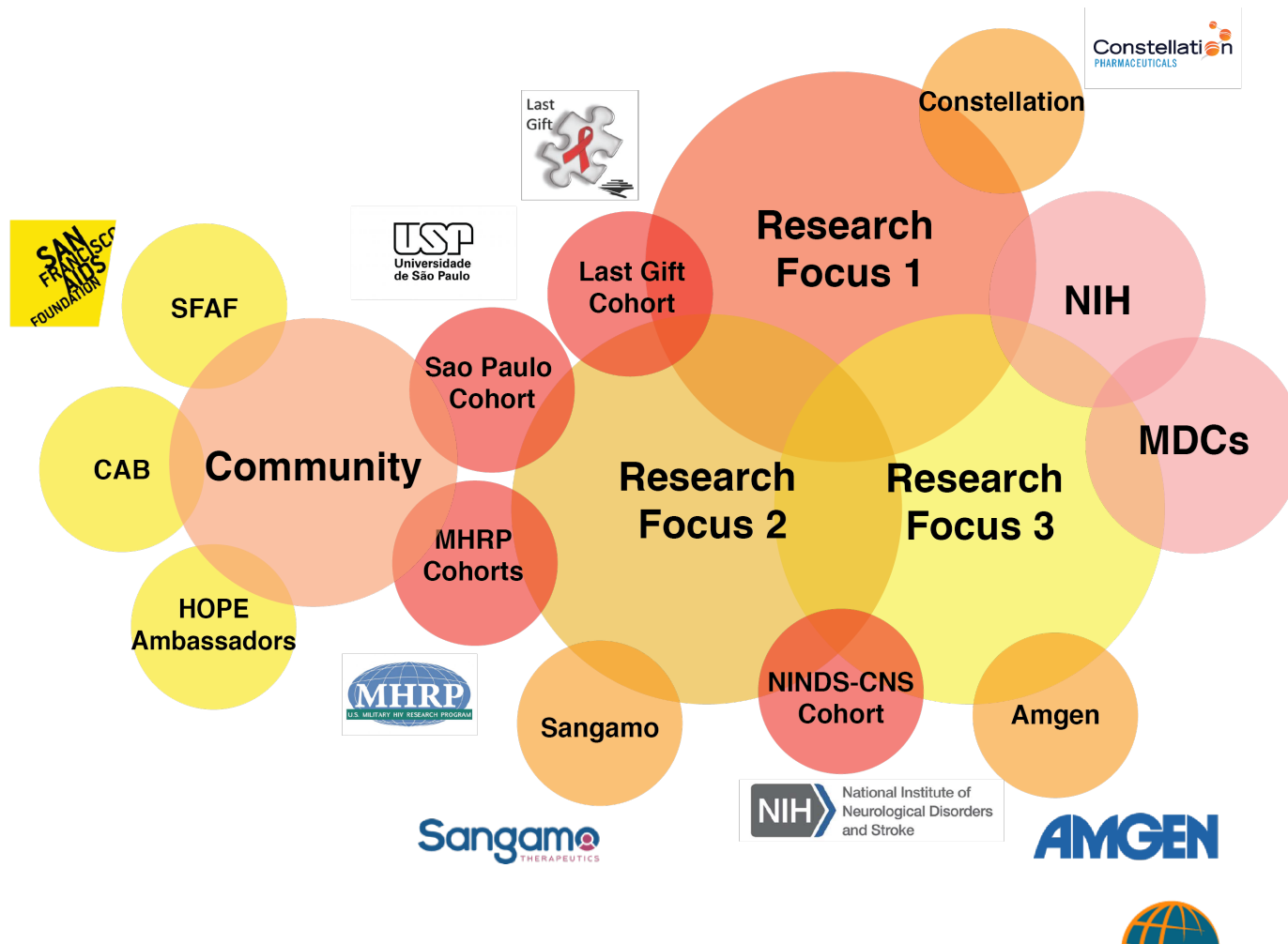


Sameshima



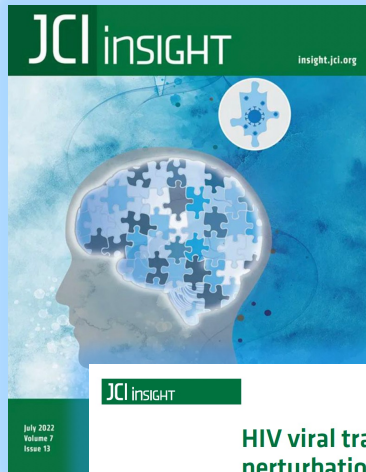
HOPE Partnerships

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Publications and IAS Abstracts

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HIV viral transcription and immune perturbations in the CNS of people with HIV despite ART

Shelli F. Farhadian,^{1,2} Ofir Lindenbaum,^{3,4} Jun Zhao,^{4,5} Michael J. Corley,^{6,7} Yunju Im,⁸ Hannah Walsh,¹ Alyssa Vecchio,⁹ Rolando Garcia-Milian,¹⁰ Jennifer Chiarella,² Michelle Chintanaphol,² Rachela Calvi,² Guilin Wang,¹¹ Lishomwa C. Ndhlovu,^{6,7} Jennifer Yoon,¹ Diane Trotta,⁶ Shuangge Ma,⁴ Yuval Kluger,^{4,12} and Serena Spudich¹

Hallmarks of Retroelement Expression in T-Cells Treated With HDAC Inhibitors

Gislaine Curty¹, Luis P. Iñiguez², Douglas F. Nixon³, Marcelo A. Soares¹ and Miguel de Mulder Rougvie^{2,3*}

¹ Oncovirology Program, Instituto Nacional de Cancer, Rio de Janeiro, Brazil; ² Division of Infectious Diseases, Department of Medicine, Weill Cornell Medicine, New York, NY, United States; ³ Department of Genetic Medicine, Weill Cornell Medicine, New York, NY, United States

Human endogenous retrovirus expression in HIV-associated diffuse large B-cell lymphoma

Matthew L. Bendall¹, Jez L. Marston¹, Bhavya Singh¹, Gislaine Curty², Luis P. Iñiguez¹, Fabio E. Leal², Ethel Cesarman³, Cedric Feschotte⁴, Douglas F. Nixon¹

¹ Division of Infectious Diseases, Department of Medicine, Weill Cornell Medicine, New York, New York, USA.

² Oncovirology Program, Instituto Nacional de Cancer, Rio de Janeiro, Brazil.

³ Department of Pathology and Laboratory Medicine, Weill Cornell Medicine, New York, New York, USA.

Off-target effects on retroelement expression in T-cells Treated with Histone deacetylase inhibitors

G. Curty¹, L.P. Iñiguez², D.F. Nixon², M.A. Soares¹, M. de Mulder Rougvie^{2,3}

¹ Instituto Nacional de Cancer, Oncovirology Program, Rio de Janeiro, Brazil; ² Weill Cornell Medicine, Division of Infectious Diseases, New York, United States; ³ Weill Cornell Medicine, Department of Genetic Medicine, New York, United States

Endogenous Retrovirus Expression Distinguishes Latent From Actively Infected Cells In Novel Dual-Reporter HIV Latency Model

Marston, Jez L.^{1,2}, Randall, Kipchoge^{2,3}, Yesmeen Elgabori⁴, Nixon, Douglas F.¹

¹ Department of Infectious Diseases, Weill Cornell Medical College, New York, NY

² Gateways to the Laboratory Program, Weill Cornell/Rockefeller/Sloan Kettering Tri-Institutional MD-PhD Program, New York, NY

³ San Jose State University, San Jose, CA

⁴ Connecticut College, New London, CT

Effect of novel latency reversal agents on transposable element expression profile in T-cell memory subsets of HIV clinical samples

G. Curty¹, L.P. Iñiguez², M.A. Soares¹, D.F. Nixon², M. de Mulder Rougvie^{2,3}

¹ Instituto Nacional de Cancer, Oncovirology Program, Rio de Janeiro, Brazil; ² Weill Cornell Medicine, Division of Infectious Diseases, New York, United States; ³ Weill Cornell Medicine, Department of Genetic Medicine, New York, United States

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