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

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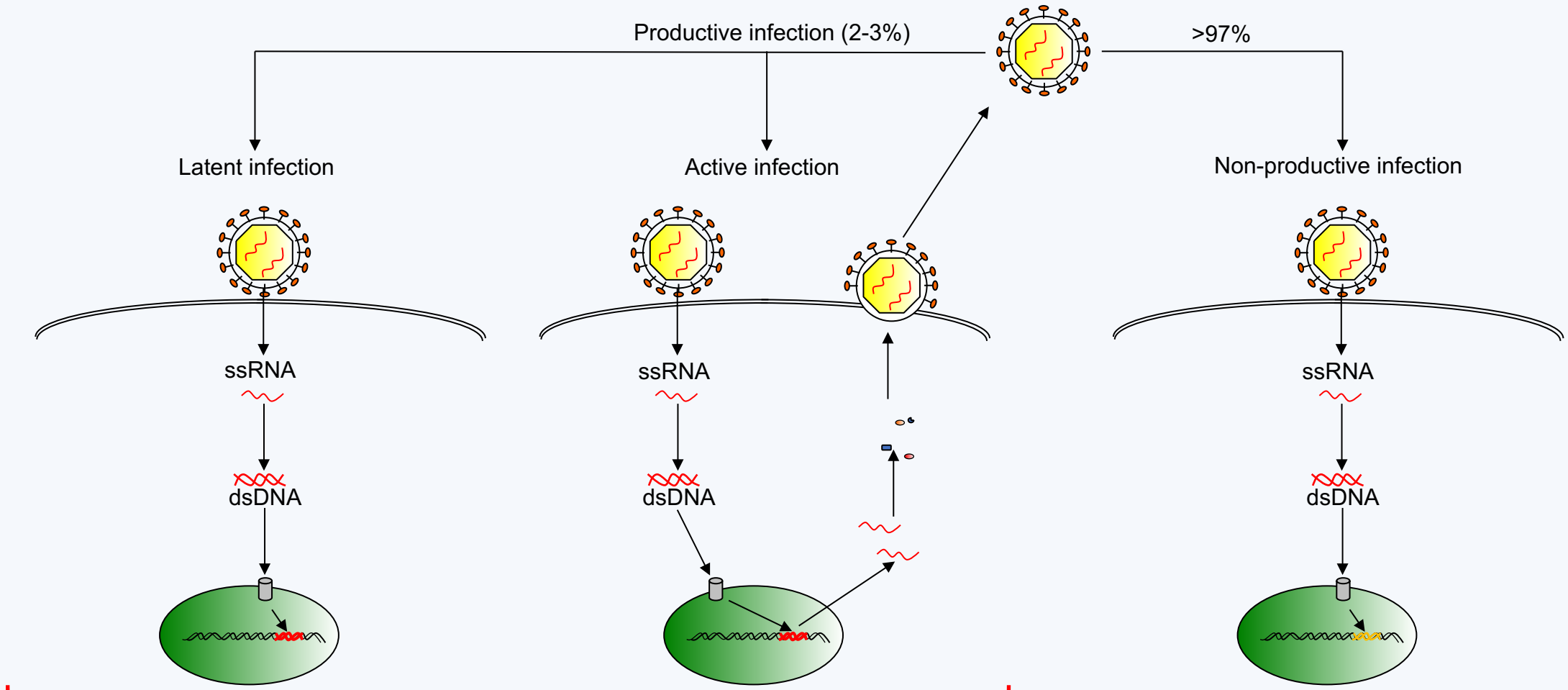
We Declare no conflict of interest

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

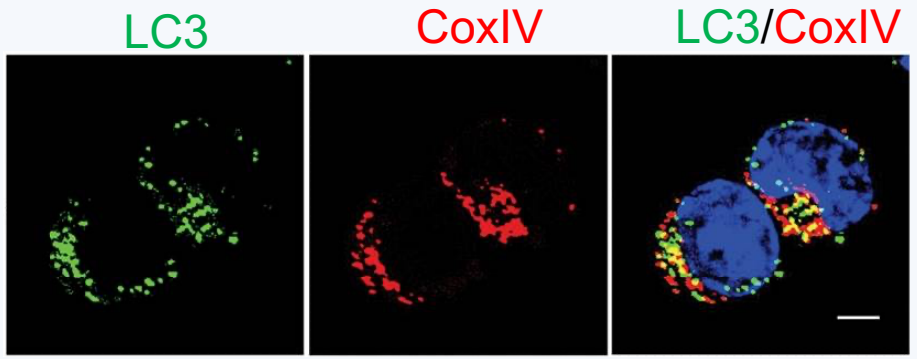


# HIV Reservoir Cells and Immune Memory Cells

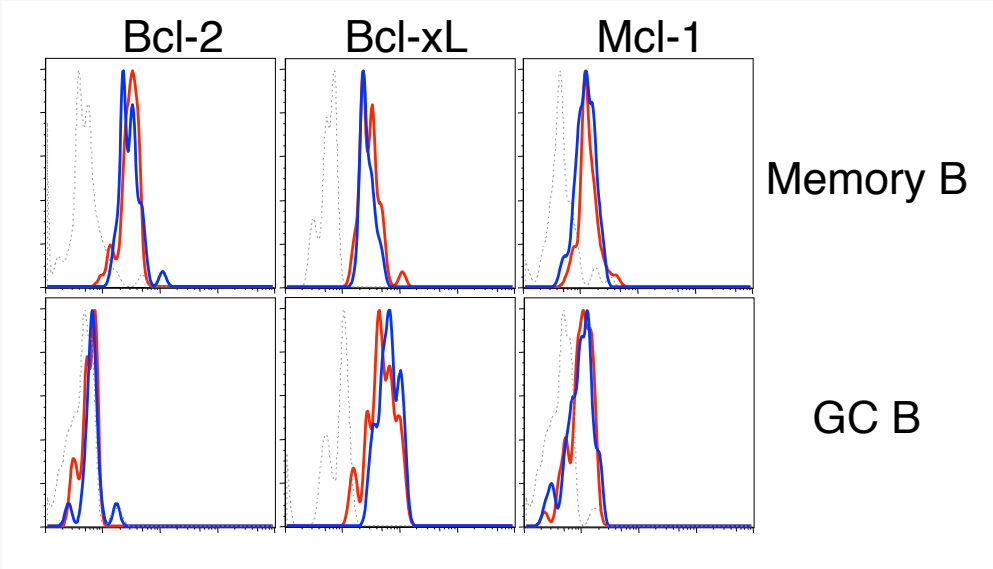
1. Quiescence

2. Longevity

# Autophagy and Anti-Apoptotic Bcl-2 Contribute to memory B cell Longevity




Memory B

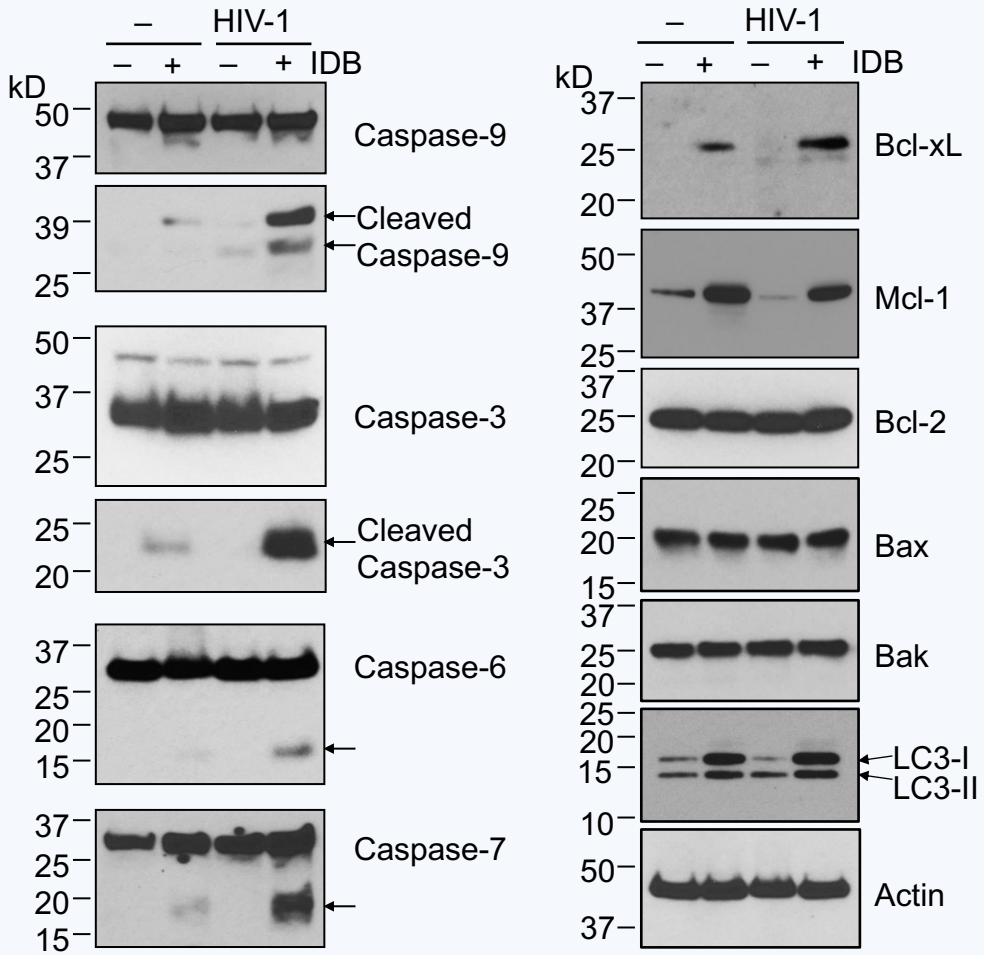


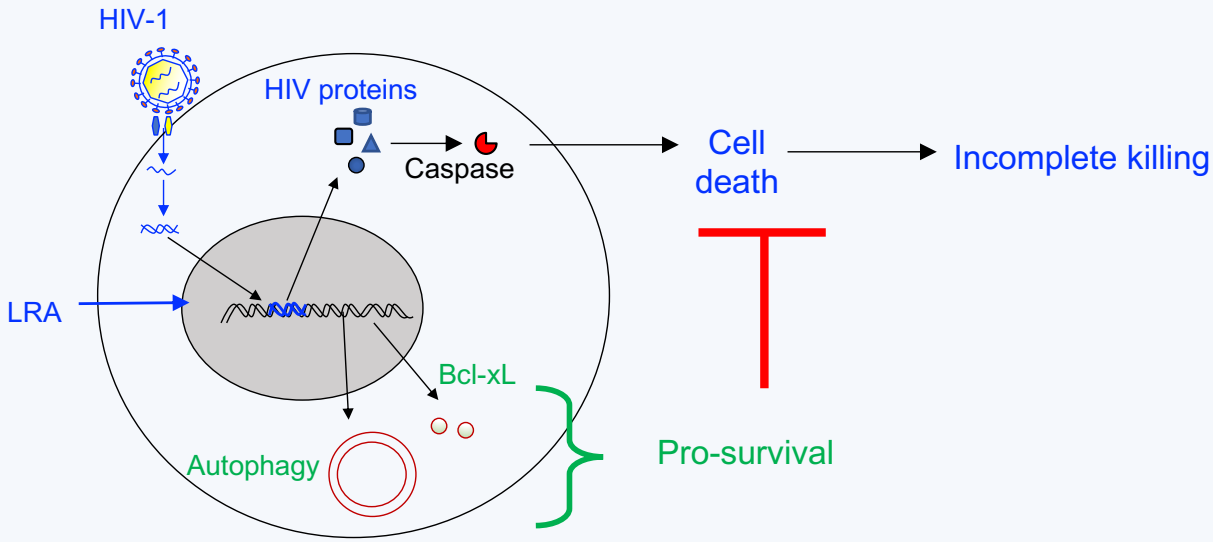

Memory B

GC B

Nature Med 20:503-510

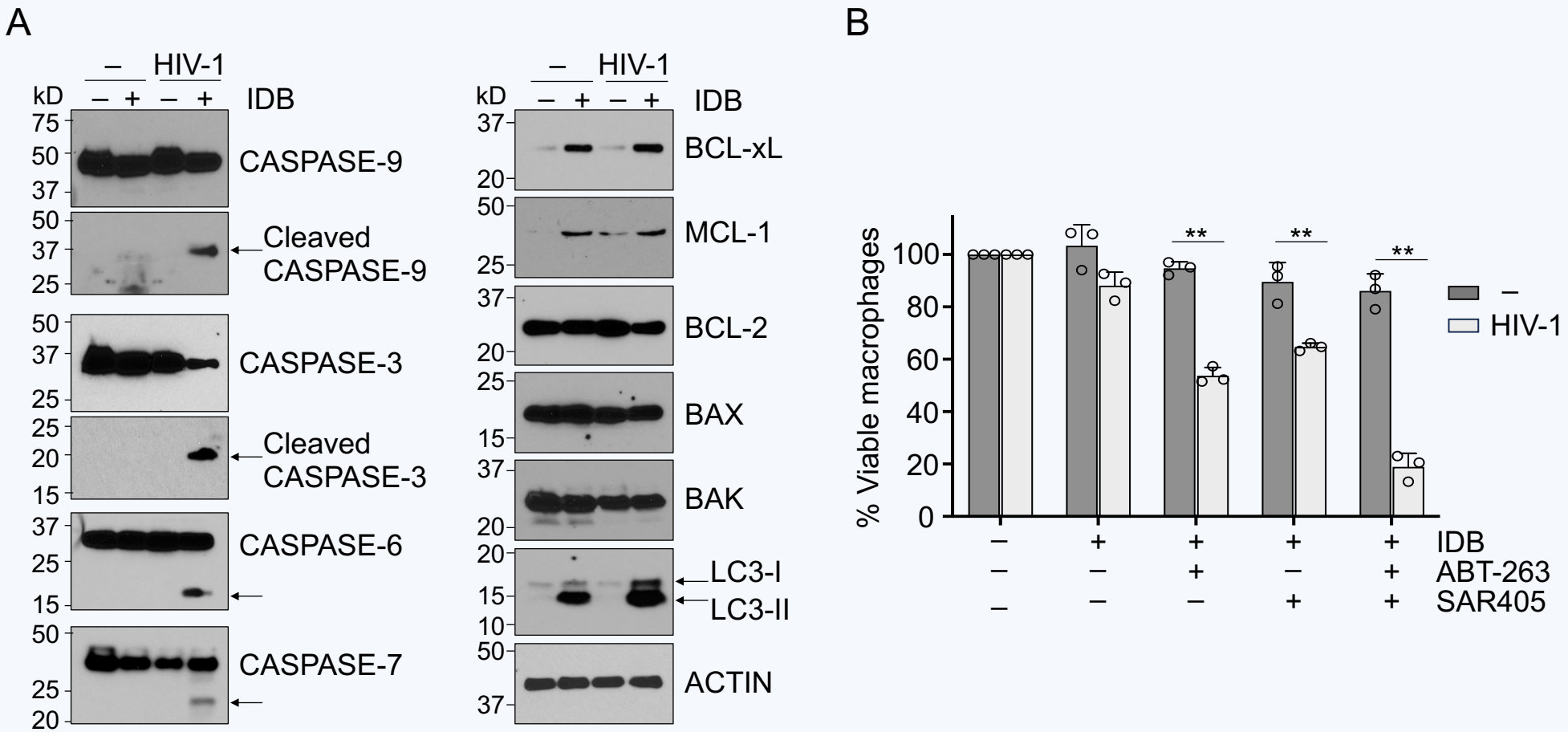
# LRA induces Both Cell death and Pro-survival Signaling in HIV-infected T cells



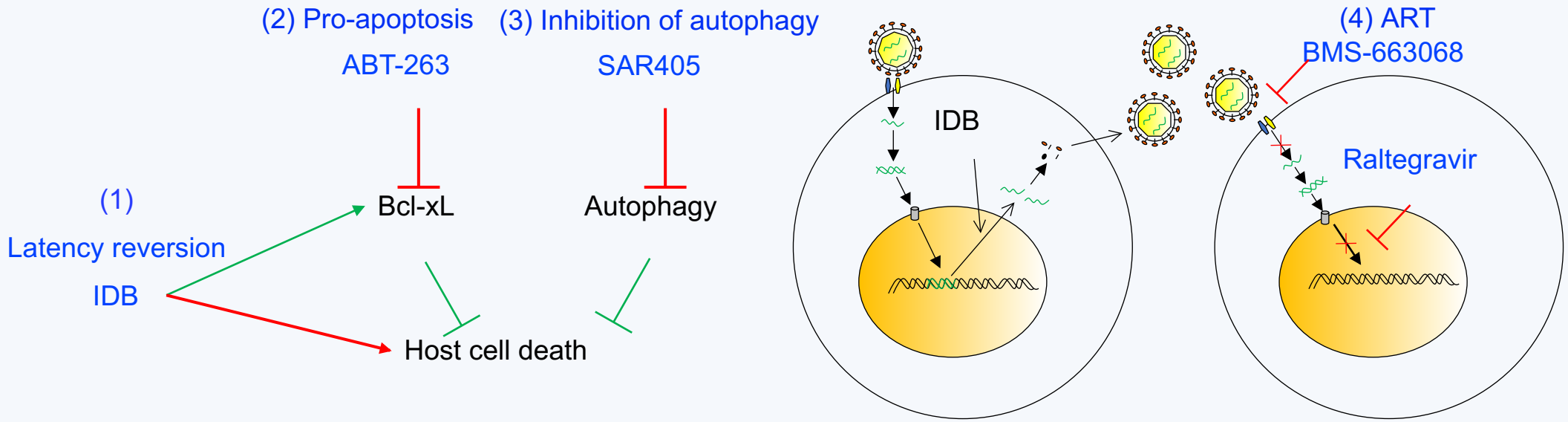

*Nature Comm 2020*

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

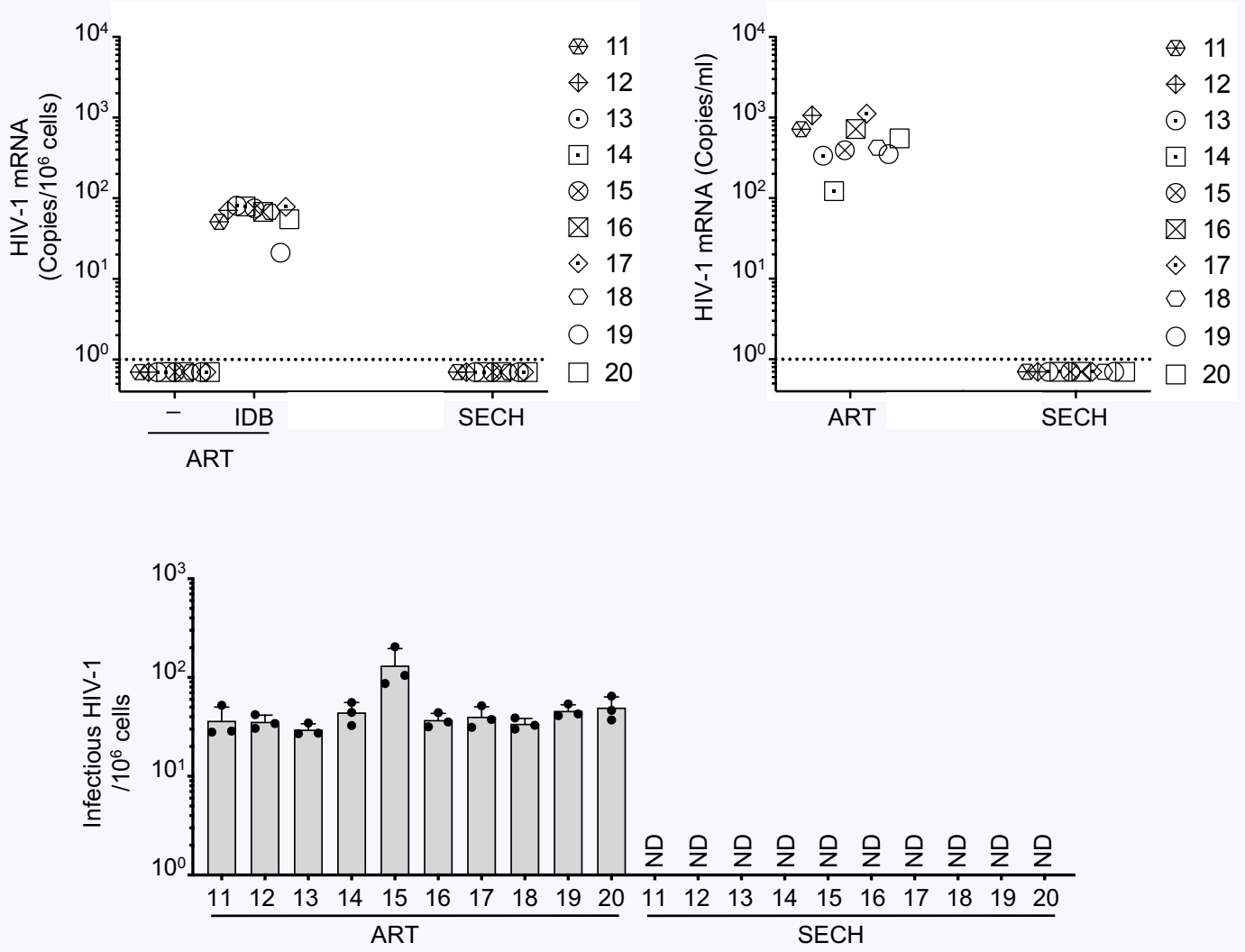



*(Unpublished observation)*

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

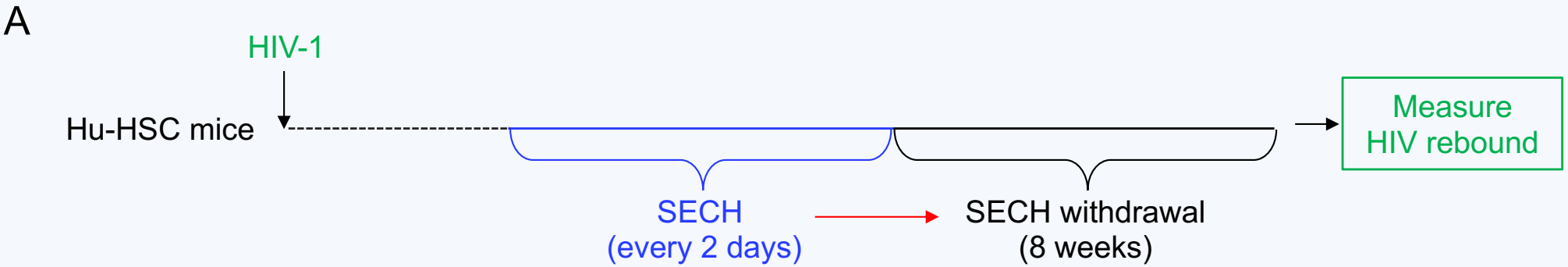


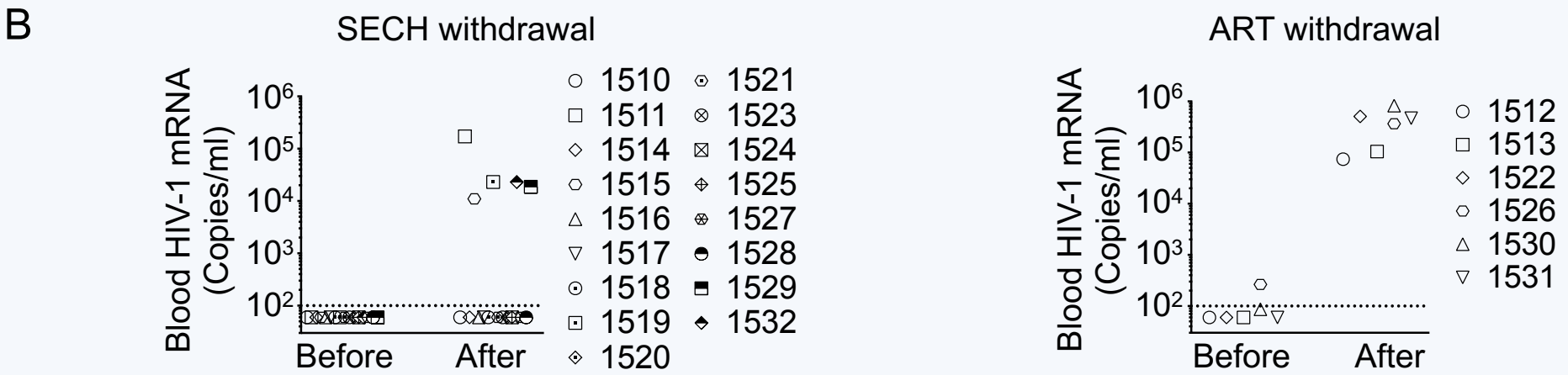
# Clearance of HIV-1 in PBMCs from PLWH by SECH




Li et al., *Nature Comm* 2020

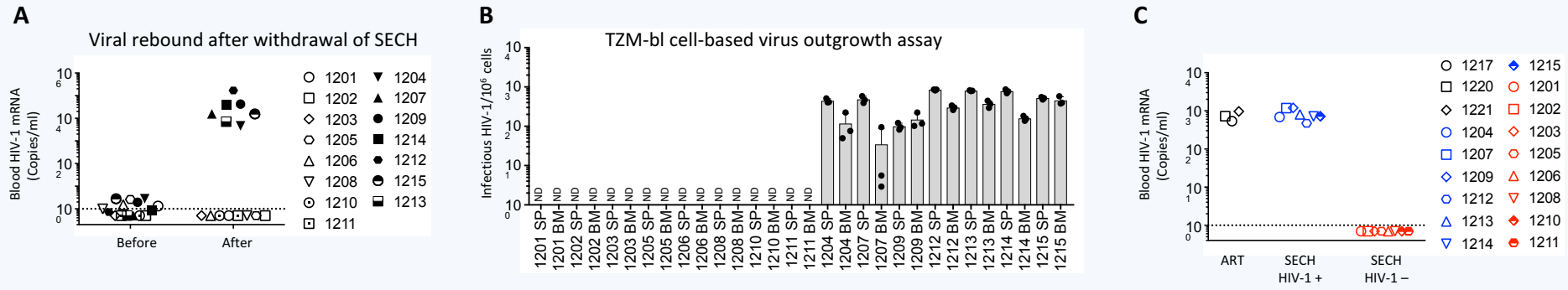
# HIV Clearance in Hu-Mice by SECH




Li et al., *Nature Comm* 2020

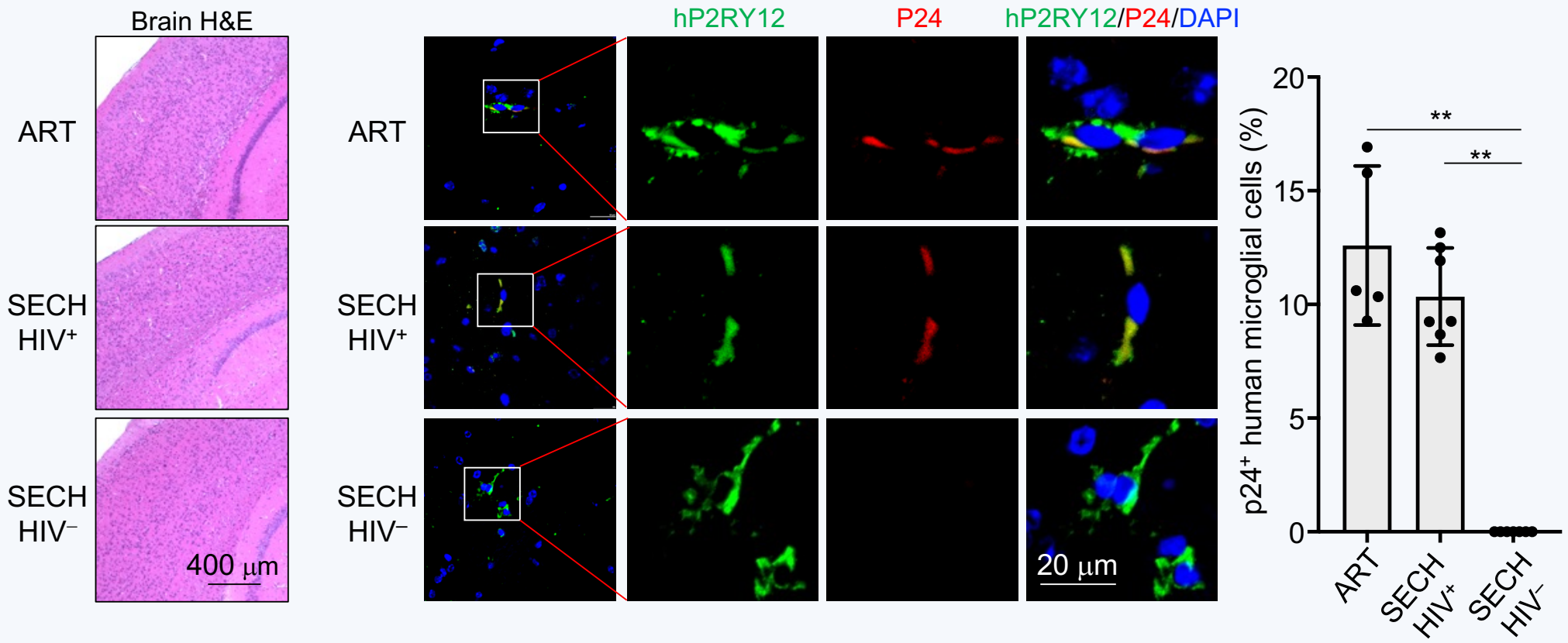
# Determination of HIV clearance




**(A)** Drug withdrawal.
(**B**) *In vitro* virus outgrowth assay.
(**C**) *In vivo* humanized mouse-based virus outgrowth assay (hmVOA).

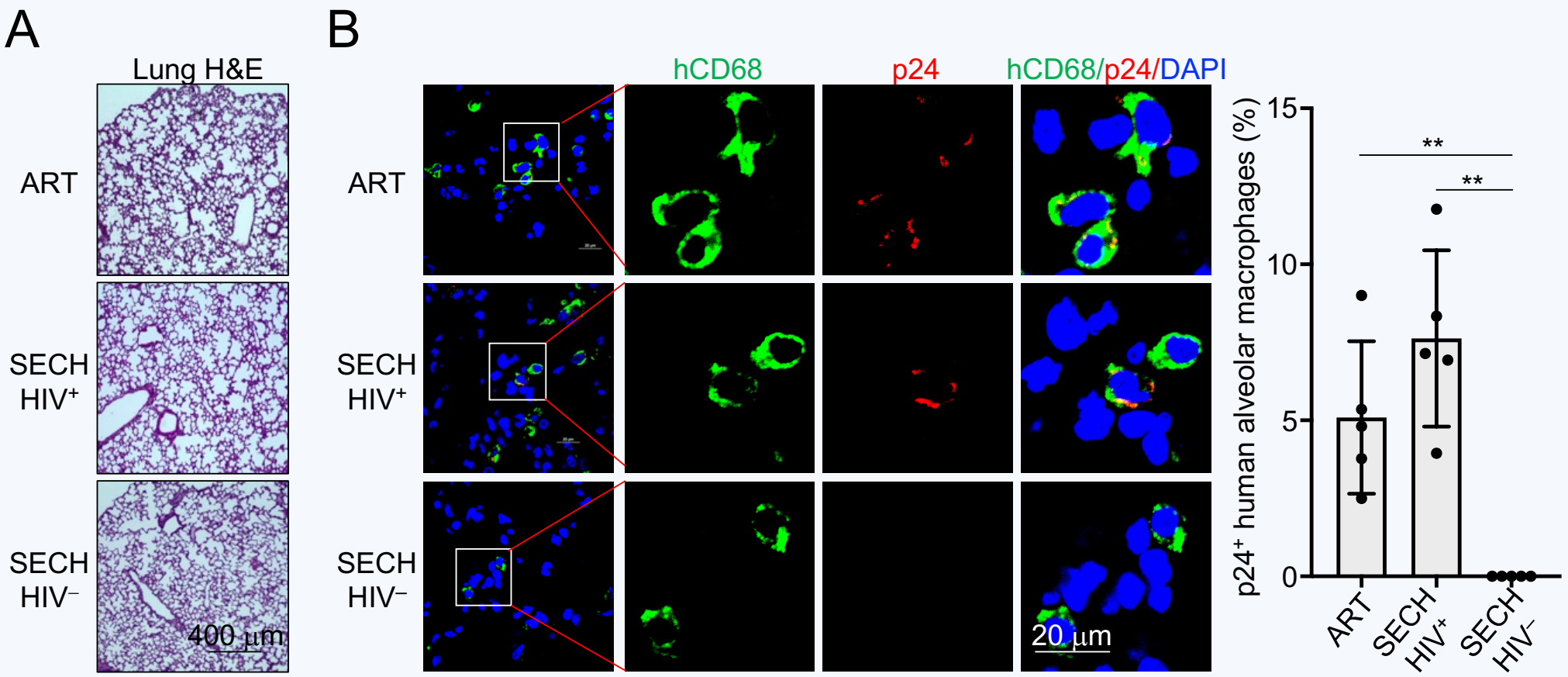
Li et al., *Nature Comm* 2020

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



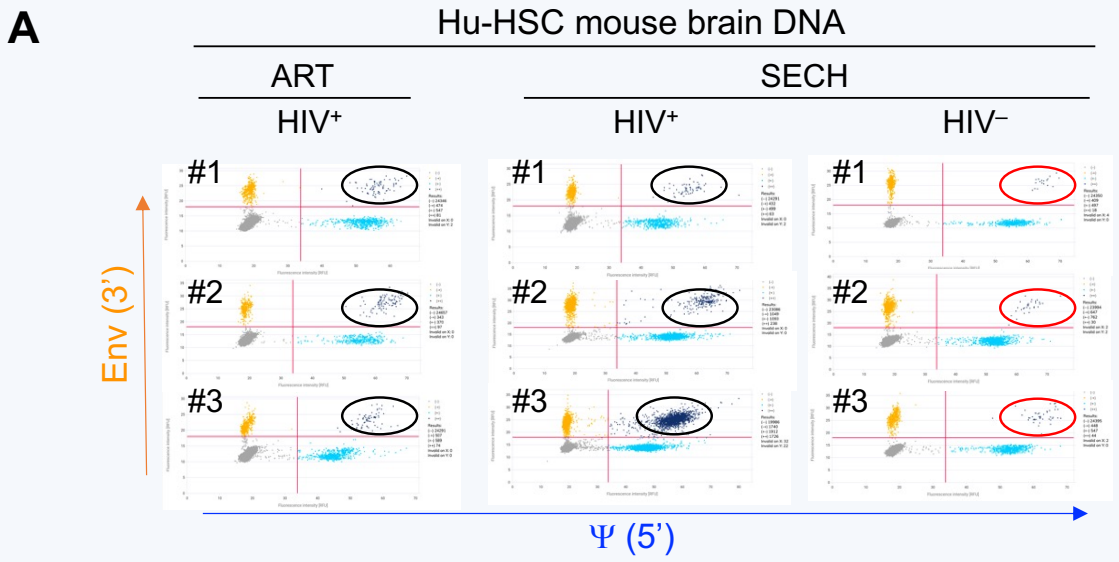

*(Unpublished observation)*

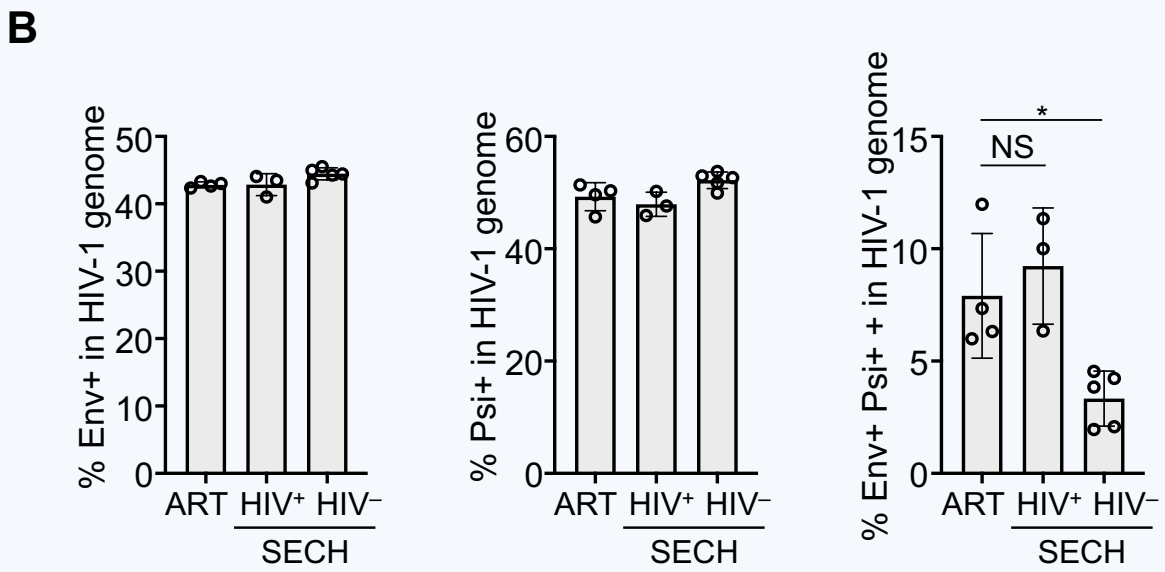
# HIV Clearance in Alveolar Macrophages of Hu-Mice by SECH




*(Unpublished observation)*

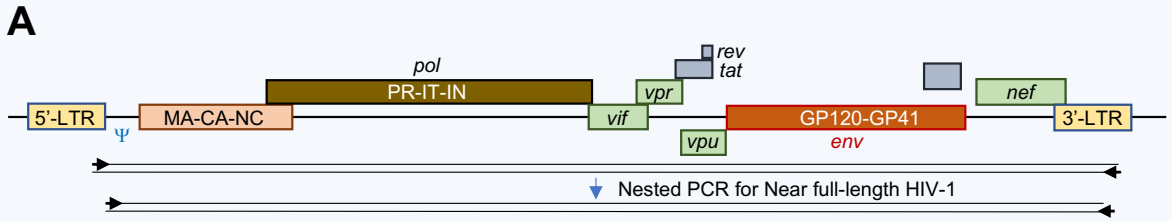
# Depletion of intact but not defective HIV-1 by SECH in the brain of Hu-mice

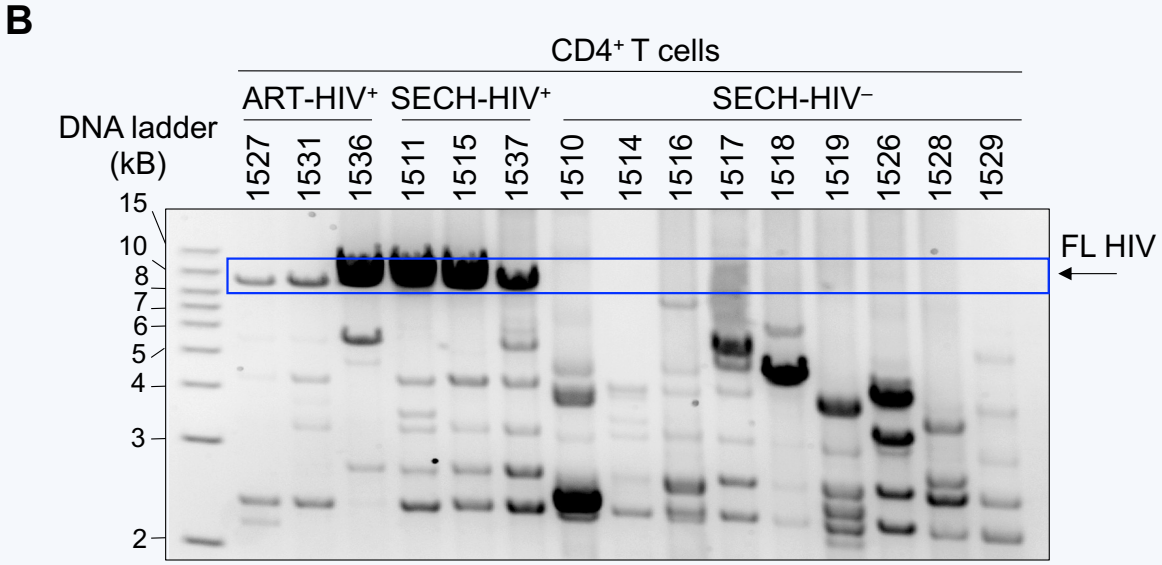


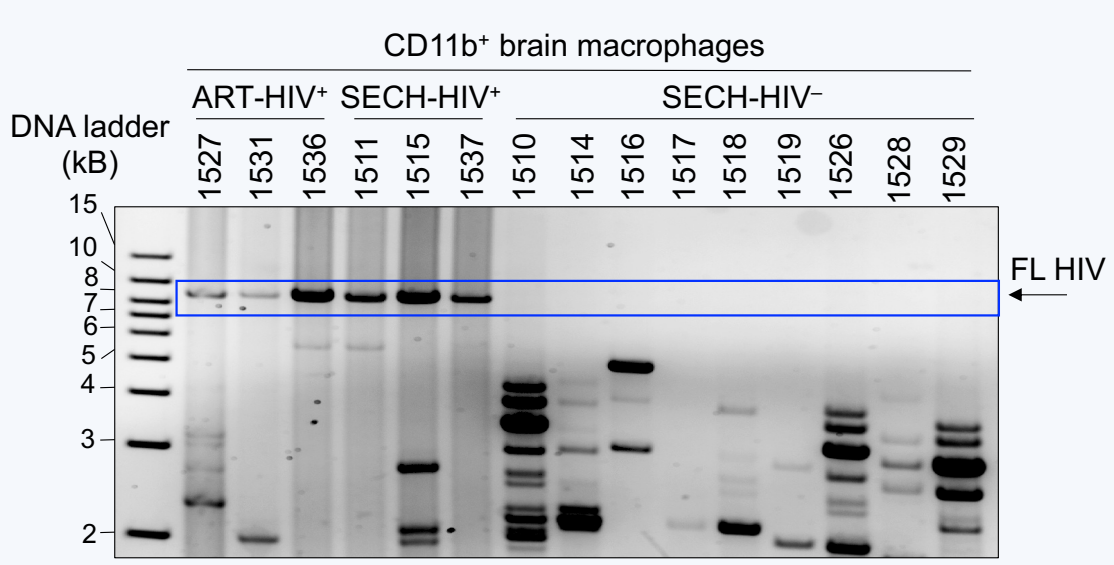




*(Unpublished observation)*

# 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

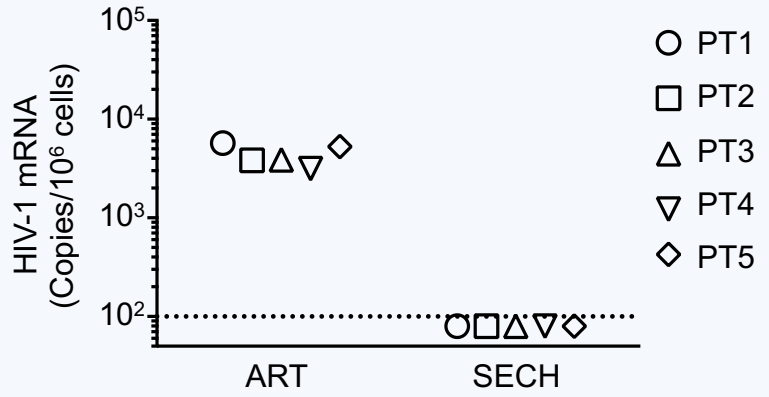
**A**

**Table. ART-experienced HIV-1 patients.**

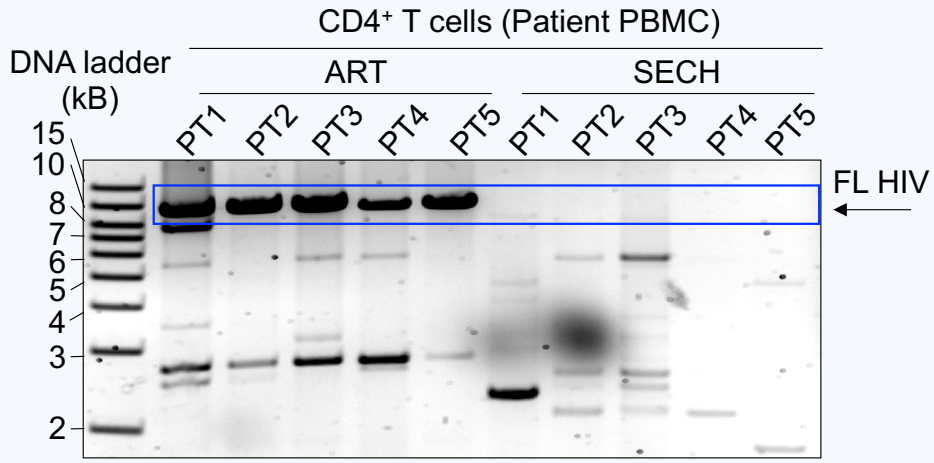
| Patient | Race | Sex | Age | CD4 Count | CD4 % | HIV RNA Levels (copies/mL) |
|---|---|---|---|---|---|---|
| PT1 | B | M | 60 | 284 | 33 | <20 |
| PT2 | C | F | 49 | 93 | 11 | ND |
| PT3 | C | M | 56 | 318 | 40 | ND |
| PT4 | B | M | 58 | 779 | 63 | ND |
| PT5 | B | F | 52 | 576 | 33 | ND |

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

**B**

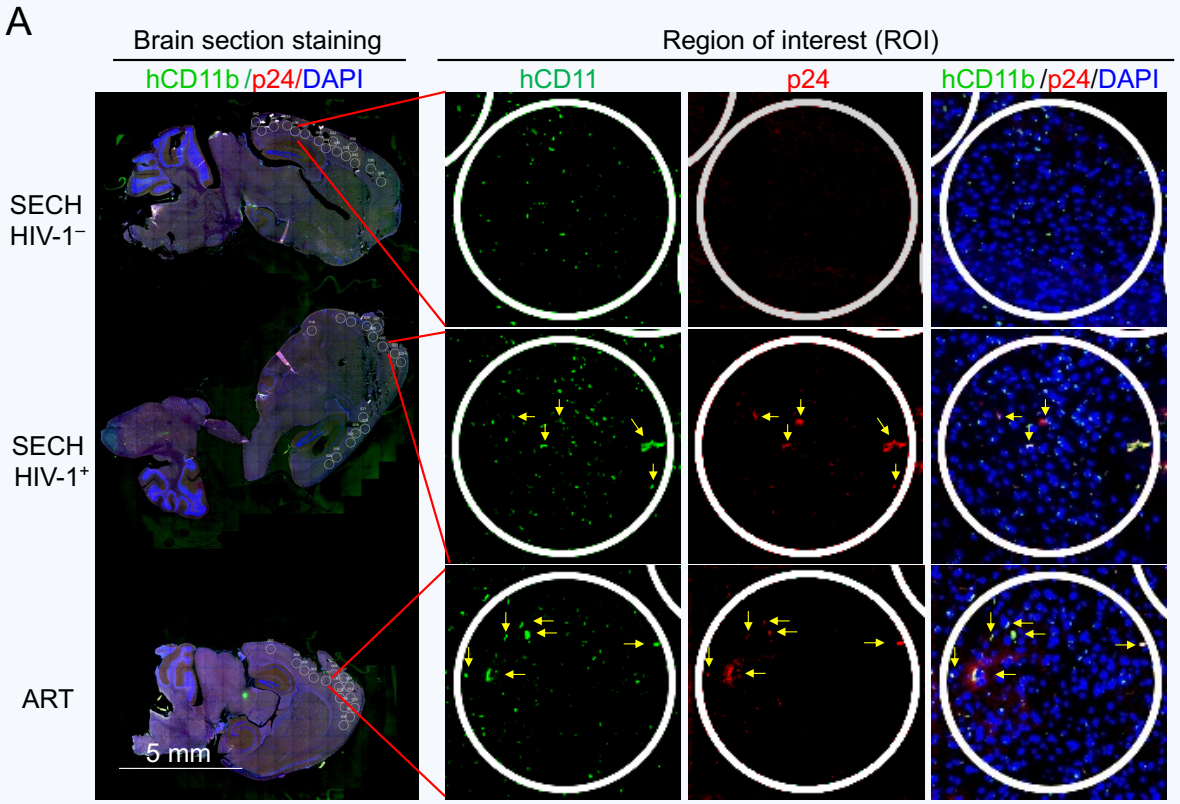


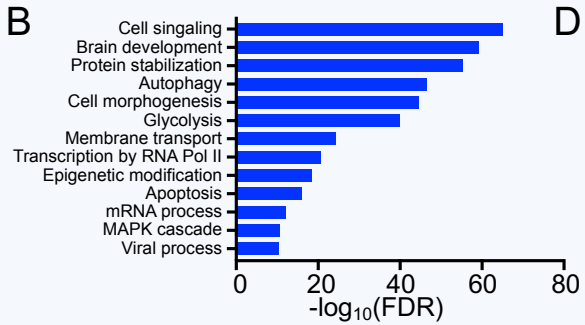

**C**

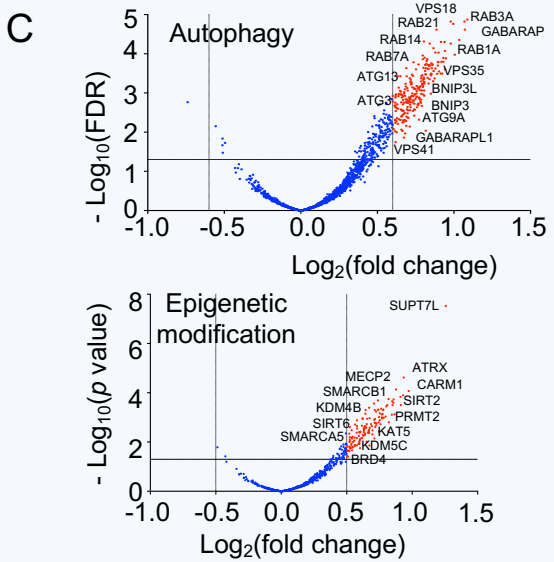


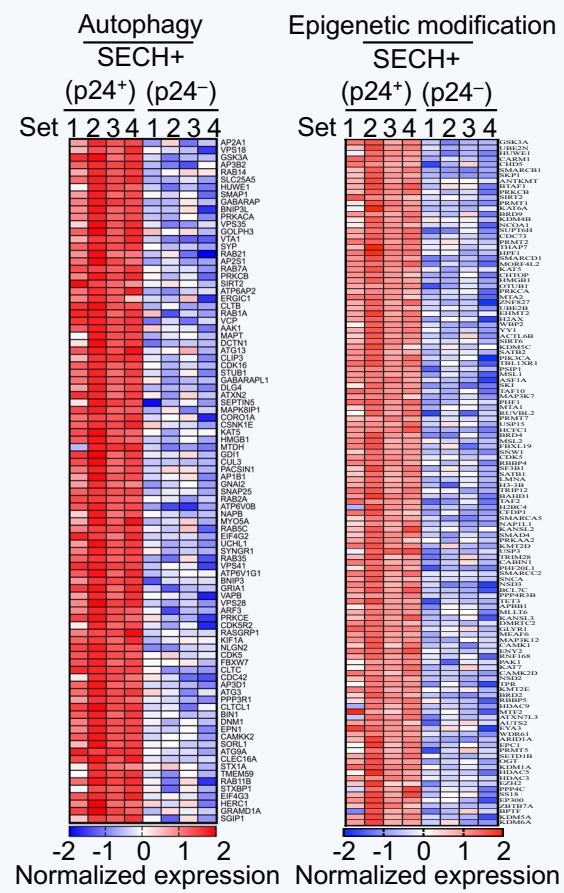

*(Unpublished observation)*

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



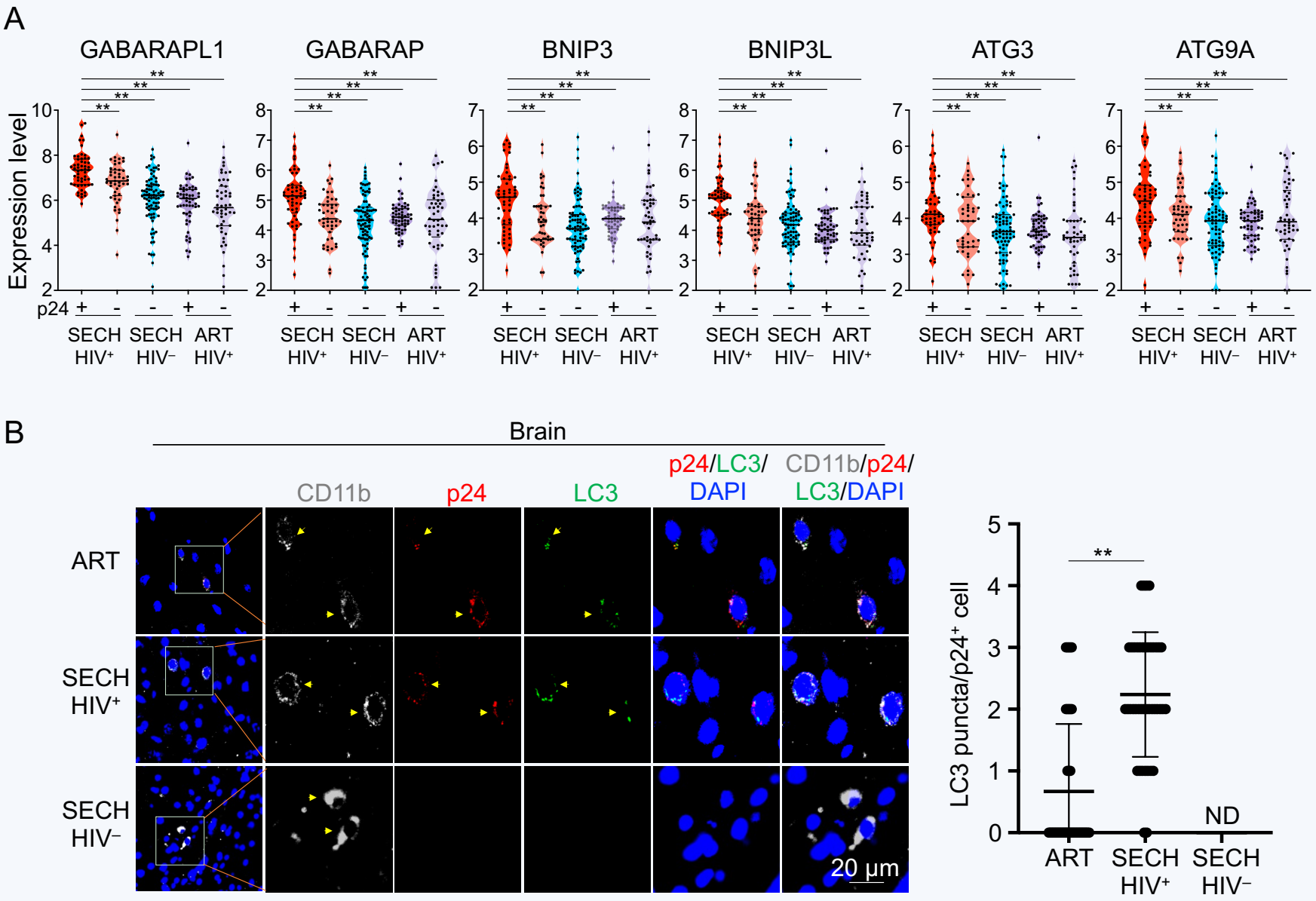



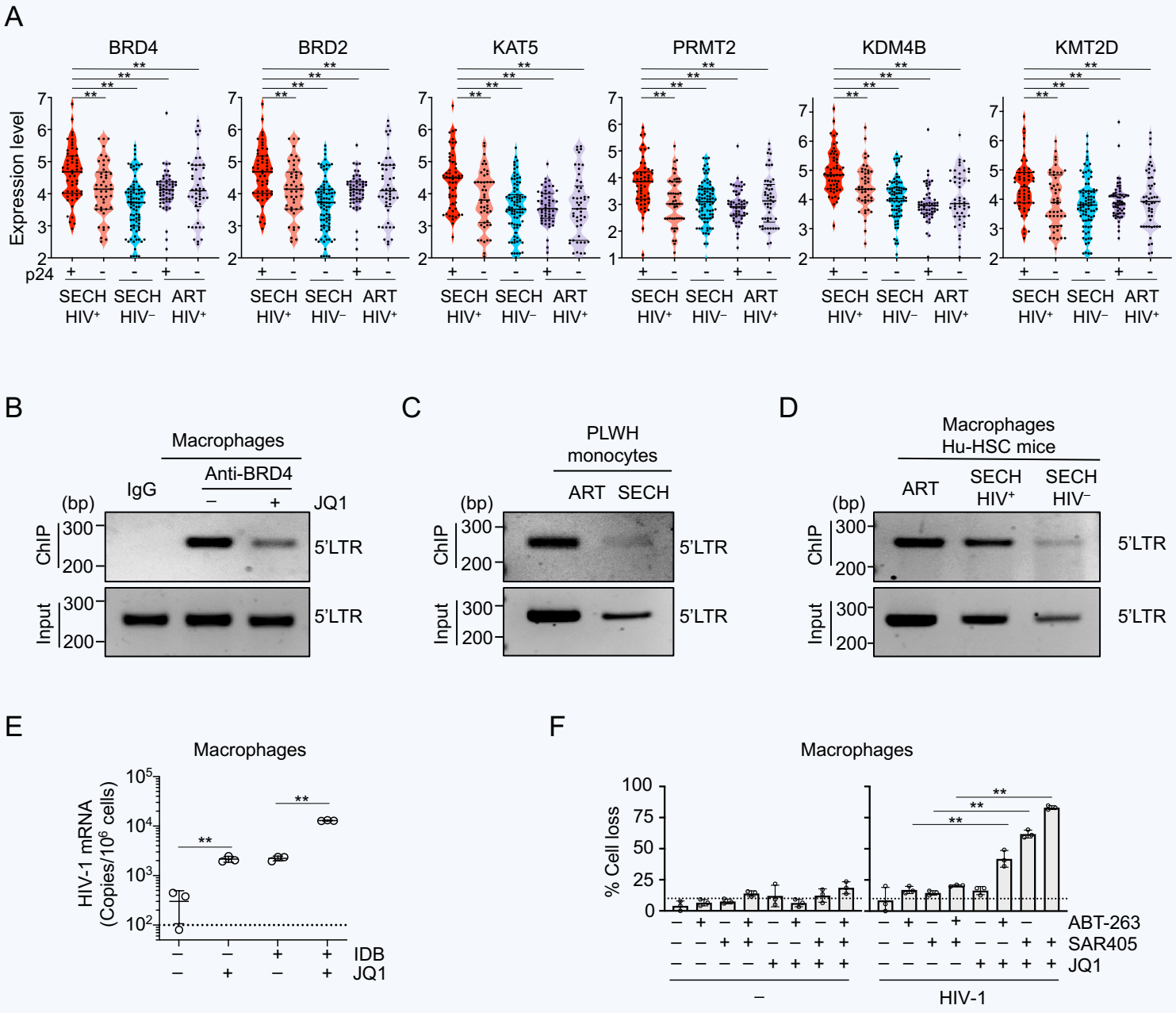

*(Unpublished observation)*

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



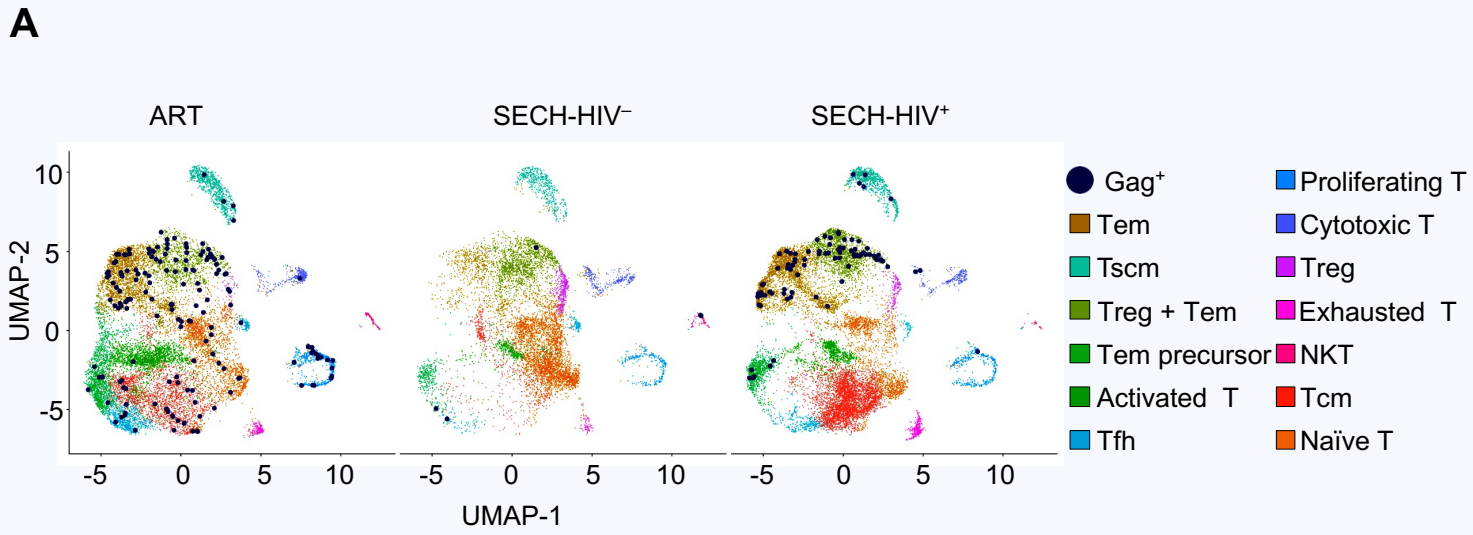

*(Unpublished observation)*

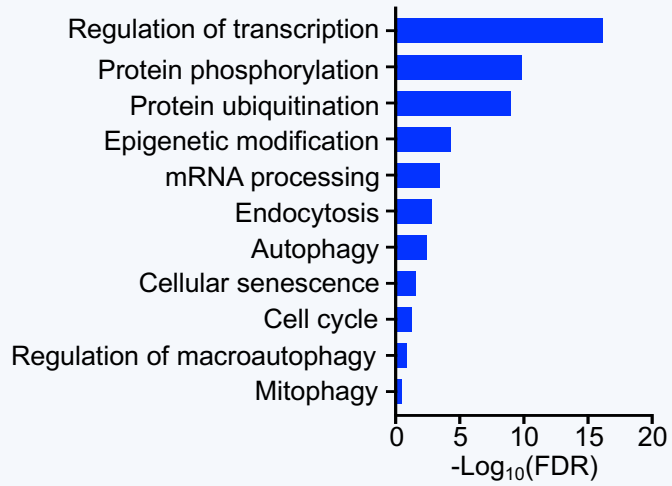
# Increased Epigenetic Modifiers in SECH-resistant Microglia of Hu-Mice

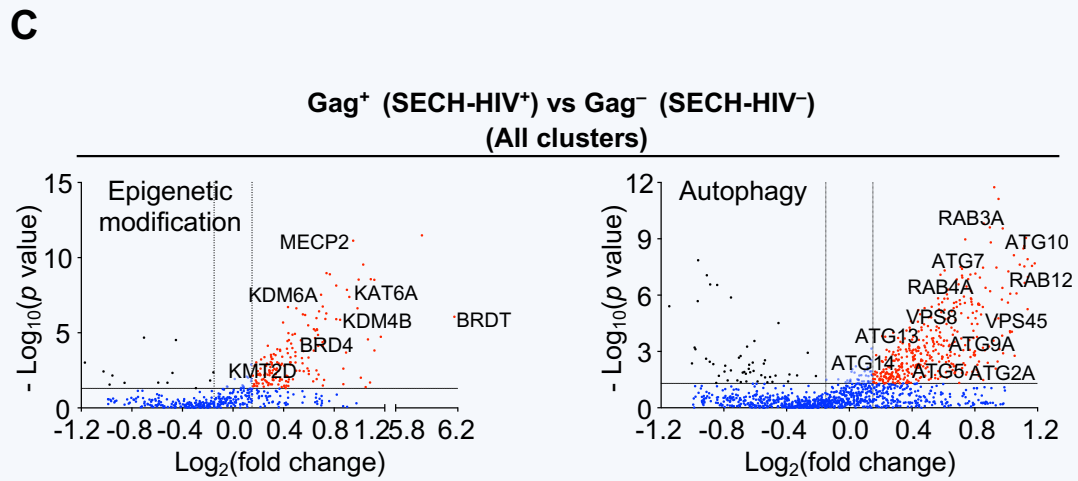


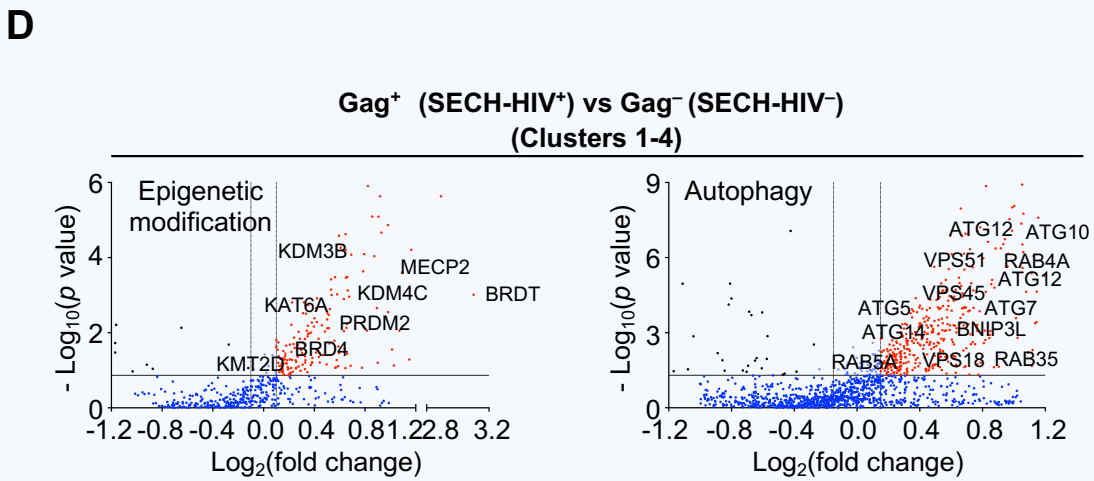

*(Unpublished observation)*

# Increased Epigenetic Modifiers and Autophagy in SECH-resistant T cells of Hu-Mice



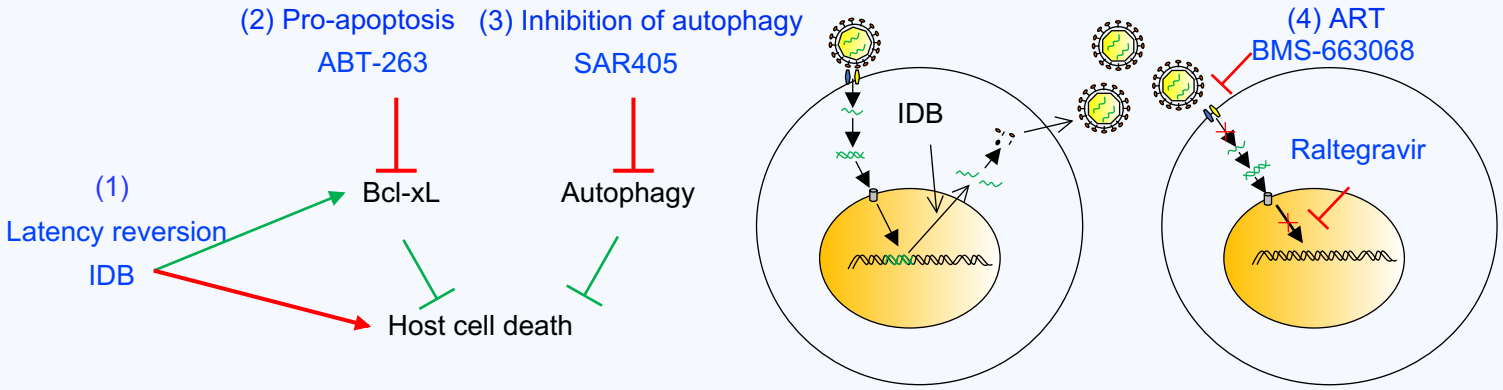




*(Unpublished observation)*

# **S**elective **E**limination of Host **C**ells Capable of Producing **H**IV-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

# Acknowledgement


HOUSTON Methodist RESEARCH INSTITUTE

Min Li
Baichao Sun
Marietta Budai
Yajing He
Wei Liu
Tonya Bauch
Matthew Vasquez
Hong Zhao
Edward A. Graviss
Laurie Minze

Baylor College of Medicine

Min Chen
Albert Jang
Jason Kimata
Khanghy Truong
Suman Sharma

Chao Cheng
Jing Dong
Andrew Rice
Thomas Giordano

UTHealth McGovern Medical School

Roberto Arduino
Olga Ortiz

utmb

Benjamin Gelman

Funding
R01 MH127979
R01 AI176558