

11<sup>TH</sup> EDITION

DECEMBER 10-13, 2024

# HIV PERSISTENCE DURING THERAPY

Reservoirs & Eradication Strategies Workshop



## Targeting the HIV-1 Reservoir in Myeloid Cells using the SECH approach

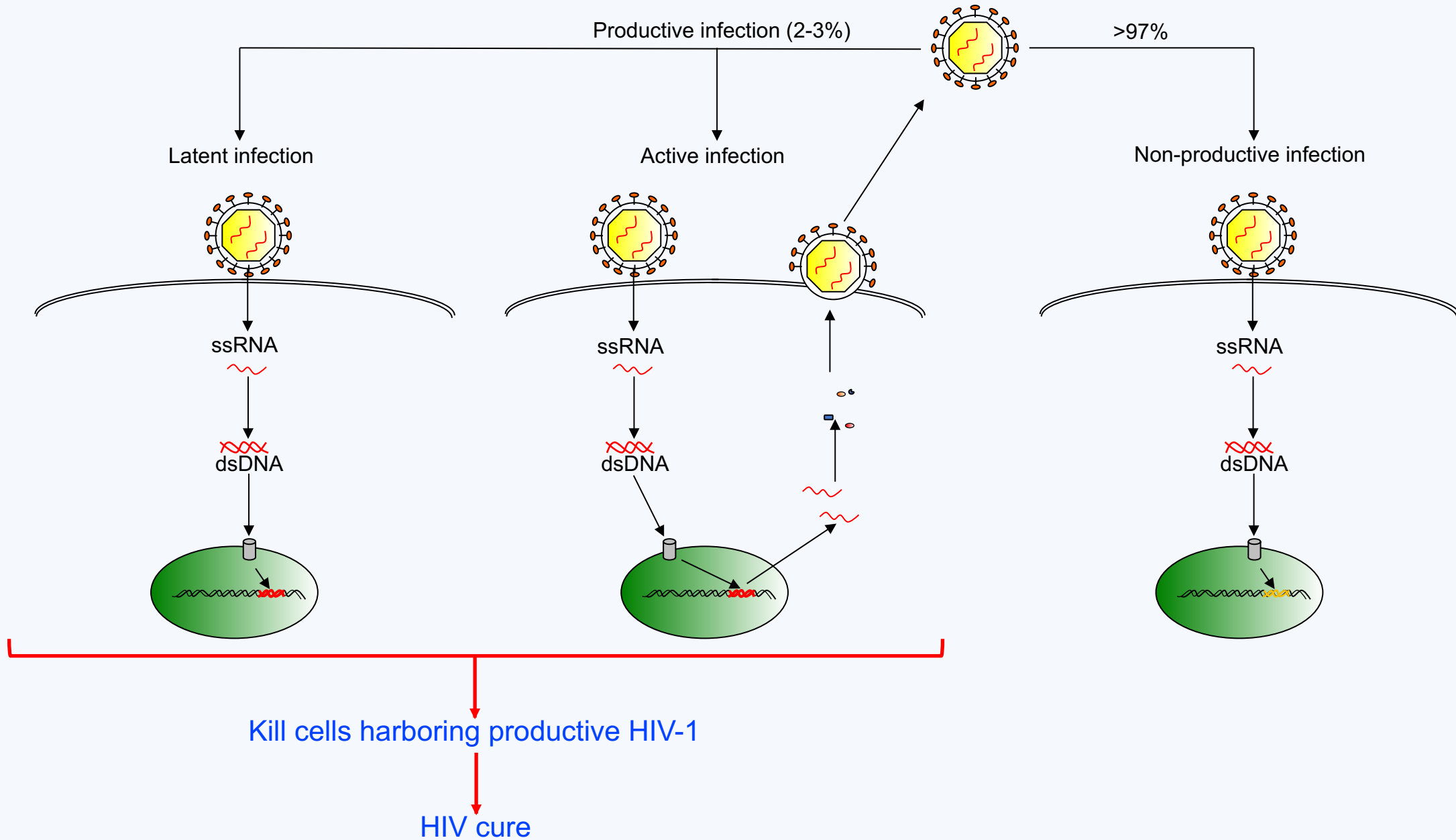
Jin Wang

Houston Methodist Research Institute

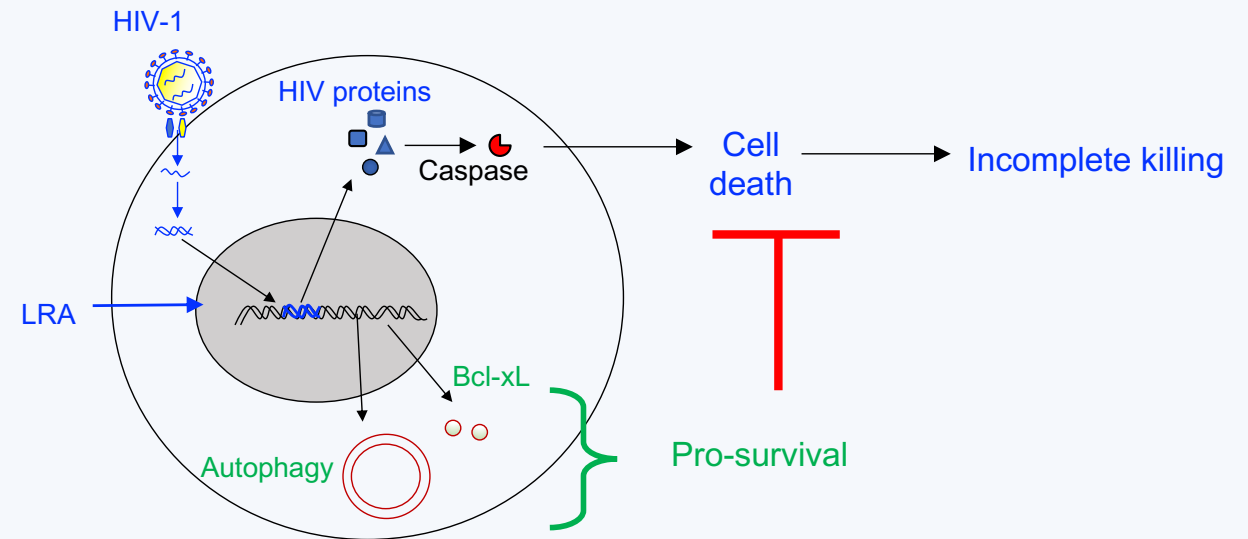
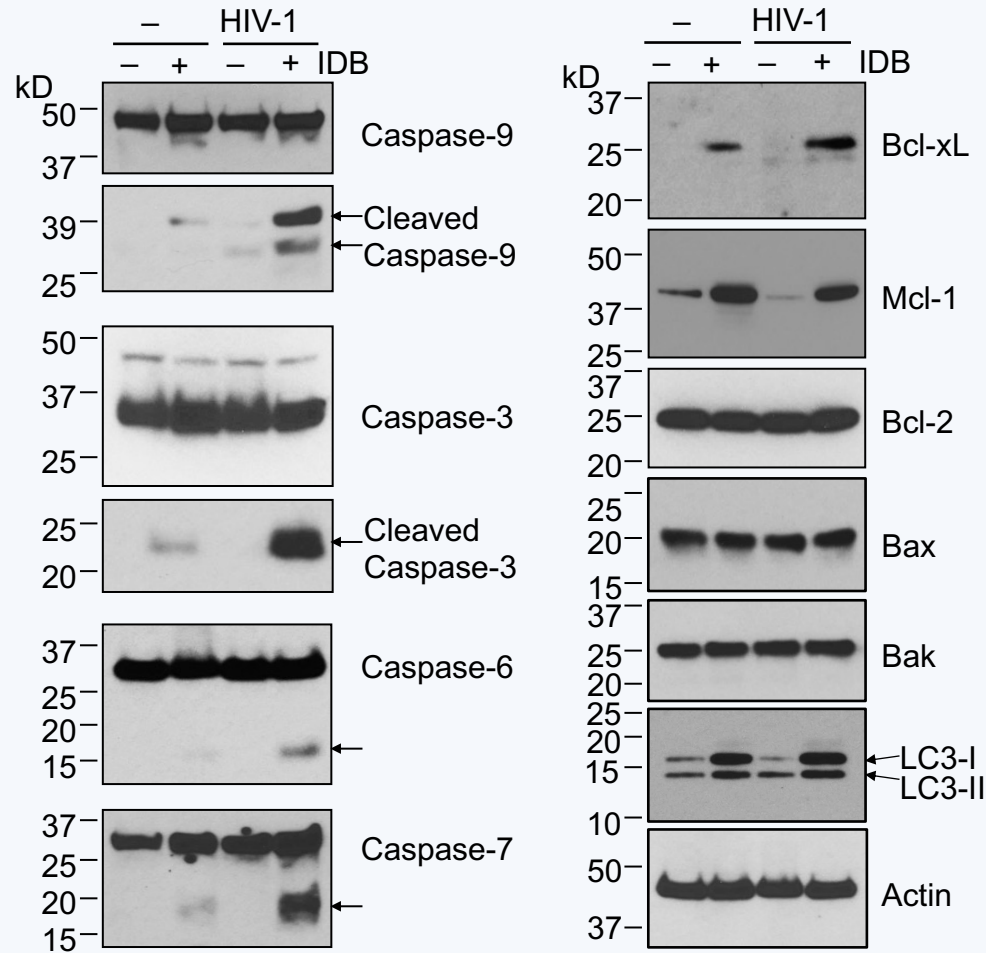
[www.hiv-persistence.com](http://www.hiv-persistence.com)

We Declare no conflict of interest

# Developing an HIV Cure by Inducing Cell Death in HIV Reservoirs

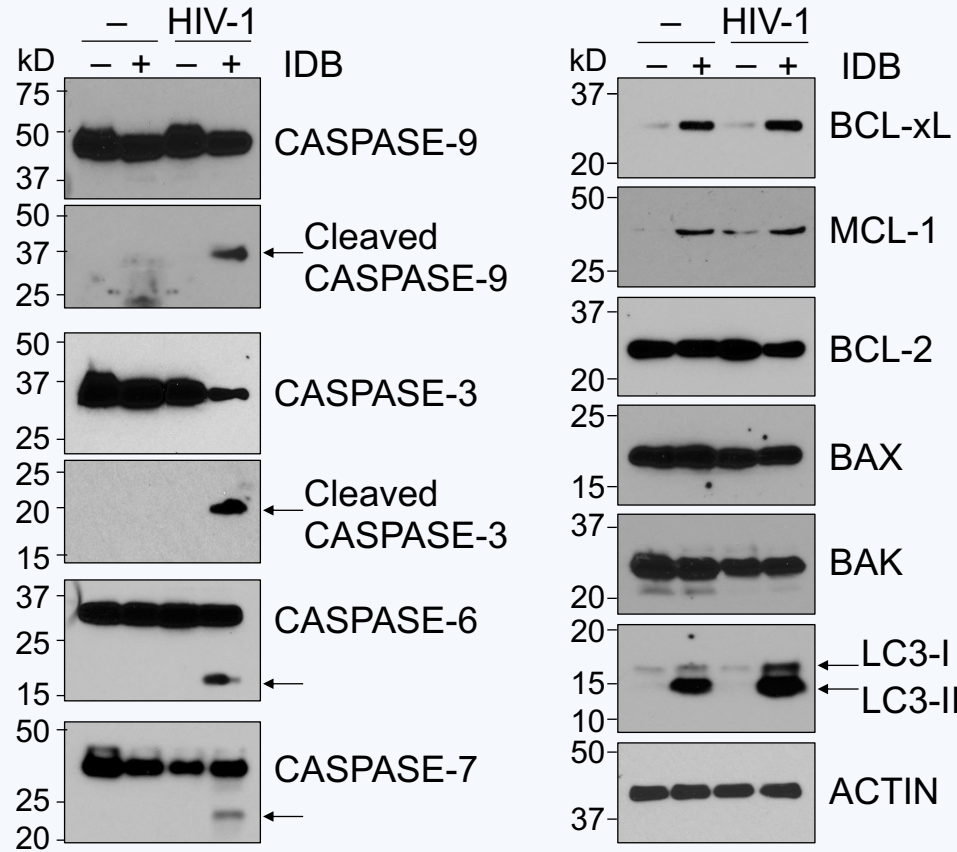


# LRA induces Both Cell death and Pro-survival Signaling in HIV-infected T cells

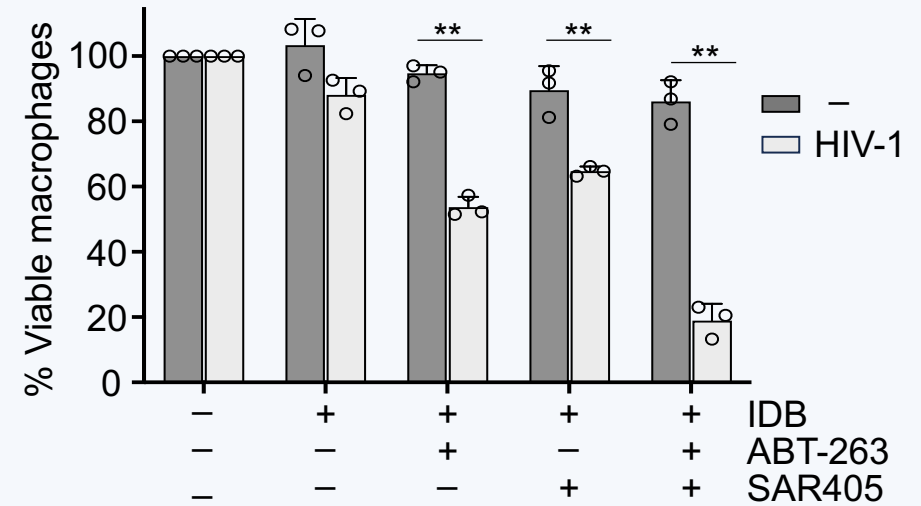


# LRA induces Both Cell death and Pro-survival Signaling in HIV-infected Macrophages

A

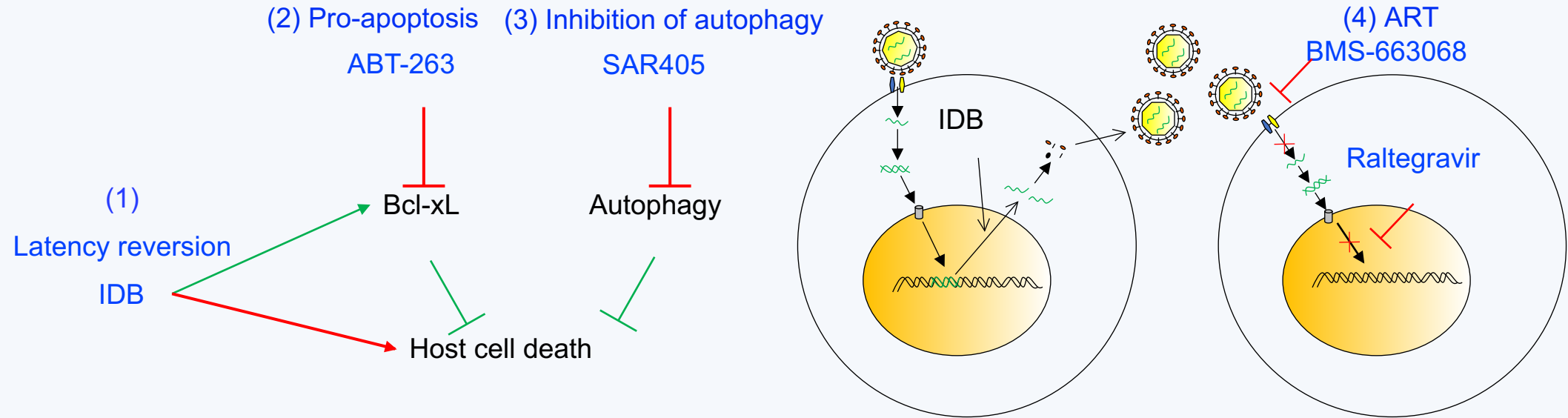


B

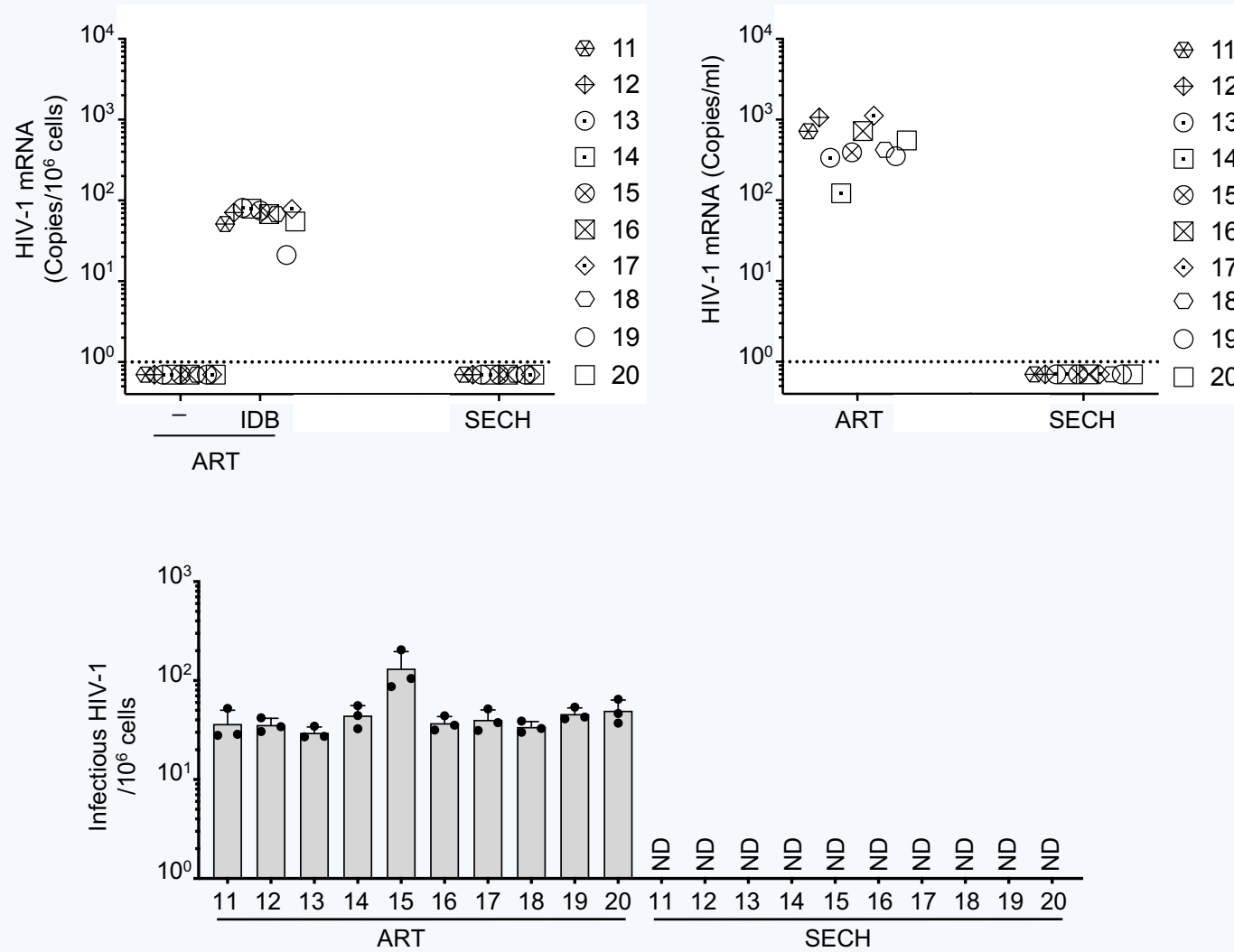


(Unpublished observation)

## Selective Elimination of Host Cells Harboring Replication-competent HIV (SECH)

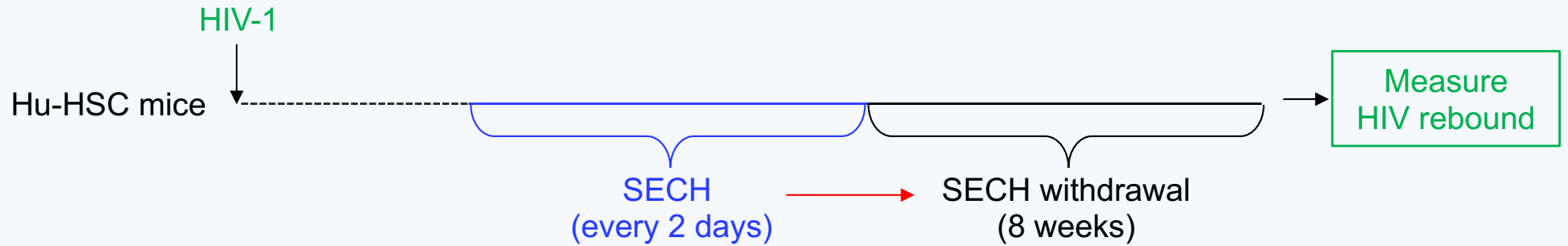


# Clearance of HIV-1 in PBMCs from PLWH by SECH



# HIV Clearance in Hu-Mice by SECH

A

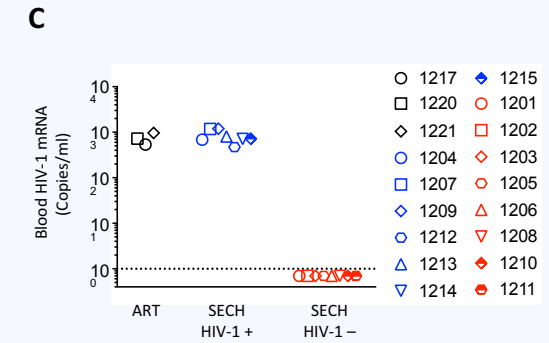
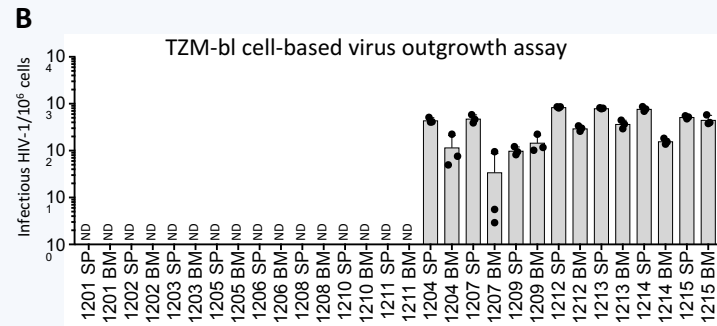
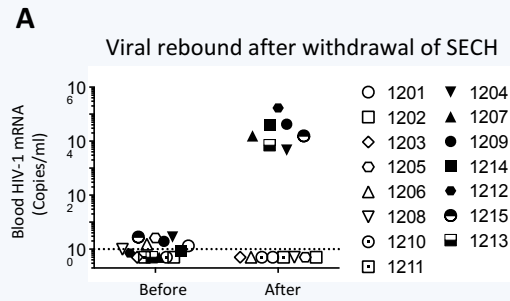


B





# Determination of HIV clearance

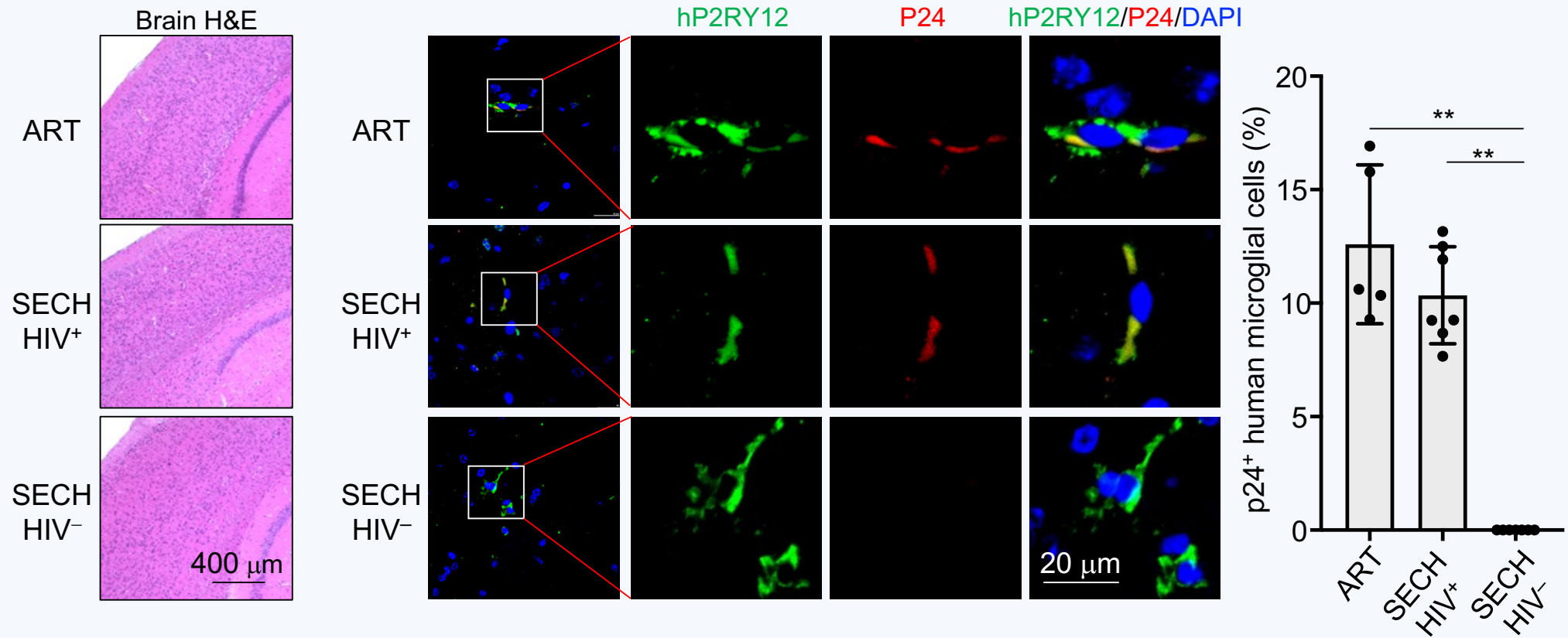


(A) Drug withdrawal.

(B) *In vitro* virus outgrowth assay.

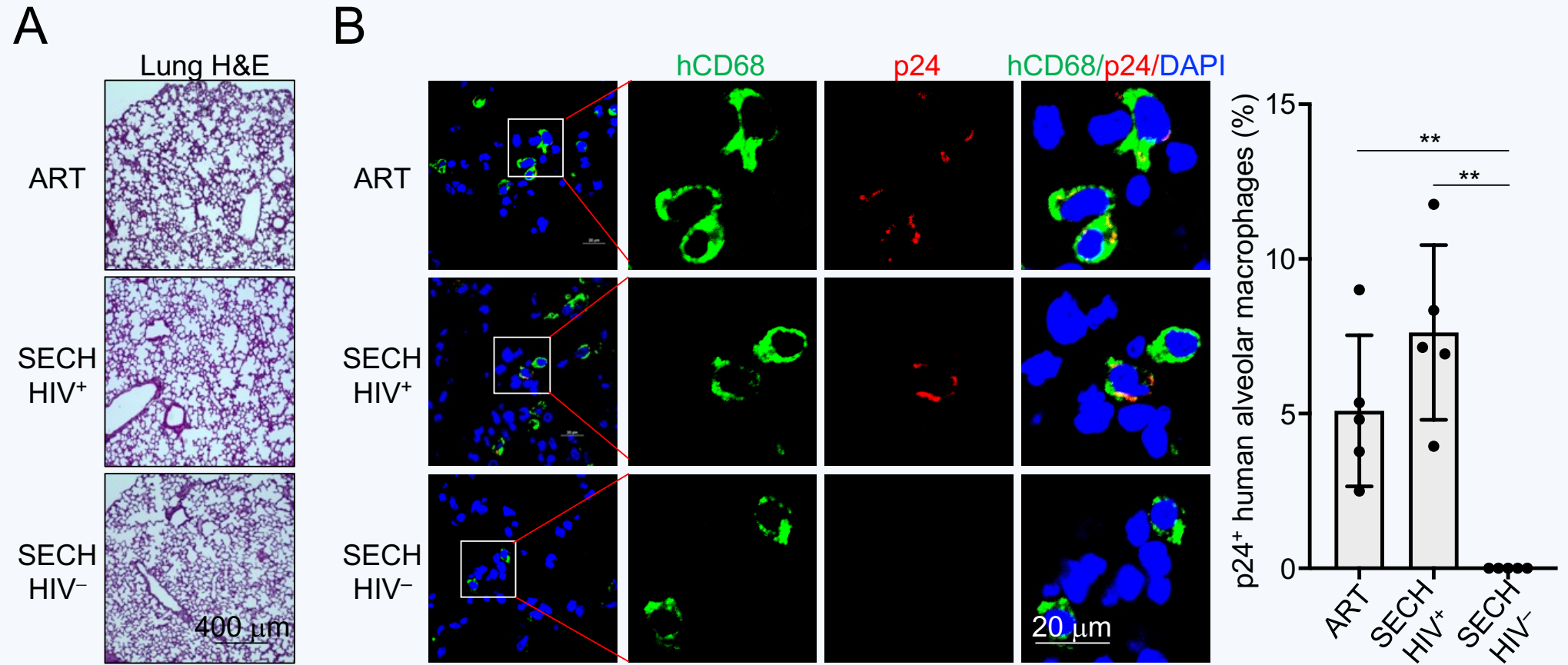
(C) *In vivo* humanized mouse-based virus outgrowth assay (hmVOA).

# HIV Clearance in Microglial Cells of Hu-Mice by SECH



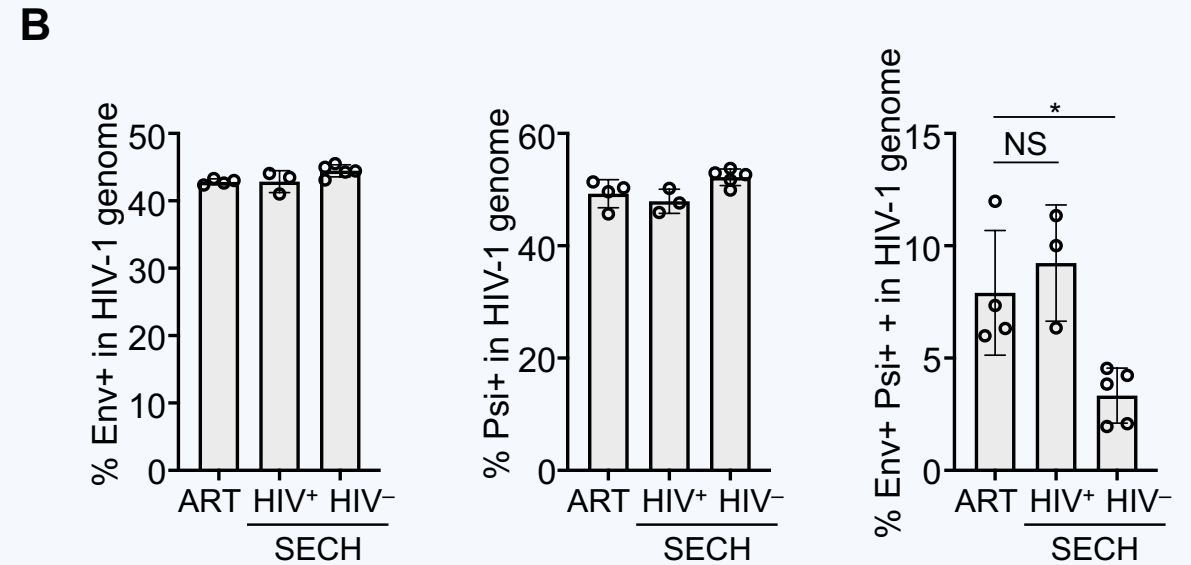
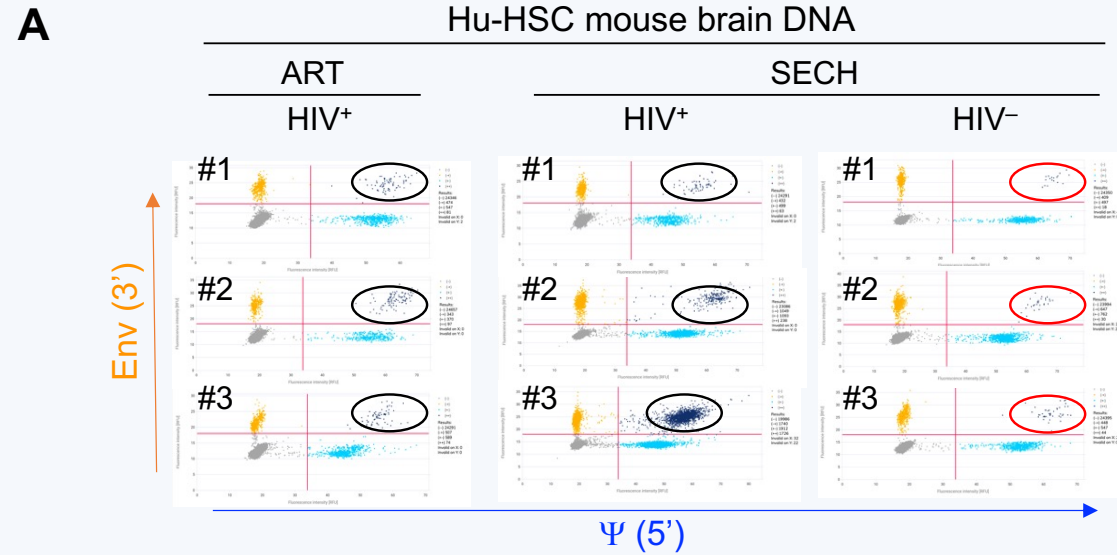
(Unpublished observation)

# HIV Clearance in Alveolar Macrophages of Hu-Mice by SECH



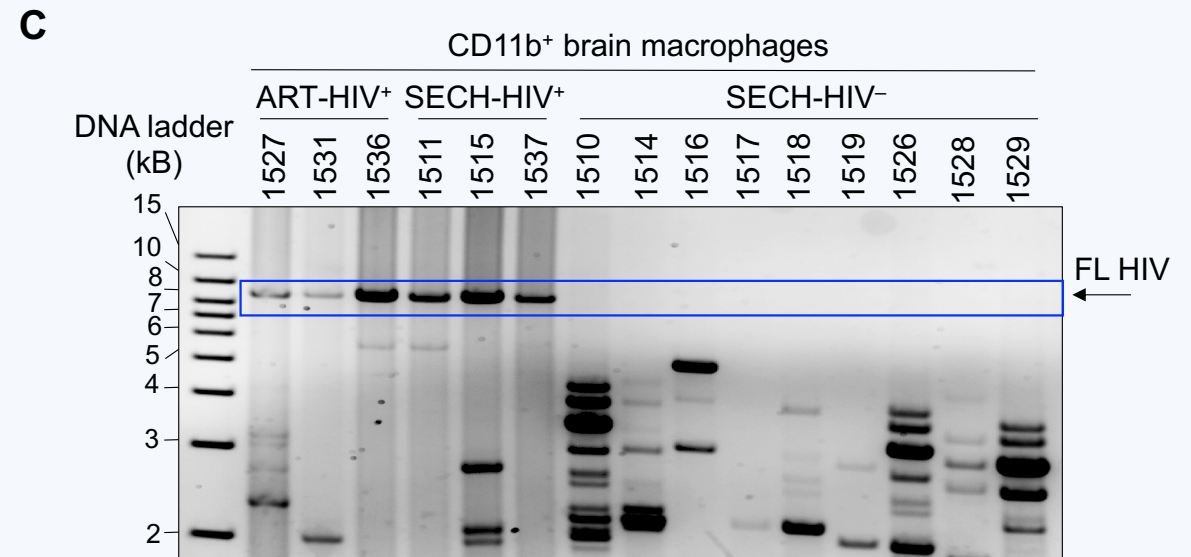
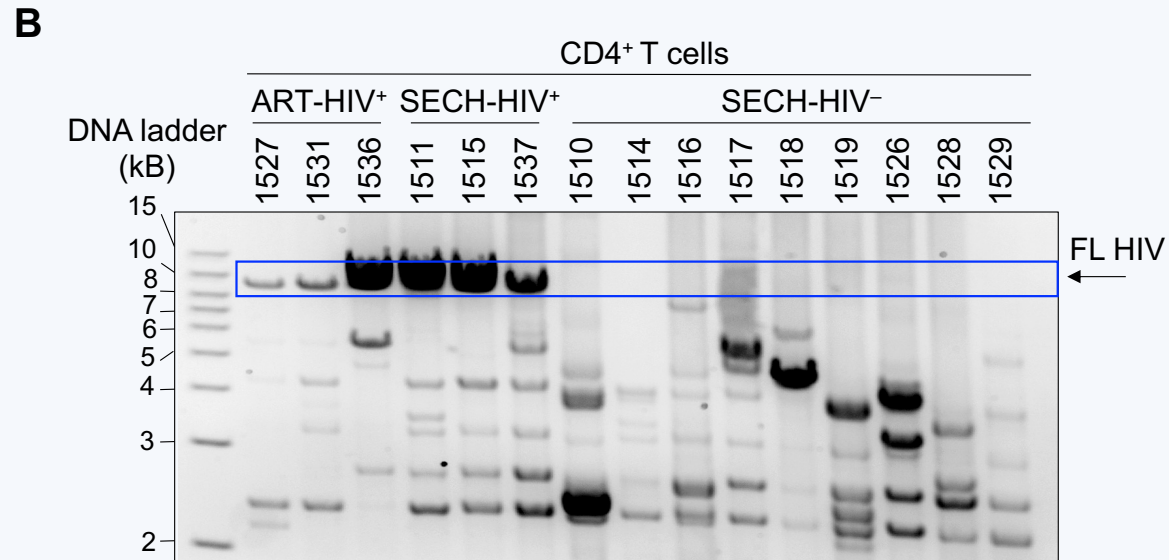
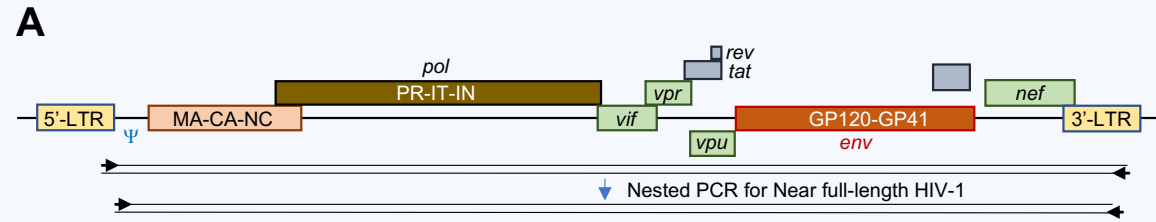
(Unpublished observation)

# Depletion of intact but not defective HIV-1 by SECH in the brain of Hu-mice



(Unpublished observation)

# Depletion of full-length but not deletion mutants of HIV-1 by SECH in Hu-mice



(Unpublished observation)

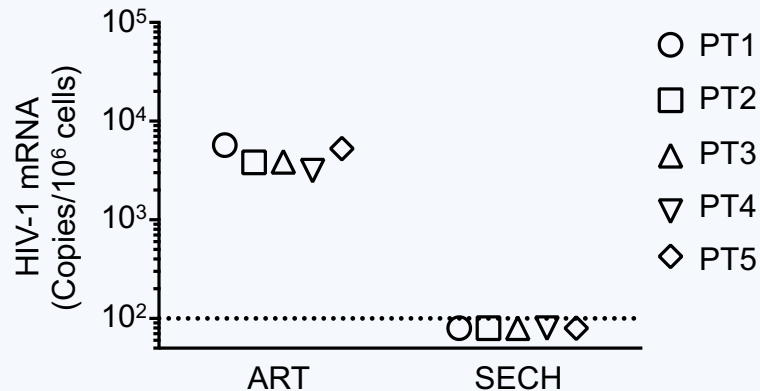
# Depletion of full-length but not deletion mutants of HIV-1 in PLWH T cells

**A**

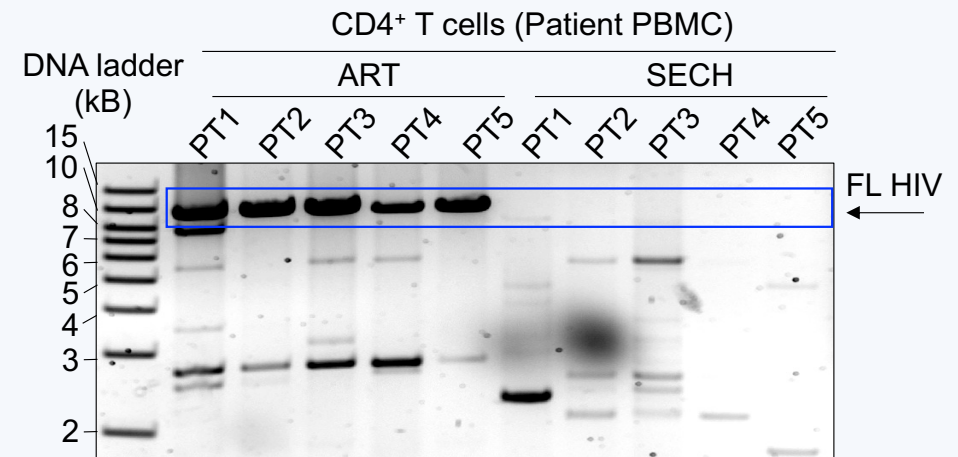
Table. ART-experienced HIV-1 patients.						
Patient	Race	Sex	Age	CD4 Count	CD4 %	HIV RNA Levels (copies/mL)
PT1	B	M	60	284	33	<20
PT2	C	F	49	93	11	ND
PT3	C	M	56	318	40	ND
PT4	B	M	58	779	63	ND
PT5	B	F	52	576	33	ND

B, black; C, caucasian; H, hispanic; ND, not detectable

**B**



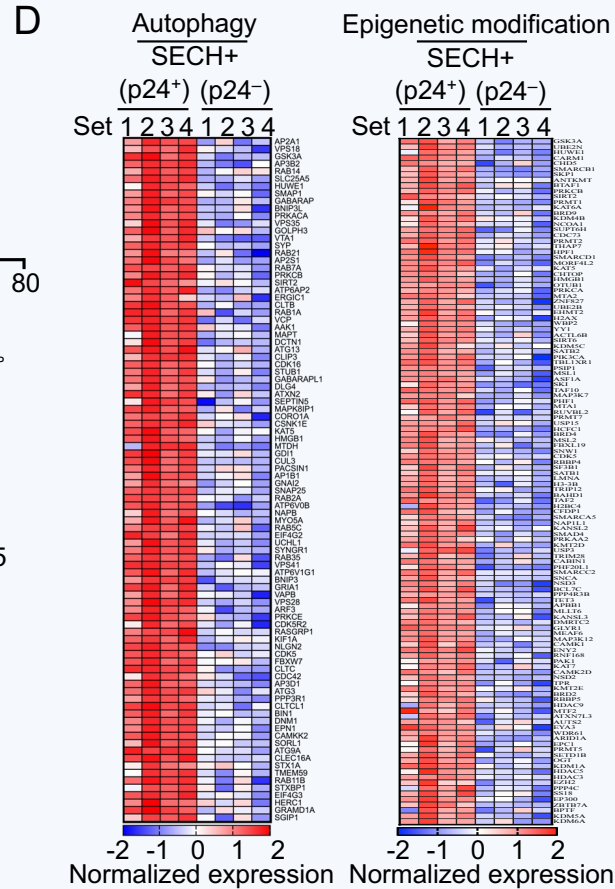
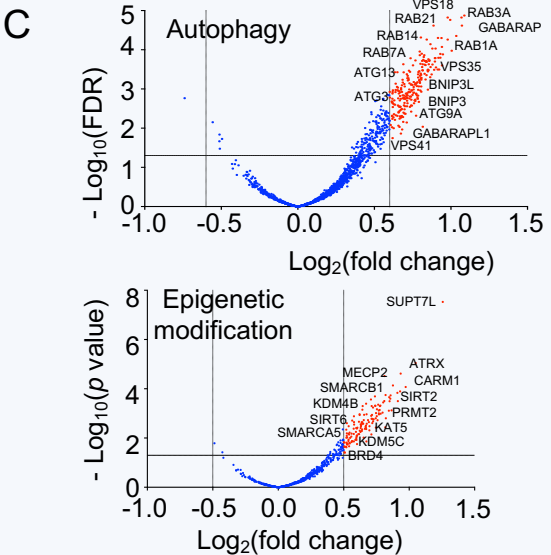
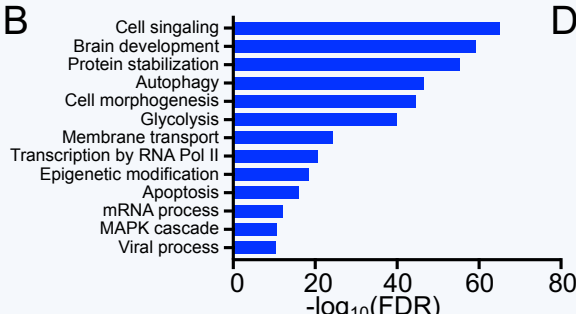
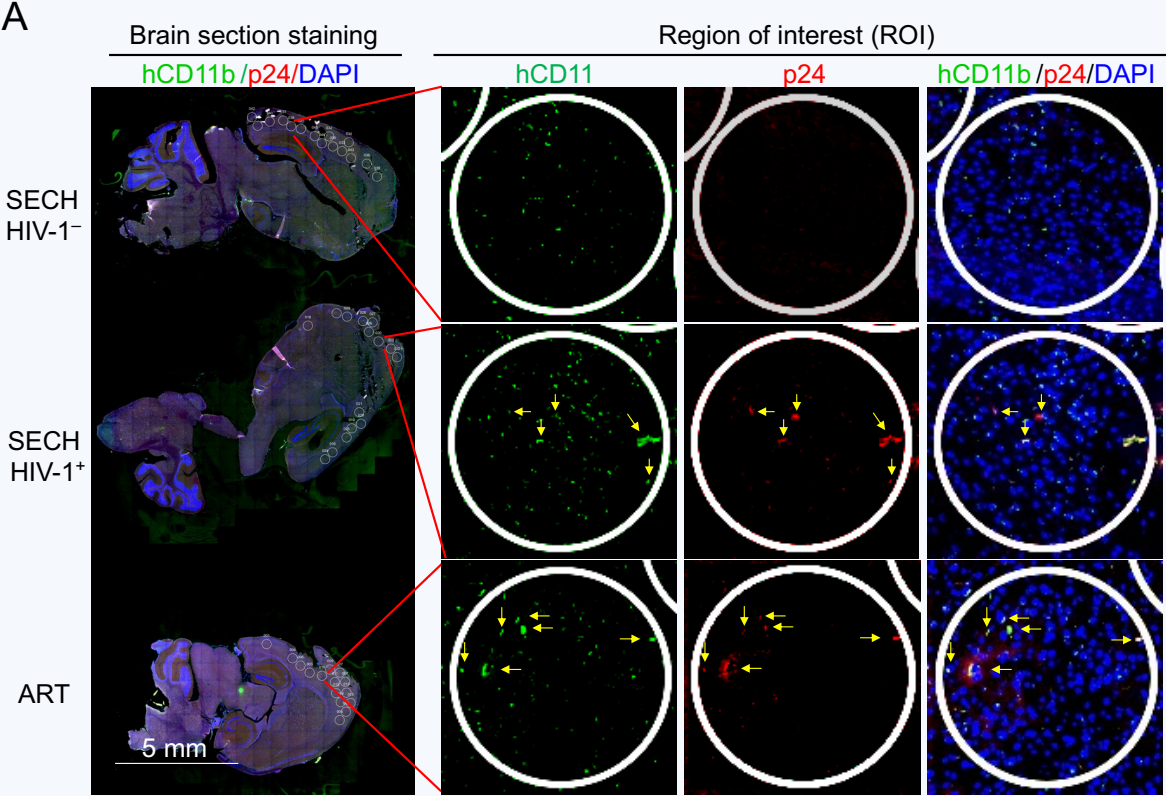
**C**



*(Unpublished observation)*

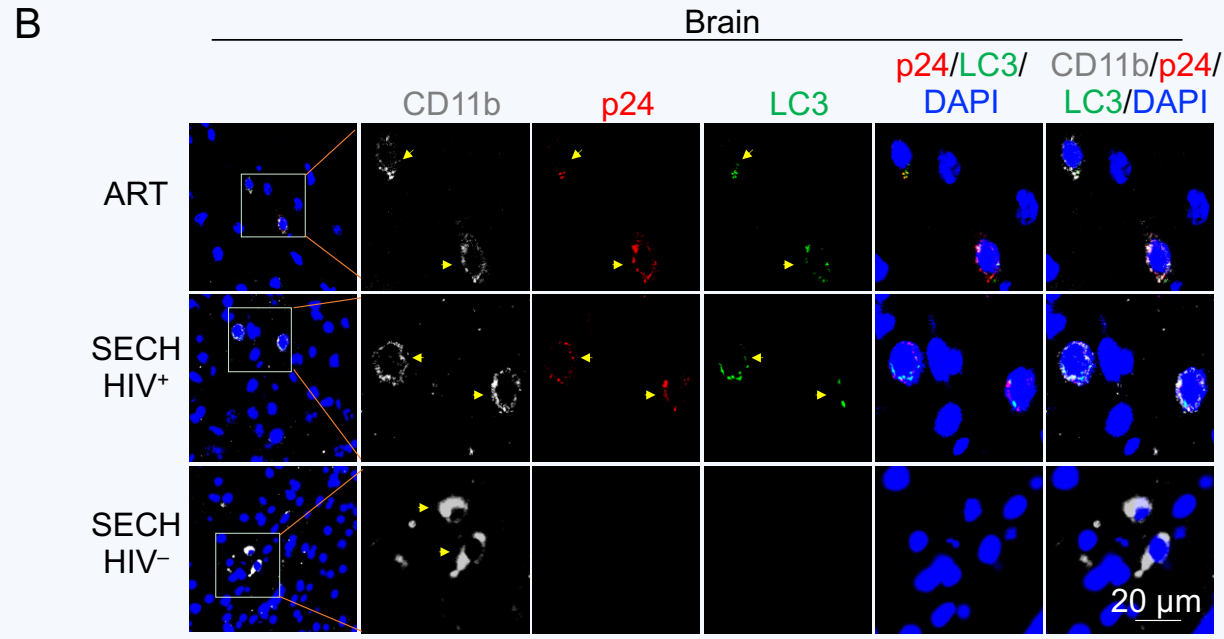
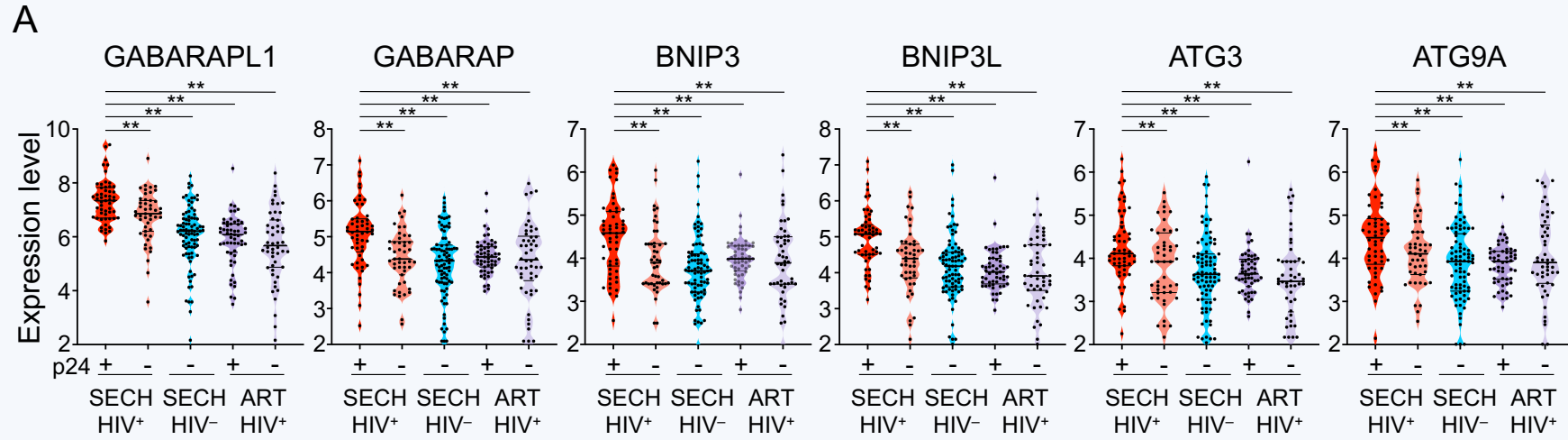


# Increased Autophagy and Epigenetic Modifiers in SECH-resistant Microglial Cells of Hu-Mice



(Unpublished observation)

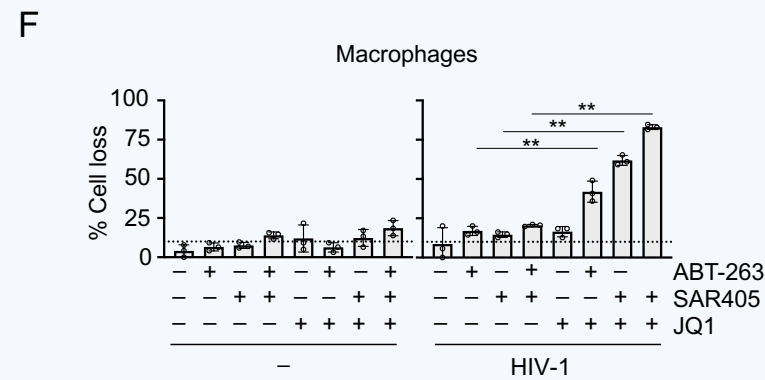
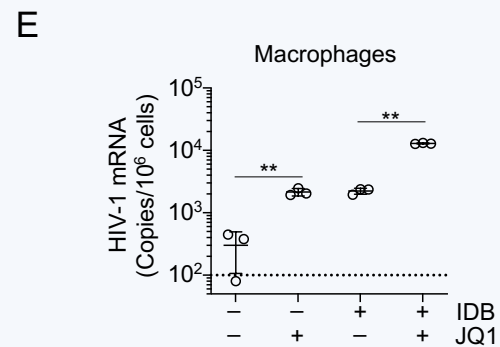
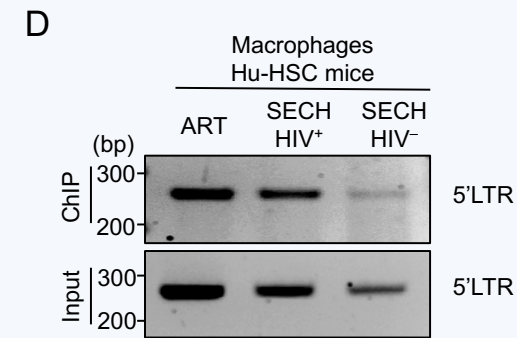
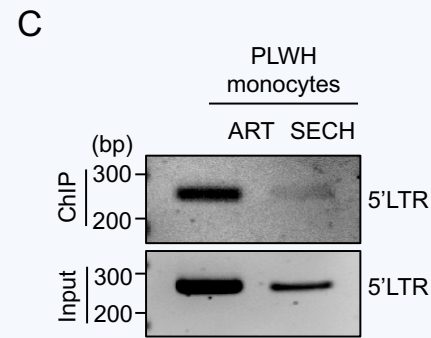
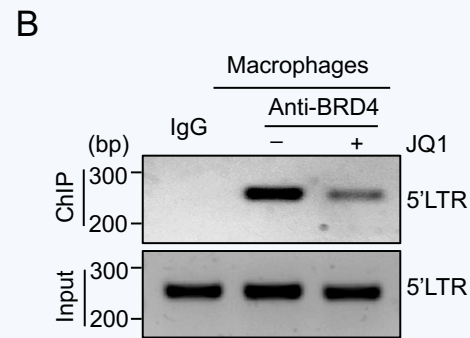
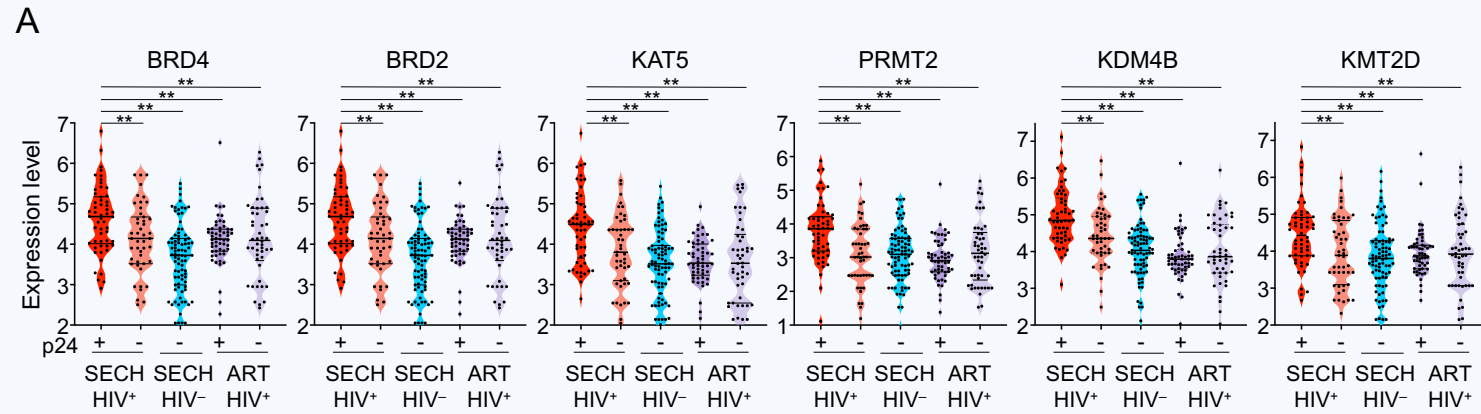
# Increased Autophagy in SECH-resistant Microglial cells of Hu-Mice



(Unpublished observation)

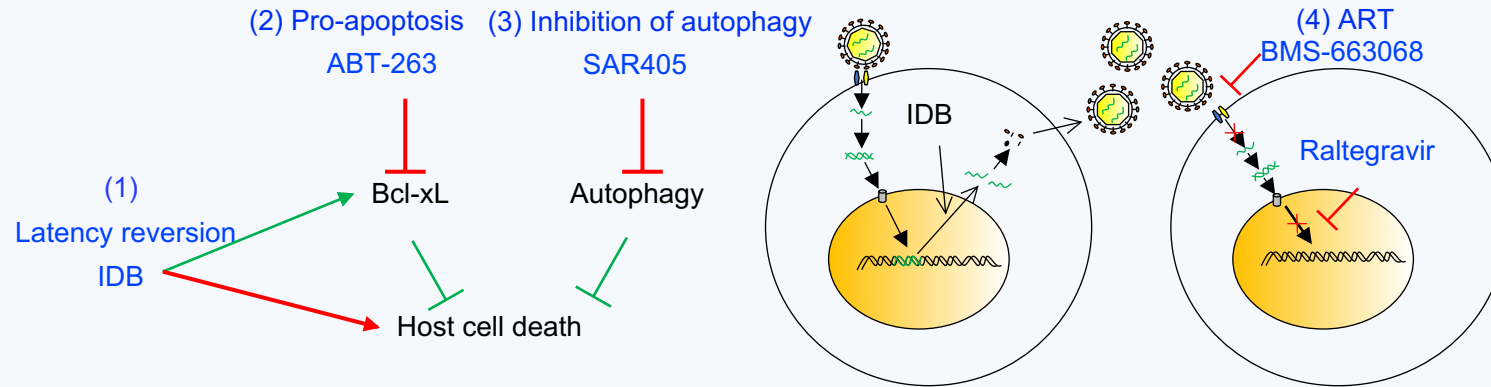


# Increased Epigenetic Modifiers in SECH-resistant Microglia of Hu-Mice



*(Unpublished observation)*

# Selective Elimination of Host Cells Capable of Producing HIV-1 (SECH)



- SECH can clear HIV reservoirs in both T cell and myeloid lineages
- SECH can clear intact but not defective HIV-1 proviruses
- To improve the clearance of HIV reservoirs
  - Targeting epigenetic modifiers for efficient HIV reactivation
  - Inhibition of autophagy

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