

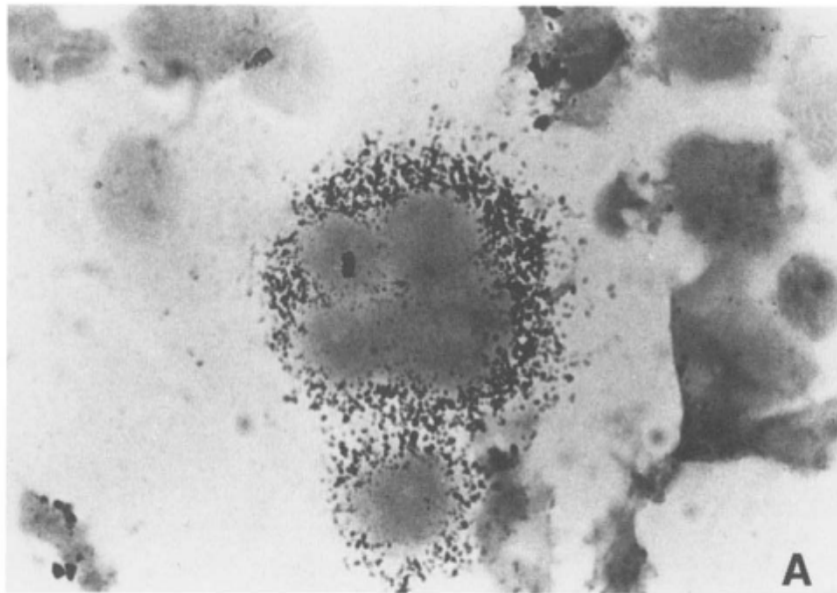


## Hommage à Dominique DORMONT



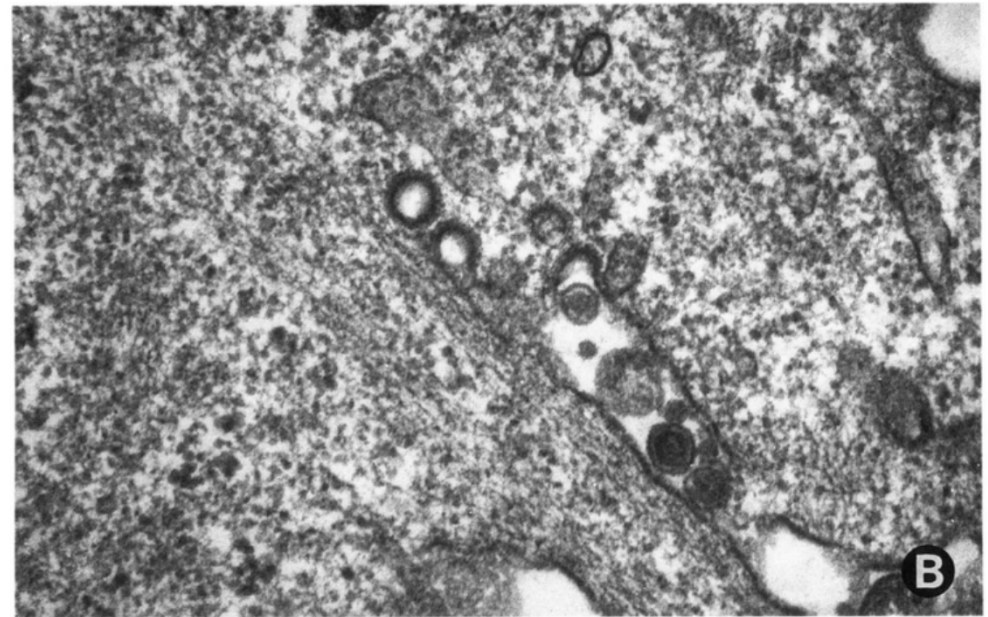
# Infection of macrophages with HTLV-1

**In situ Hybridization**



X650

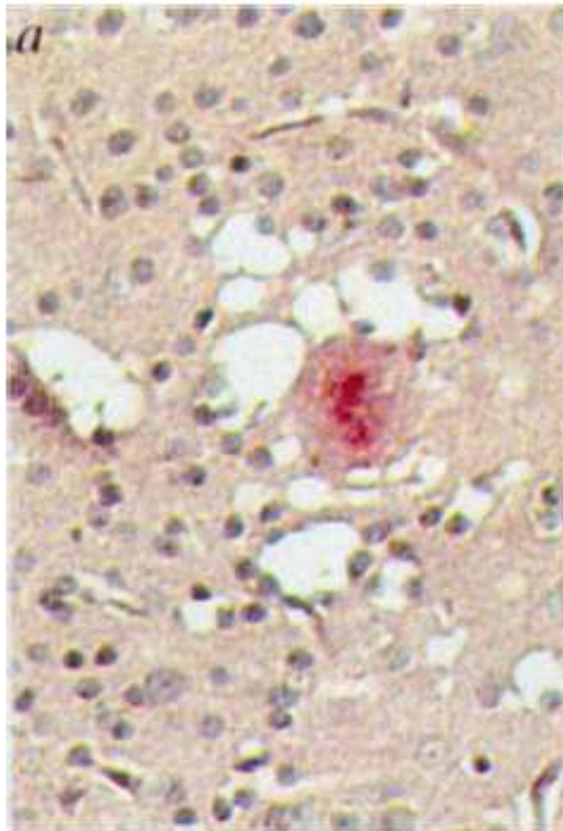
**Electron Microscopy**



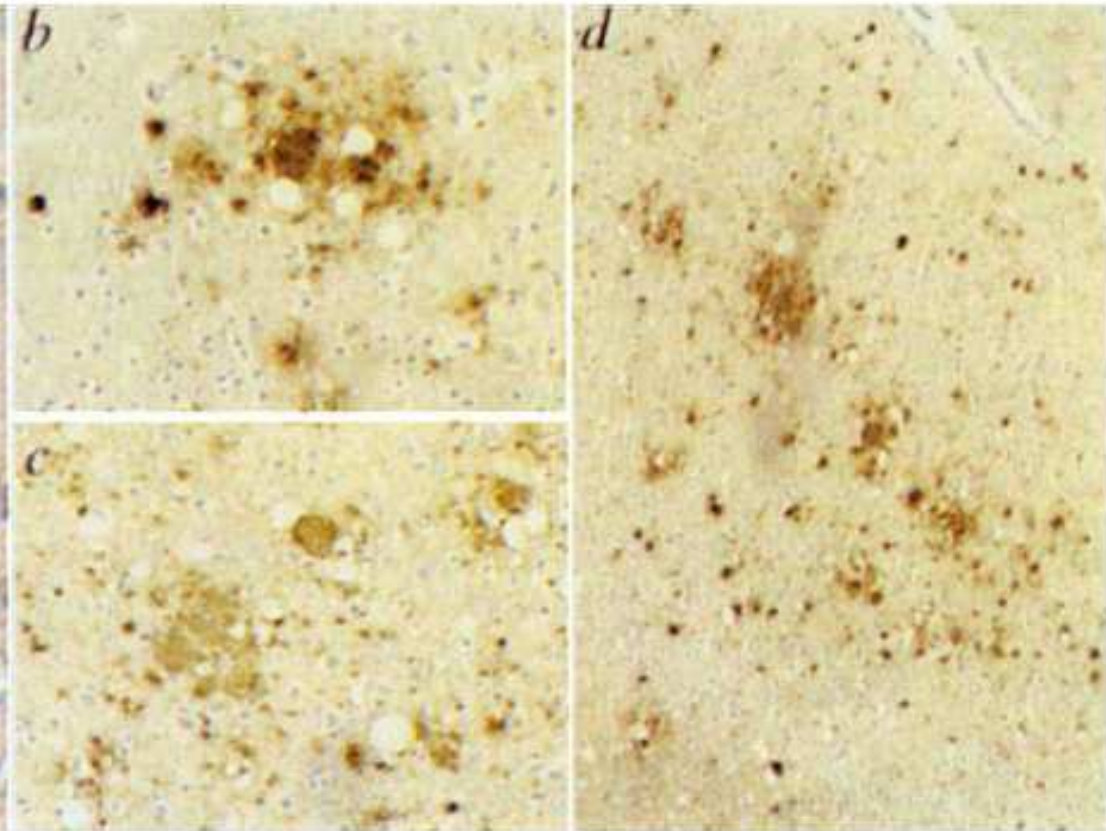
X78,000

# BSE Transmission To Macaques

vCJD Florid Plaques



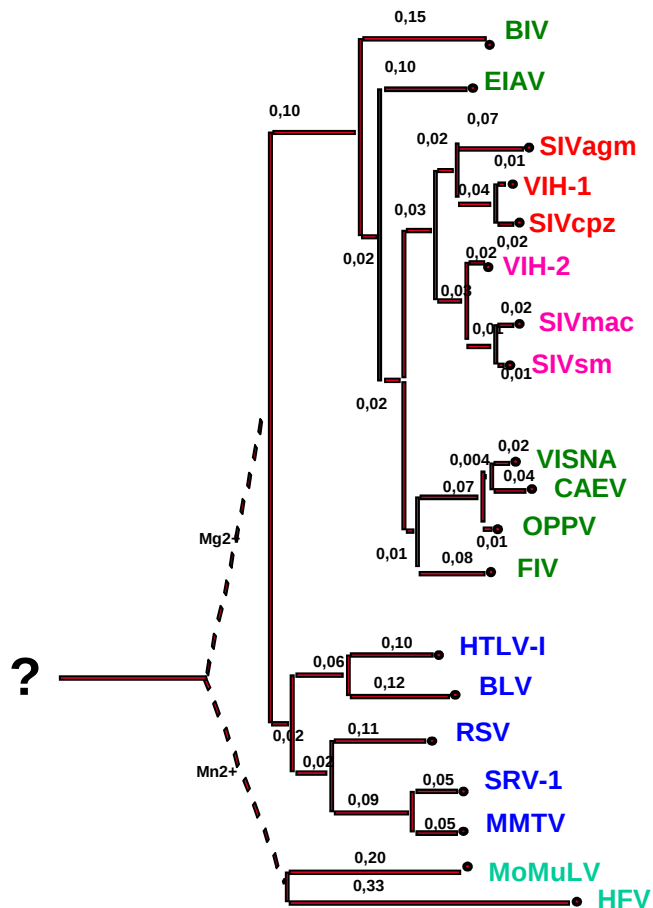
PrP Immuno-chemistry



**Pathological signature of BSE agent in cynomolgus macaques is identical to that of vCJD in British cases**

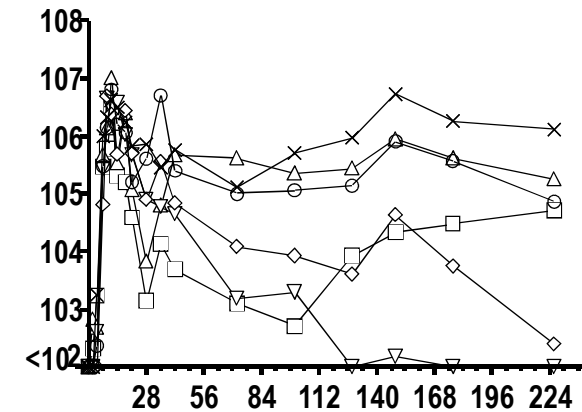
# SIVmac251 of Mauritian Cynomolgus Macaques

## RT nucleotide sequences *From Gonda et al, 1992*

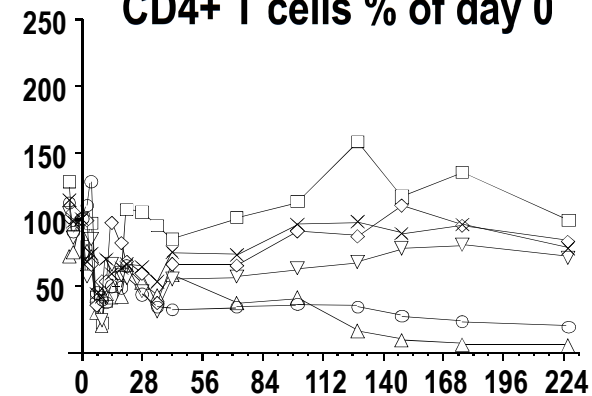


## Experimental infection of macaques

### Plasma viral load (RNA copies/ml)



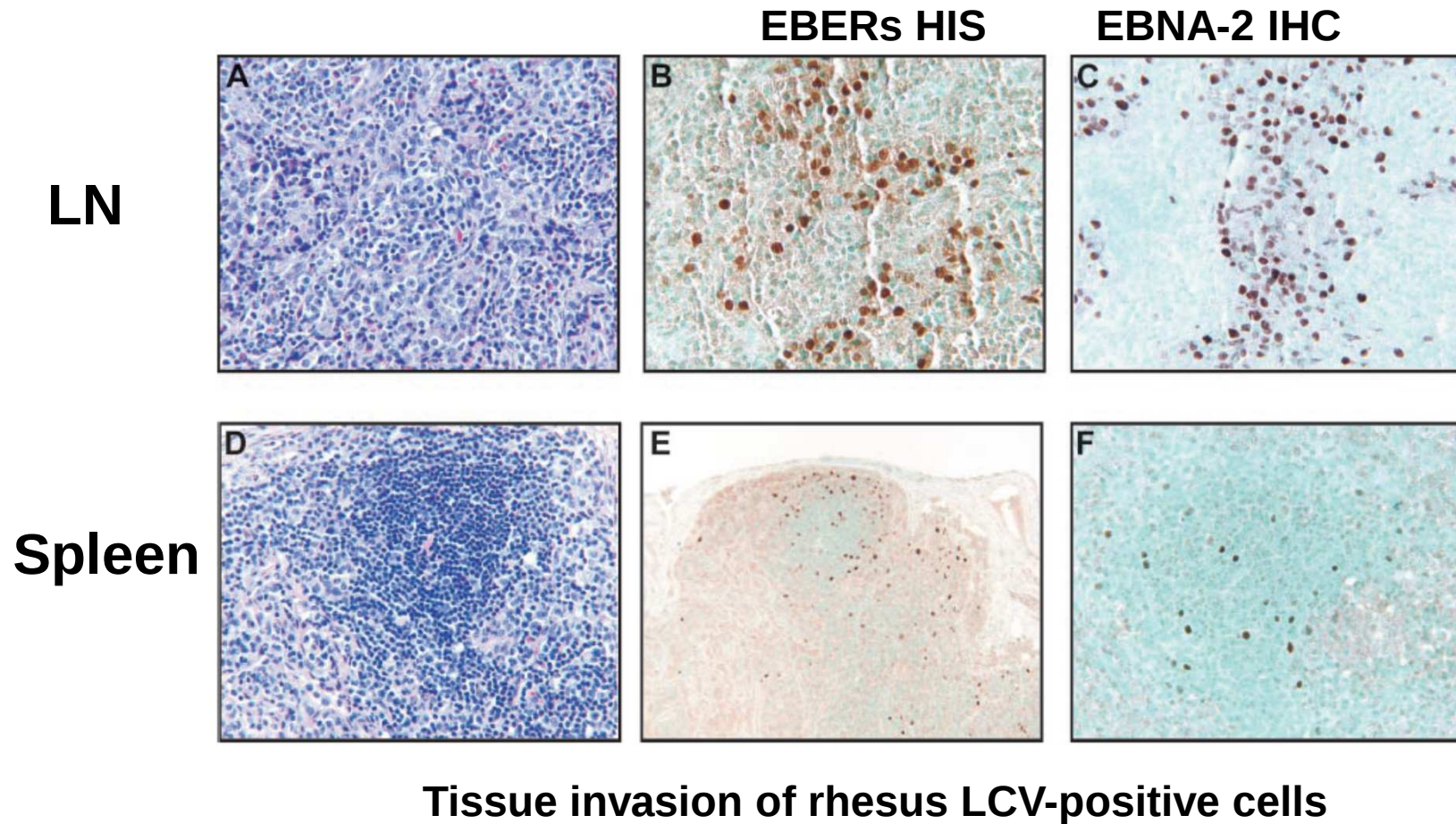
### CD4+ T cells % of day 0



Days after SIVmac251 inoculation  
*(Karlsson et al, 2007)*

## Lymphocryptovirus infection in SHIV immunosuppressed macaques

An animal model for EBV pathogenesis in the immunosuppressed host



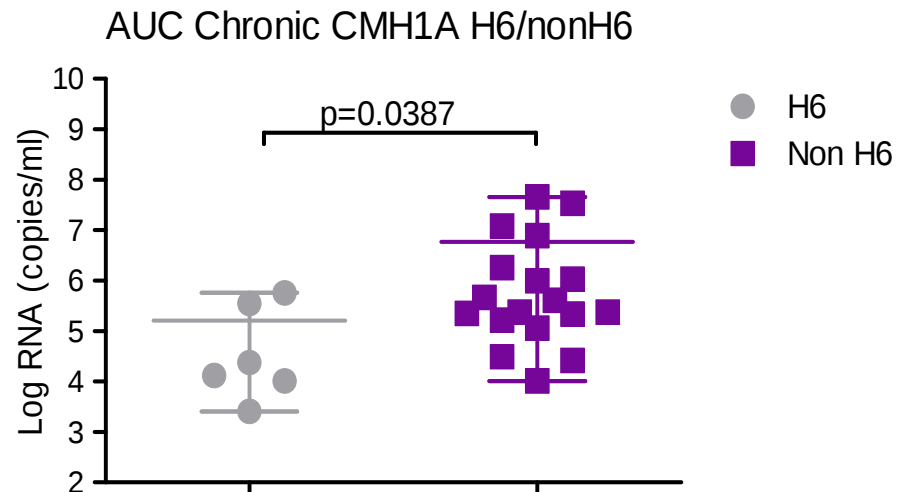
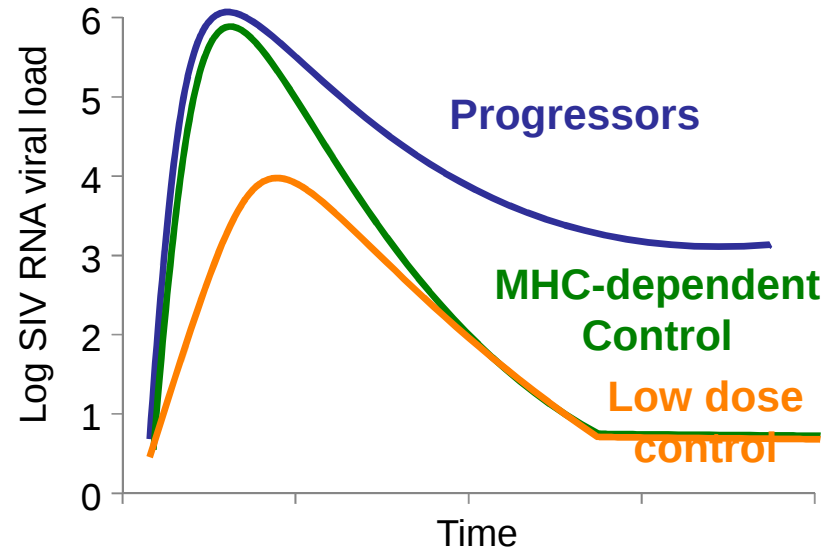
# Non-Human Primate models of SIV infection



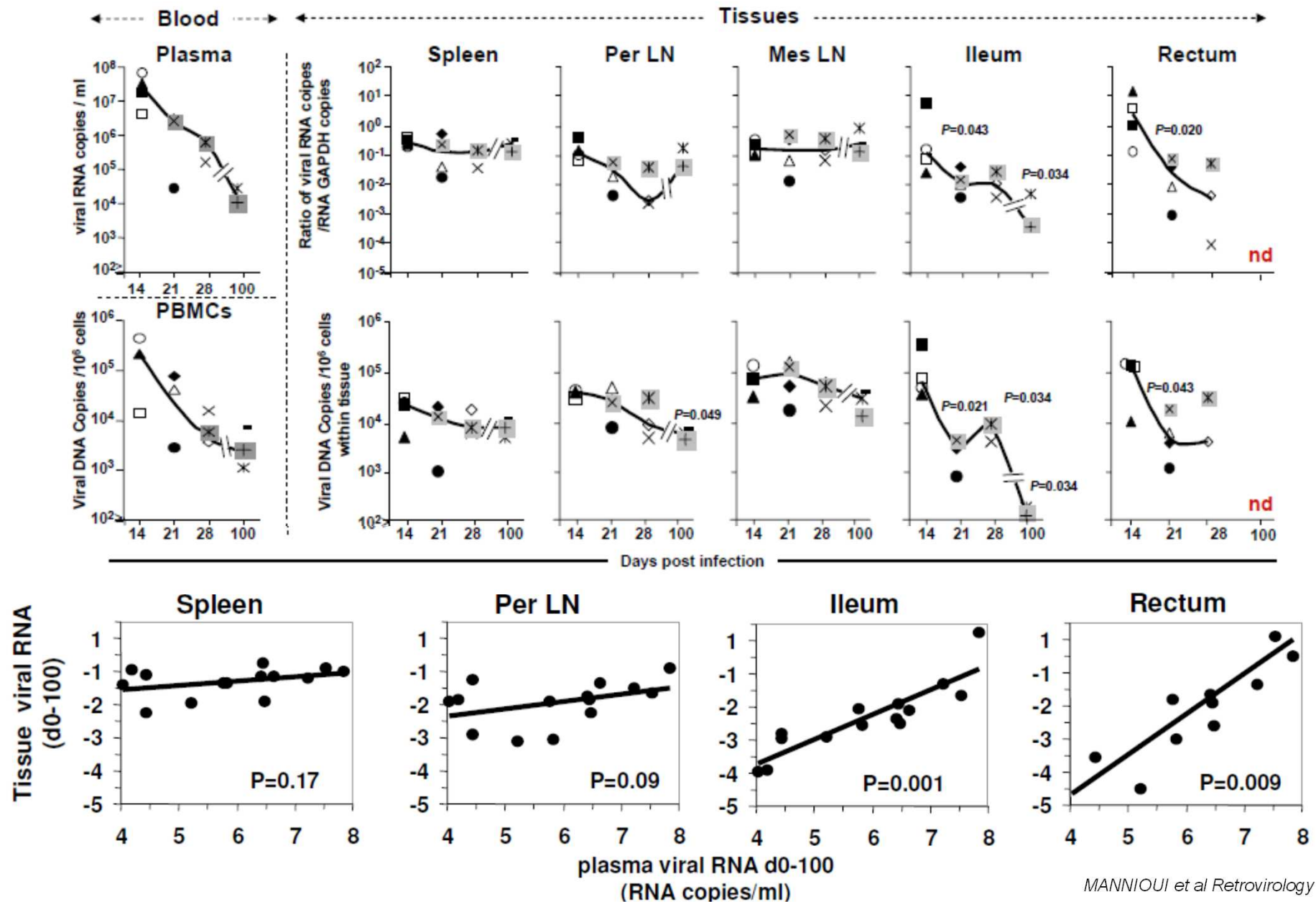
Asian  
Species

Cynomolgus Mac  
SIVmac251

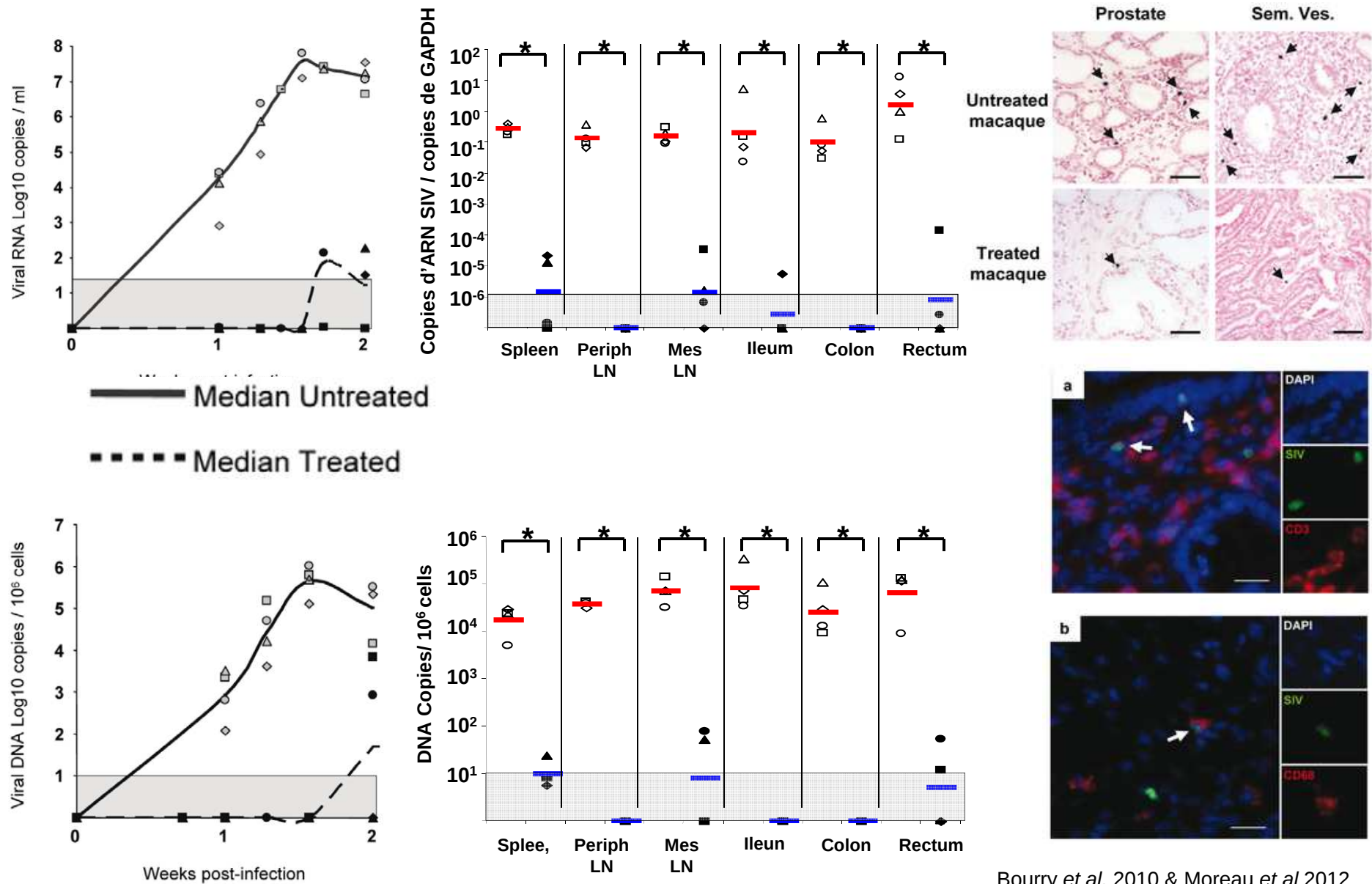
↓  
AIDS



# SIVmac251 replication and dissemination in the tissues of macaques during primary infection

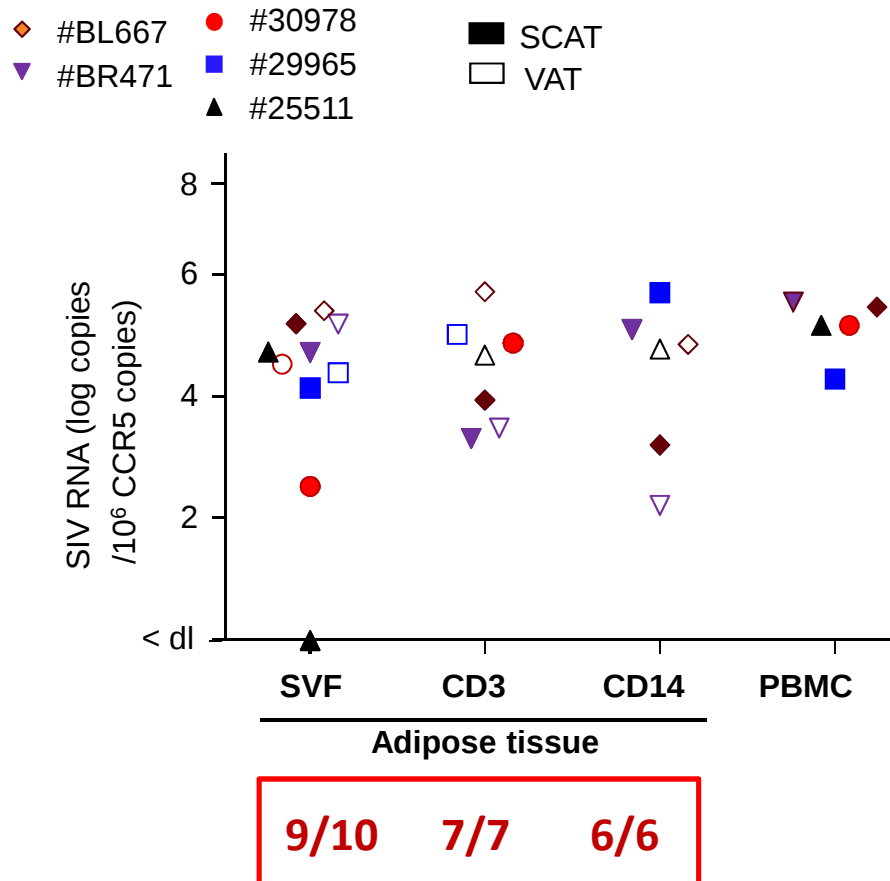


# Effect of HAART during SIVmac251 acute infection 4h/14 days

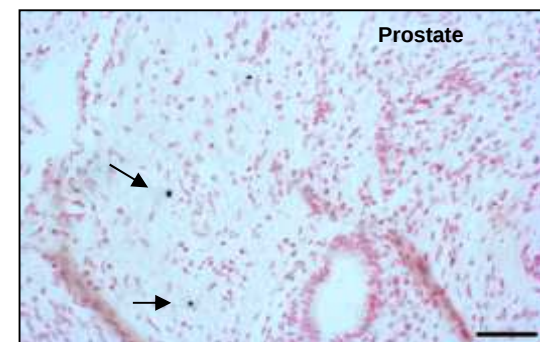
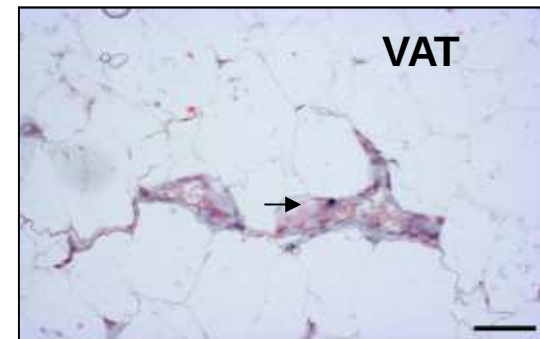
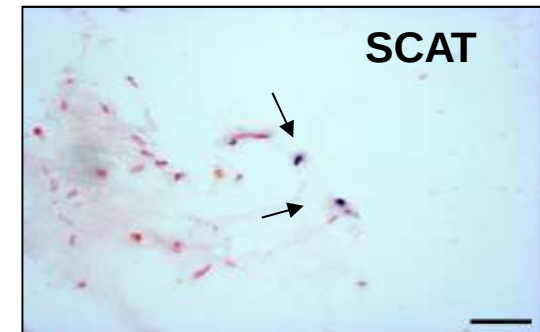


# Adipose tissue includes SIV infected cells

## SIV RNA quantification in SVF and in sorted cells



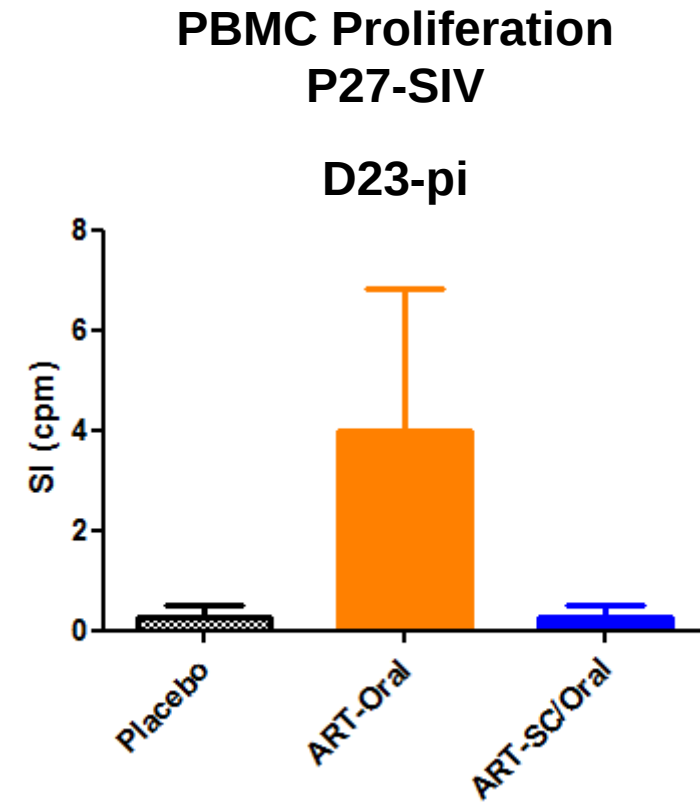
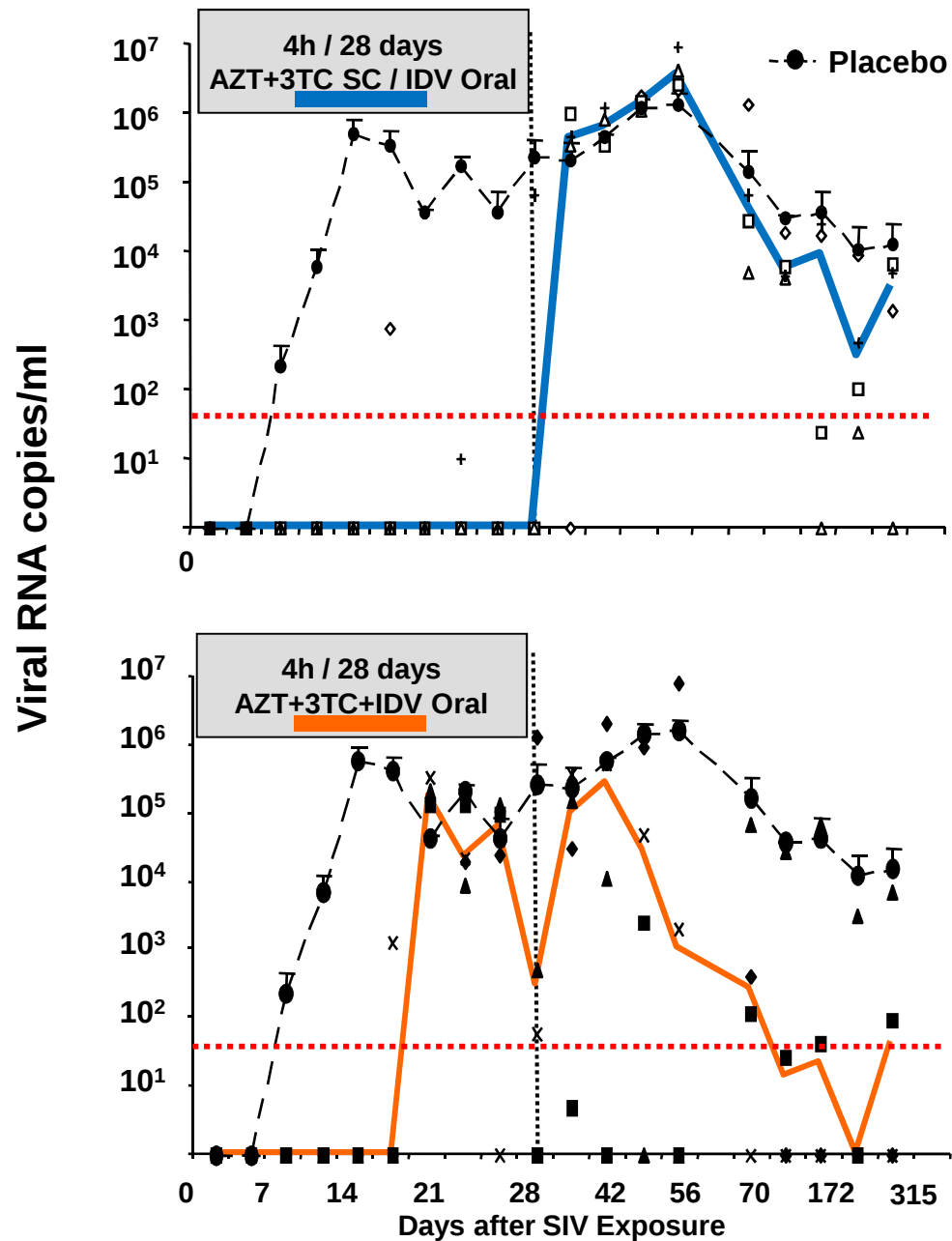
*In situ* SIV  
RNA  
hybridization



In 5 chronically SIV+ untreated macaques,

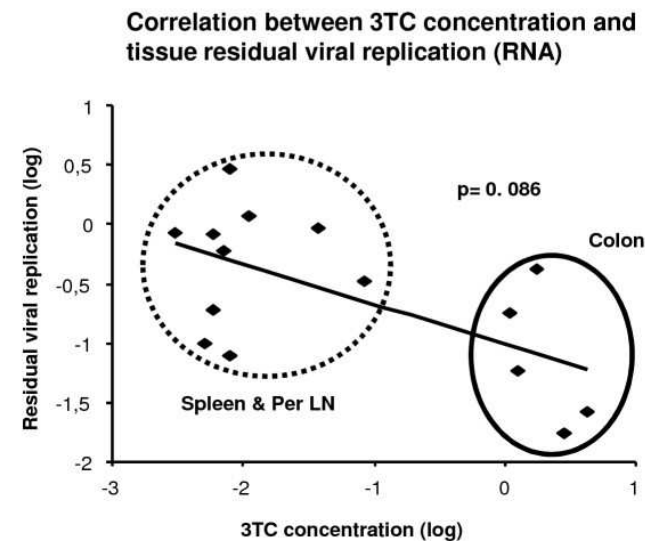
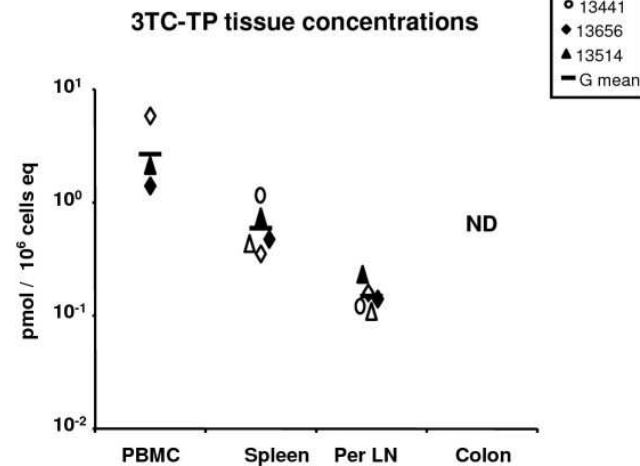
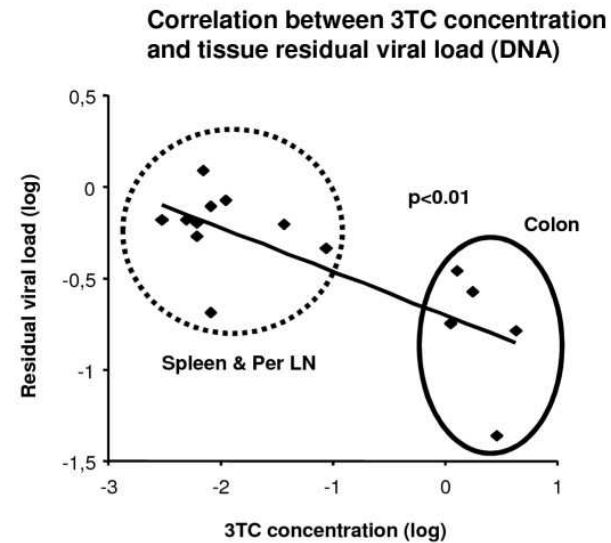
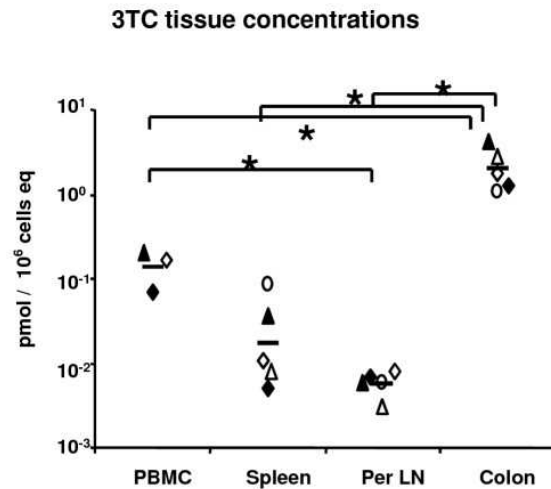
- SIV RNA detected in SVF collected from 9/10 samples (5 animals)
- SIV RNA detected in all CD3+ sorted fraction and CD14+ sorted fraction

# Post-Exposure Prophylaxis in macaques exposed IV to SIVmac251



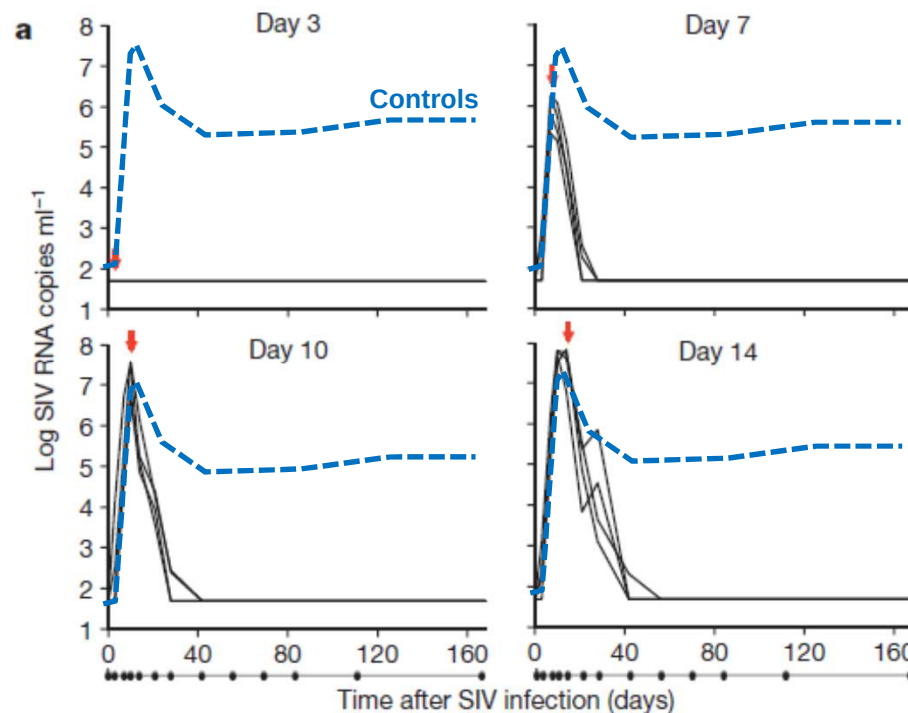
# Diffusion of antiretrovirals and other molecules

## Optimal suppression in tissues

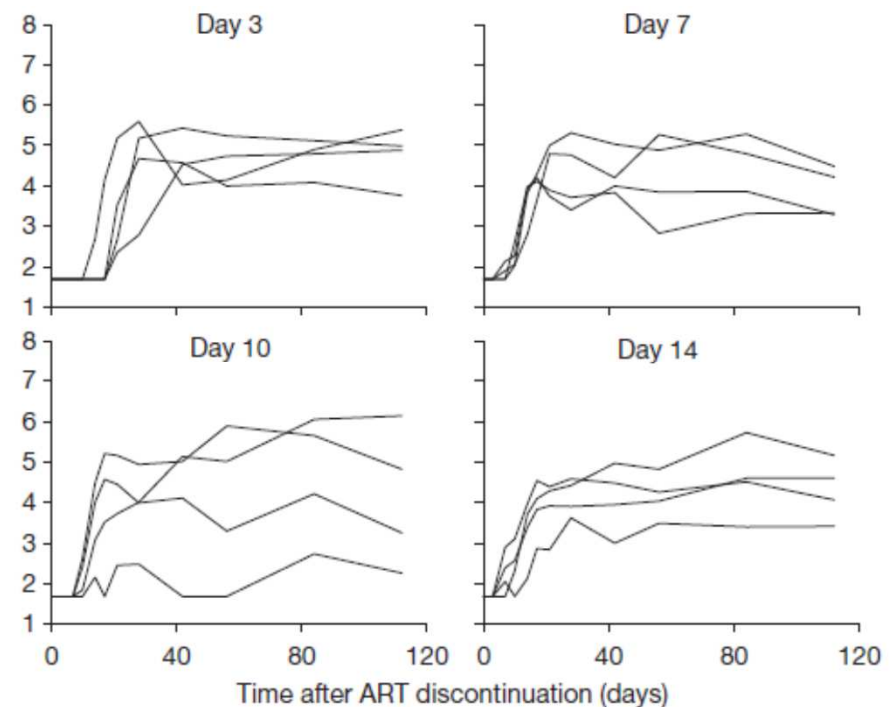


# Rapid seeding of the viral reservoir in SIV infected macaques

## Viral decay kinetics after treatment with ART

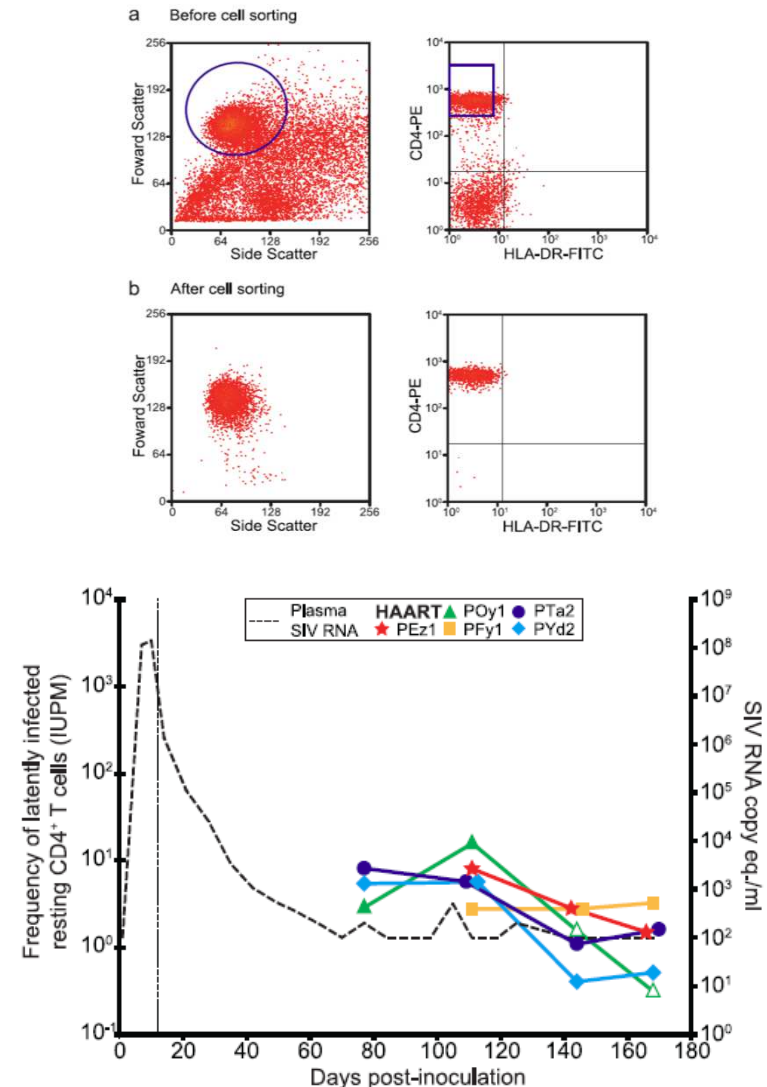
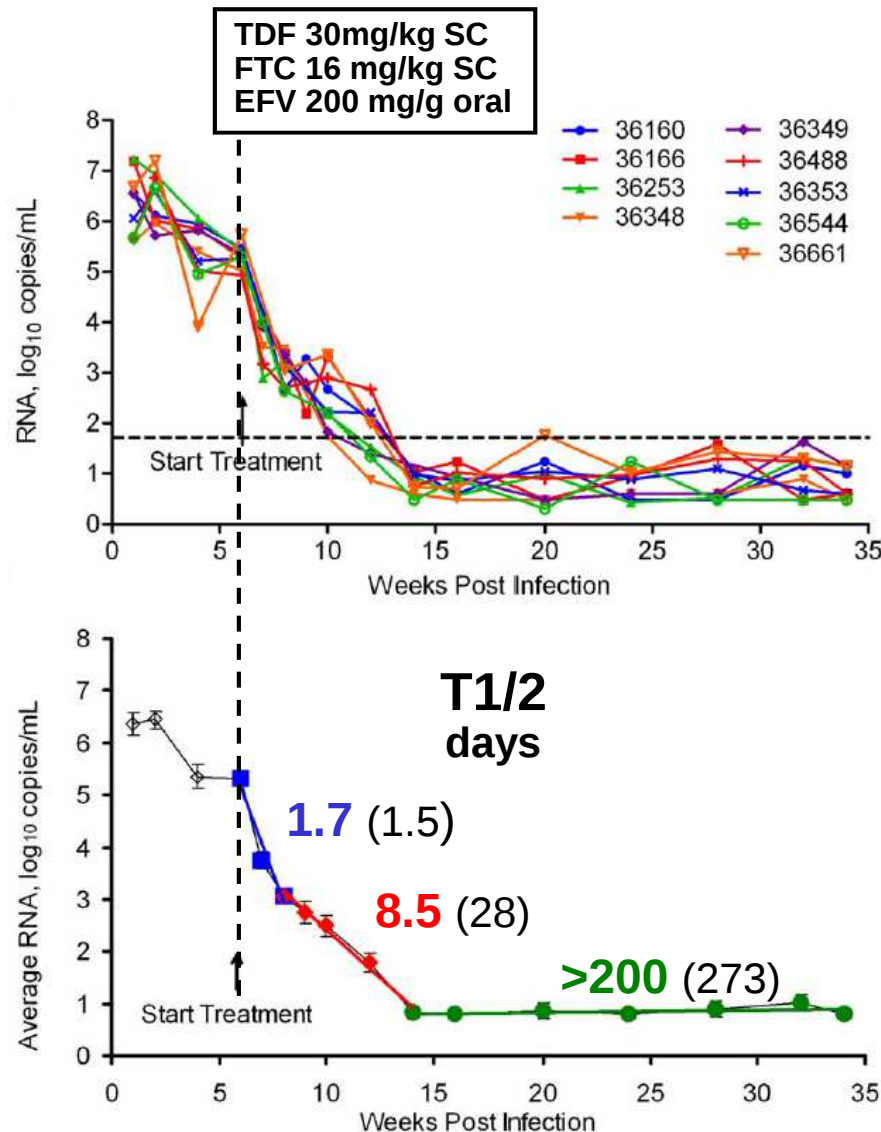


## Viral rebound after ART discontinuation

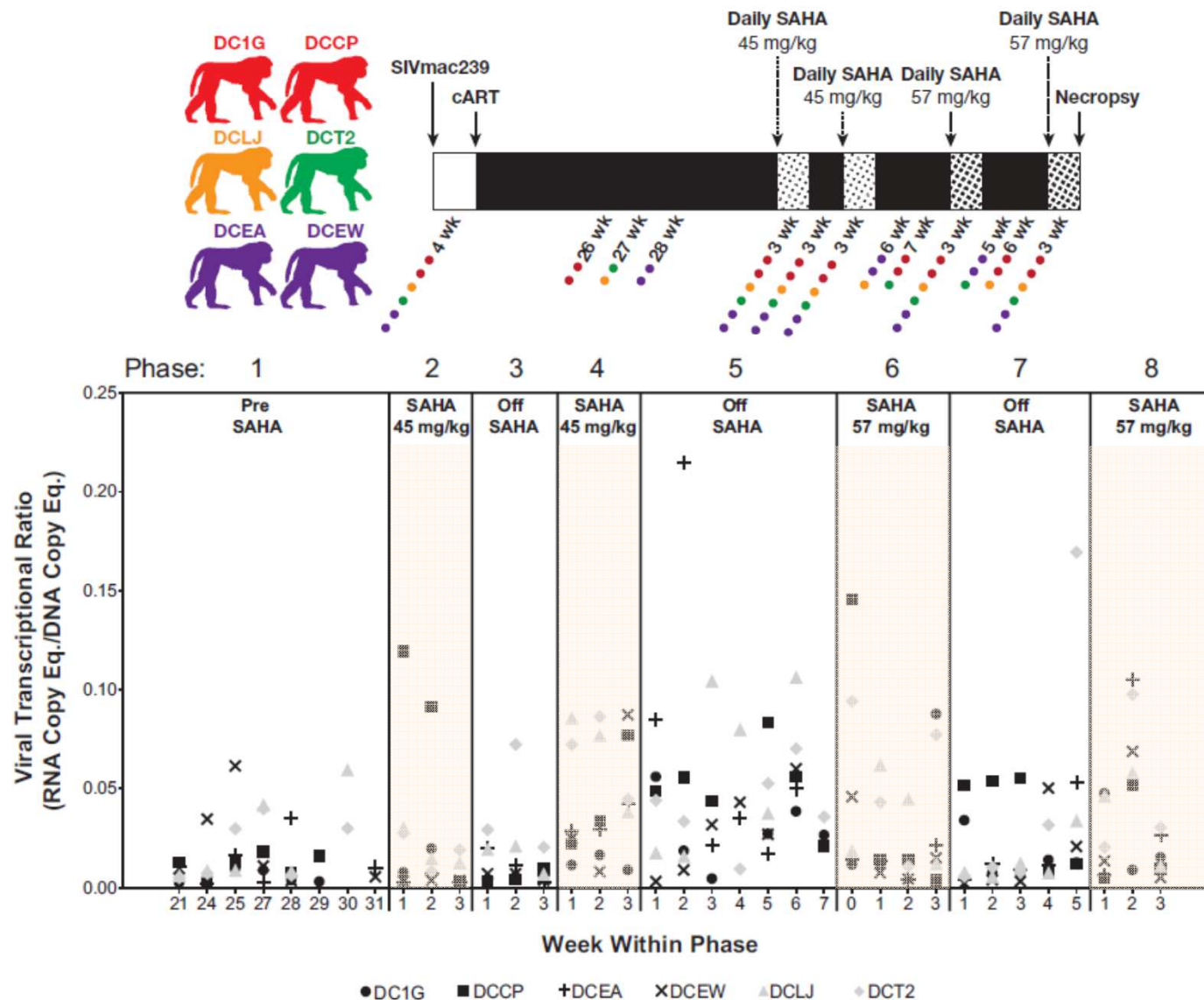


TDF – FTC – DTG  
SC administration

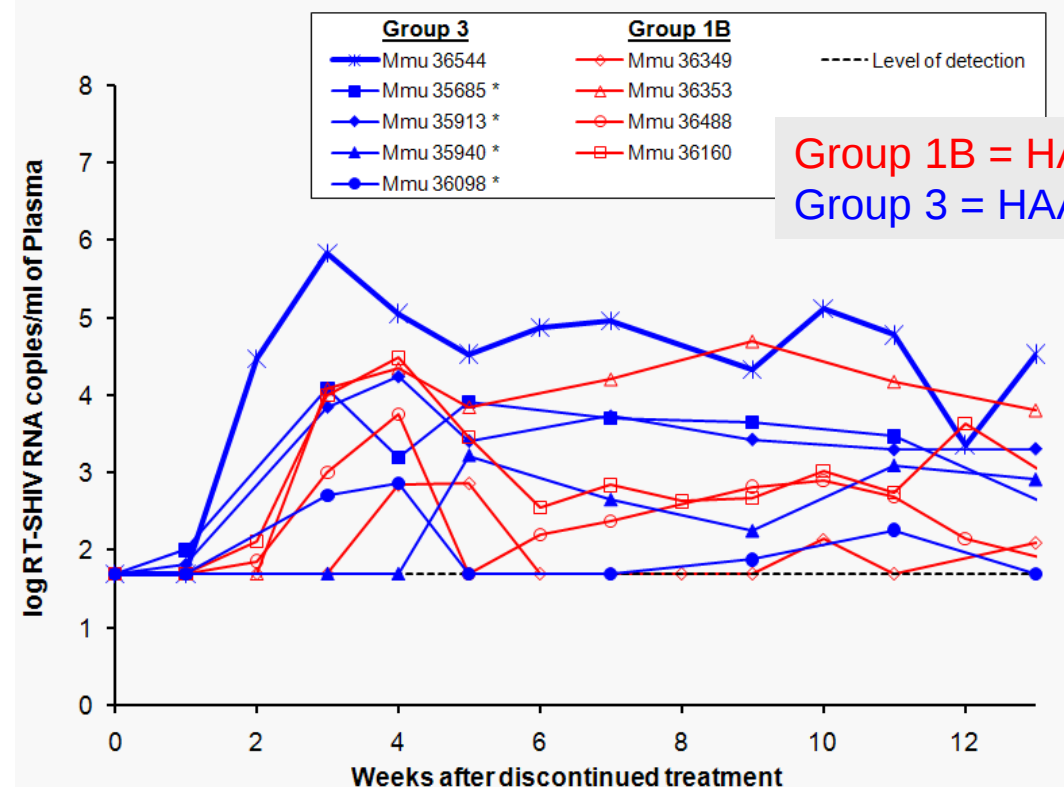
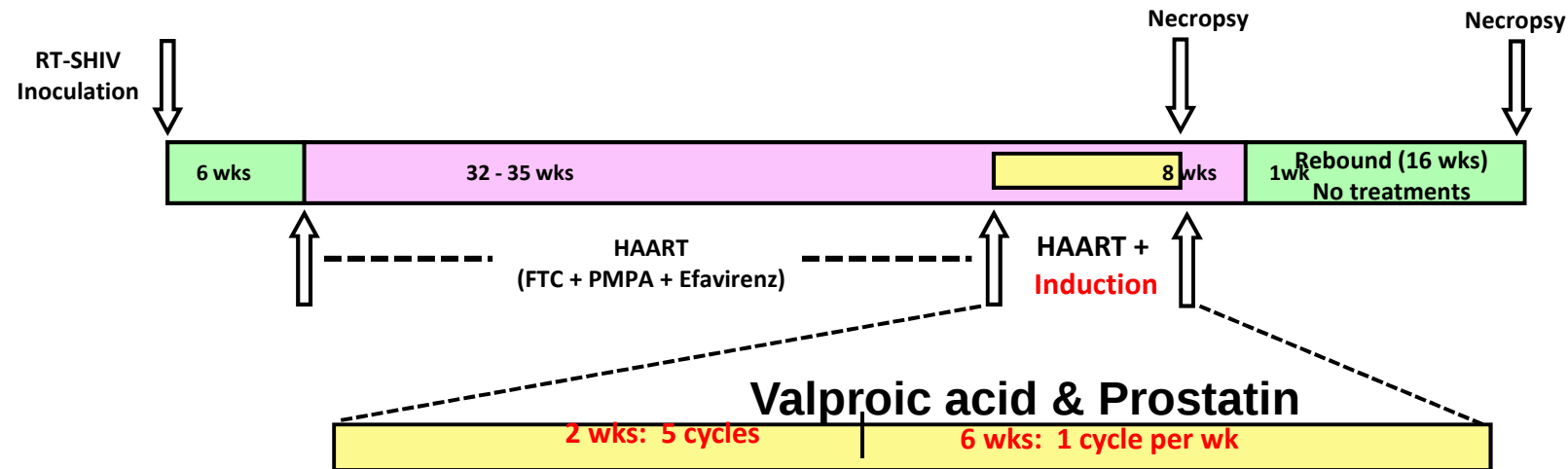
# Frequency of circulating resting CD4+ T cells harboring replication-competent RT-SHIV



# HDACi suberoylanilide hydroxamic acid (SAHA-Vorinostat) in SIV infected macaques under ART

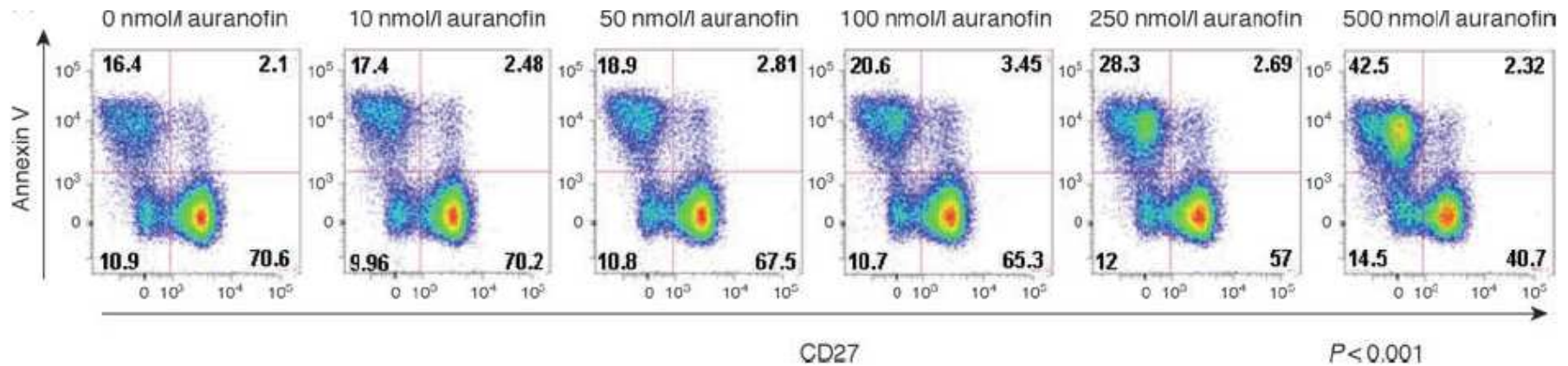


# HAART and Induction HDACi & PKC activator

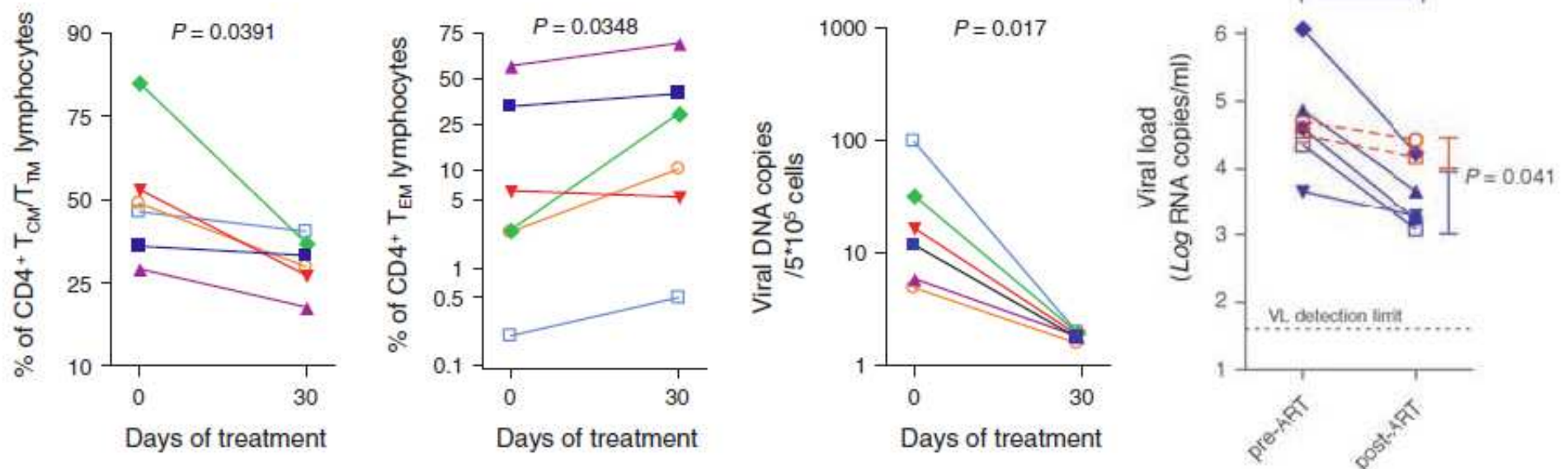


Group 1B = HAART plus induction  
Group 3 = HAART only

# Auranofin induces cell death and CD27 down-modulation in primary CD4+ T cells

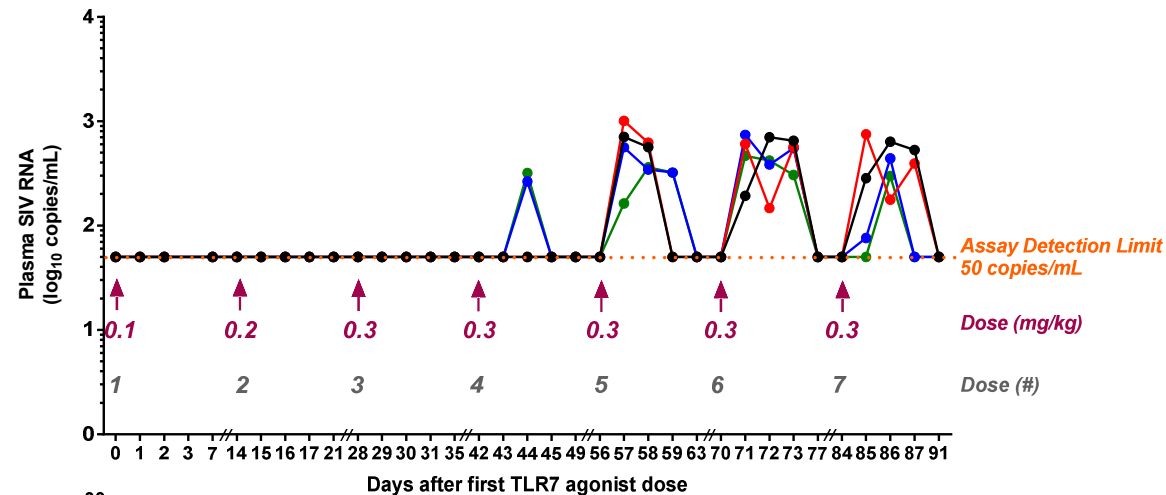


Combined effect with ART in SIVmac251 infected macaques

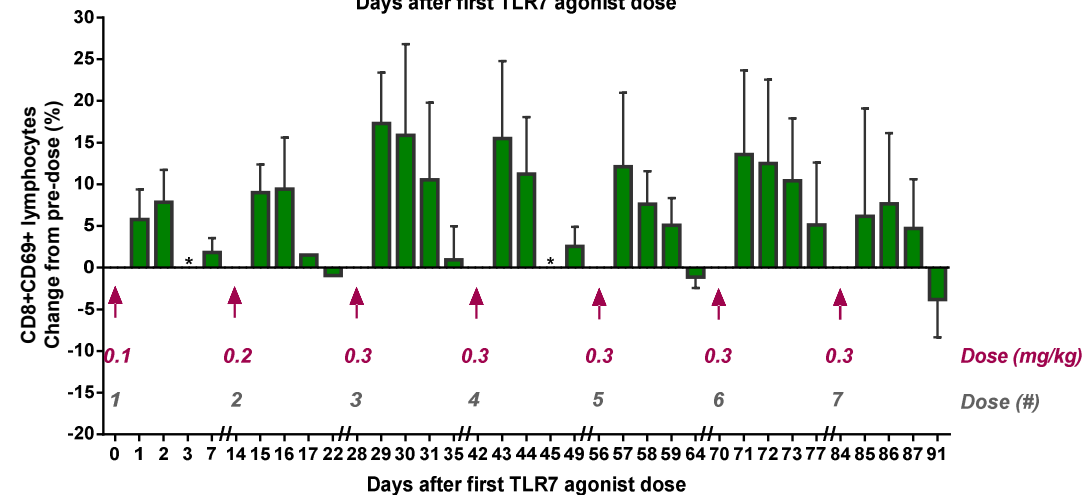


# TLR7 agonist administration in SIV infected macaques

Plasma SIV  
RNA

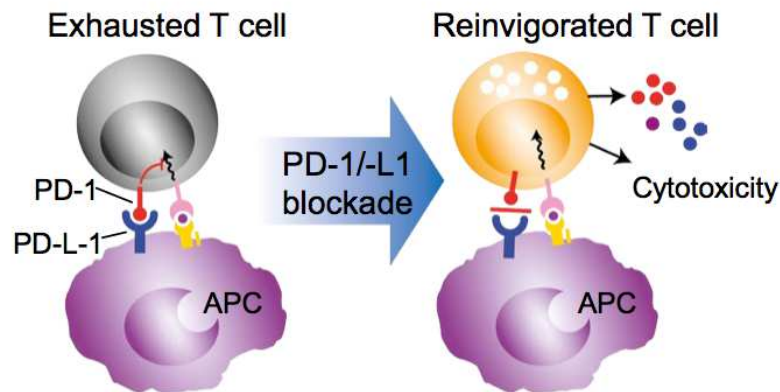


CD8 T cell  
activation

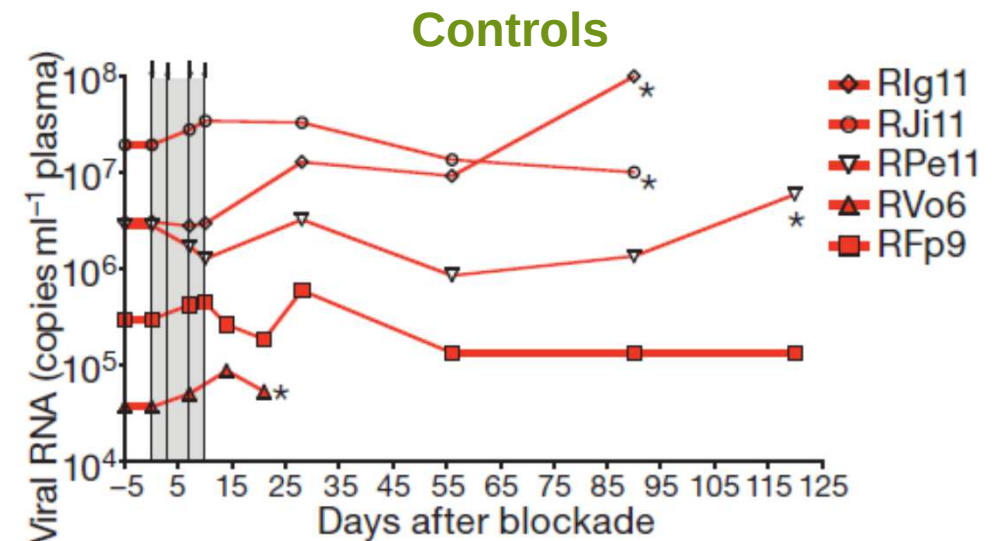
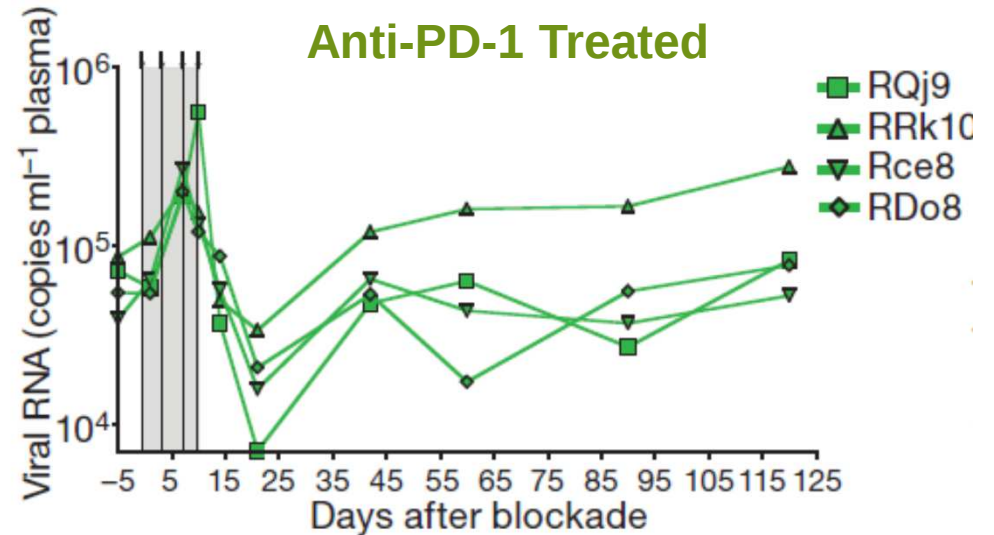
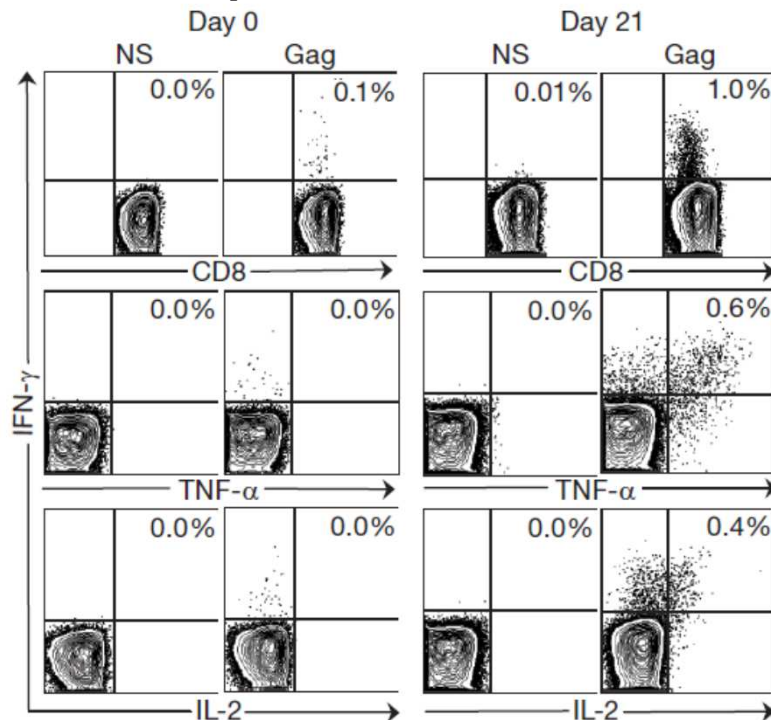


➤ TLR7 agonist induces viral production and increases CD8 T cell activation

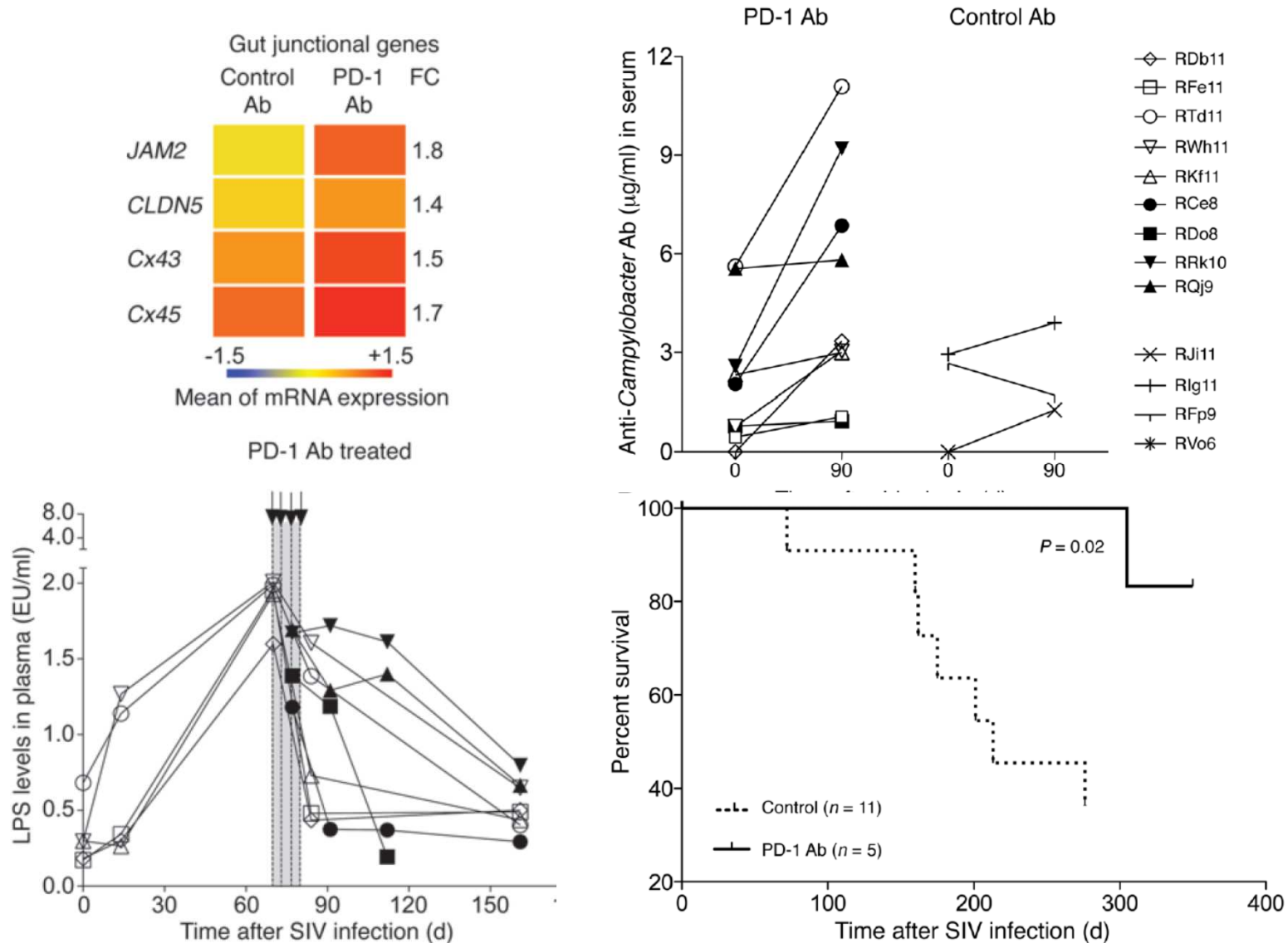
# Enhancing SIV-specific immunity *in vivo* by PD-1 blockade



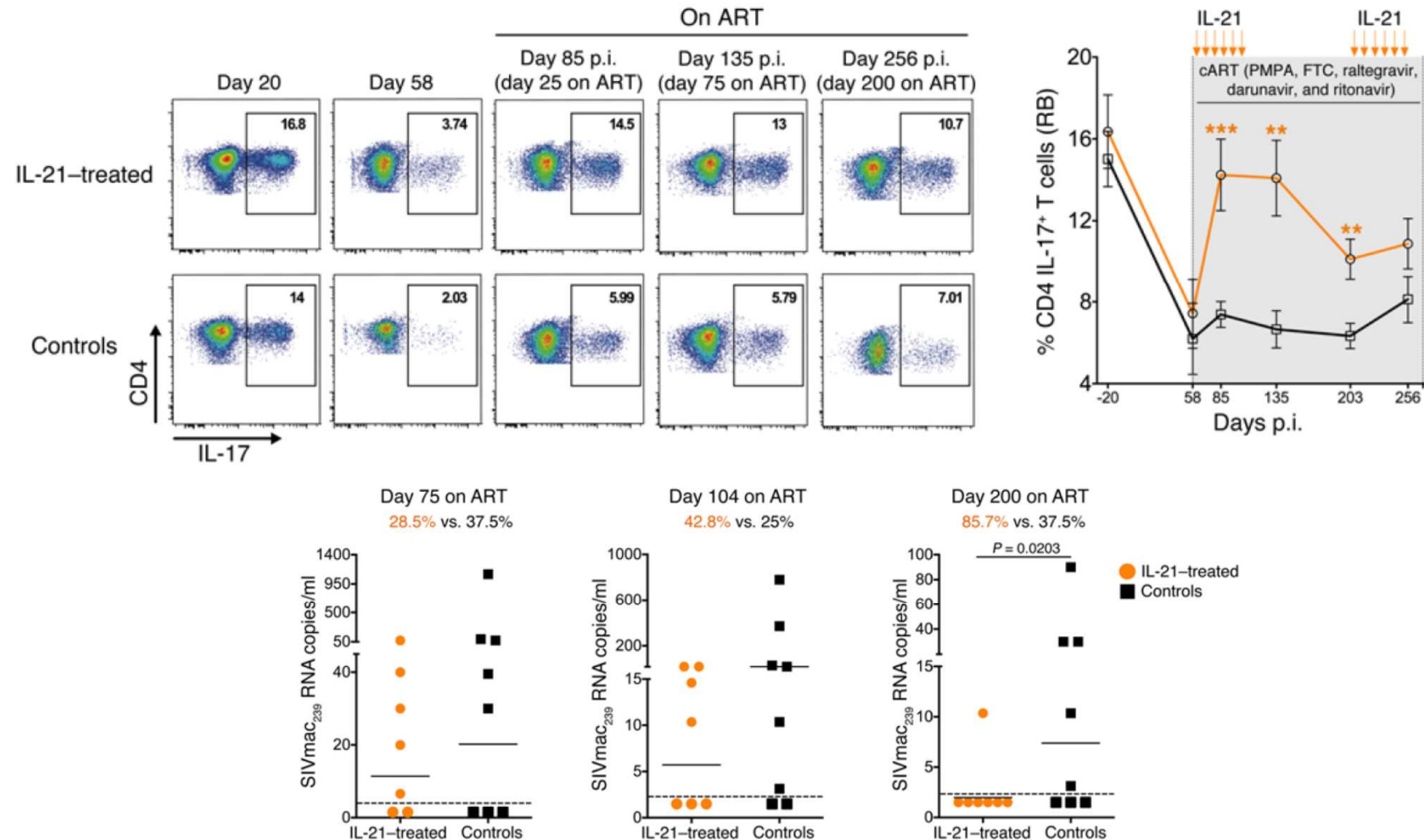
## SIV-specific CD8<sup>+</sup> T cells



# PD-1 blockade during chronic SIV infection reduces hyperimmune activation and microbial translocation in rhesus macaques



# Interleukin-21 combined with ART reduces inflammation & viral reservoir in SIV-infected macaques



Residual viremia decrease over time is higher in IL-21-treated vs. control RMs ( $P = 0.03$ )

# Immunology of Viral Infections & Autoimmune Diseases

UMR1184

Integrated Preclinical & Clinical Research



**CEA-FAR**



**Hôpital de Bicêtre**





## Infectious diseases

- HIV/AIDS
- Flu
- Dengue & Chikungunya
- Tuberculosis
- Chlamydia
- Pertussis
- Malaria

## New technologies

- FlowCyTech
- *in vivo* imaging

## Education

- Master in imaging
- European course of cytometry
- « Vaccinology »



# IDMIT

Infectious Diseases Models for Innovative Therapies

<http://www.idmitcenter.fr/>

Services

Vaccines

New Therapies



Research

International  
collaborations



**Inserm**  
Institut national  
de la santé et de la recherche médicale



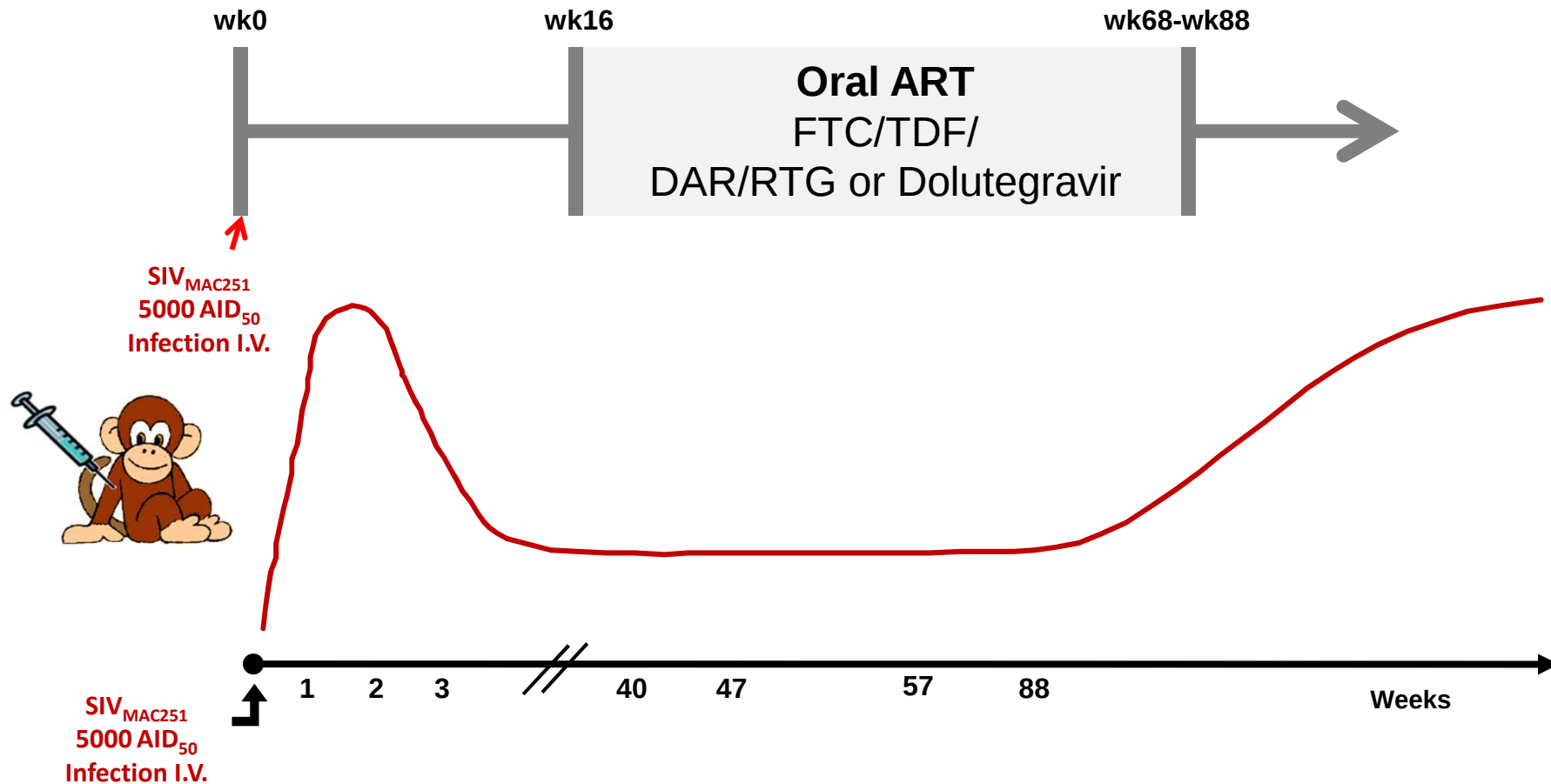
UNIVERSITÉ  
**PARIS  
SUD**

**anRS**  
France  
Recherche  
Nord & sud  
Sida-hiv  
Hépatites  
Agence autonome de l'Inserm

**bertin  
pharma**

# SIVART NHP Cohort

## A common resource for ANRS HIV/SIV Programs N=12

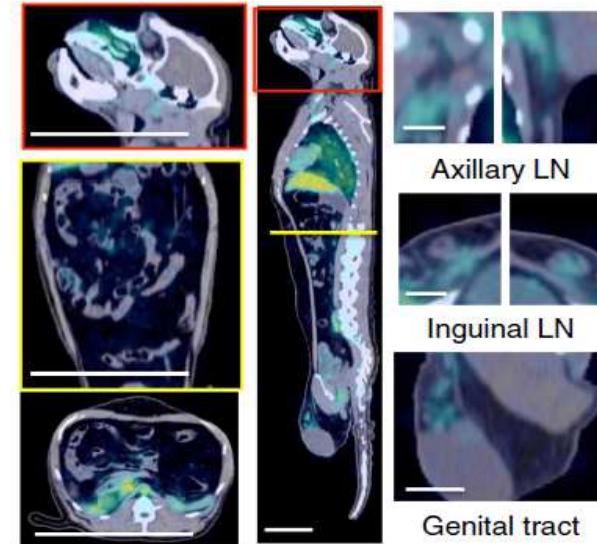


## PET-CT whole body imaging

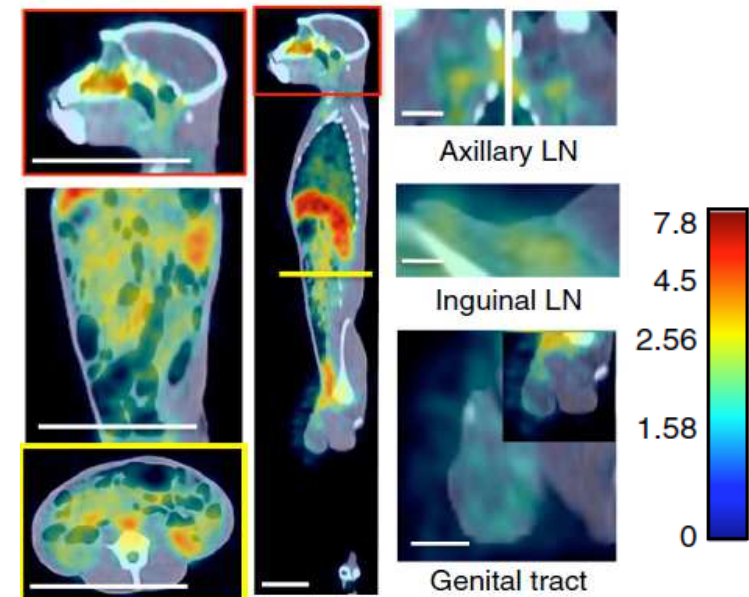


## Visualizing SIV replication

Control Animal



Infected Animal



Santangelo et al 2015



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Christine Bourgeois  
Abdelraouf Damouche  
Anne-Marie Taburet  
Bruno Vaslin  
Benoit Favier

### Immunity&Transmmision

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Olivier Bourry  
Pierre Sellier  
Pierre Roques  
Karim Mannioui



### Core Laboratories

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Patrick Flament  
Claire Torres  
Sophie Even  
Benoît Delache  
Aurélien Corneau  
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Sébastien Langlois  
Sabrina Guenounou  
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