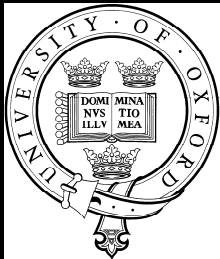
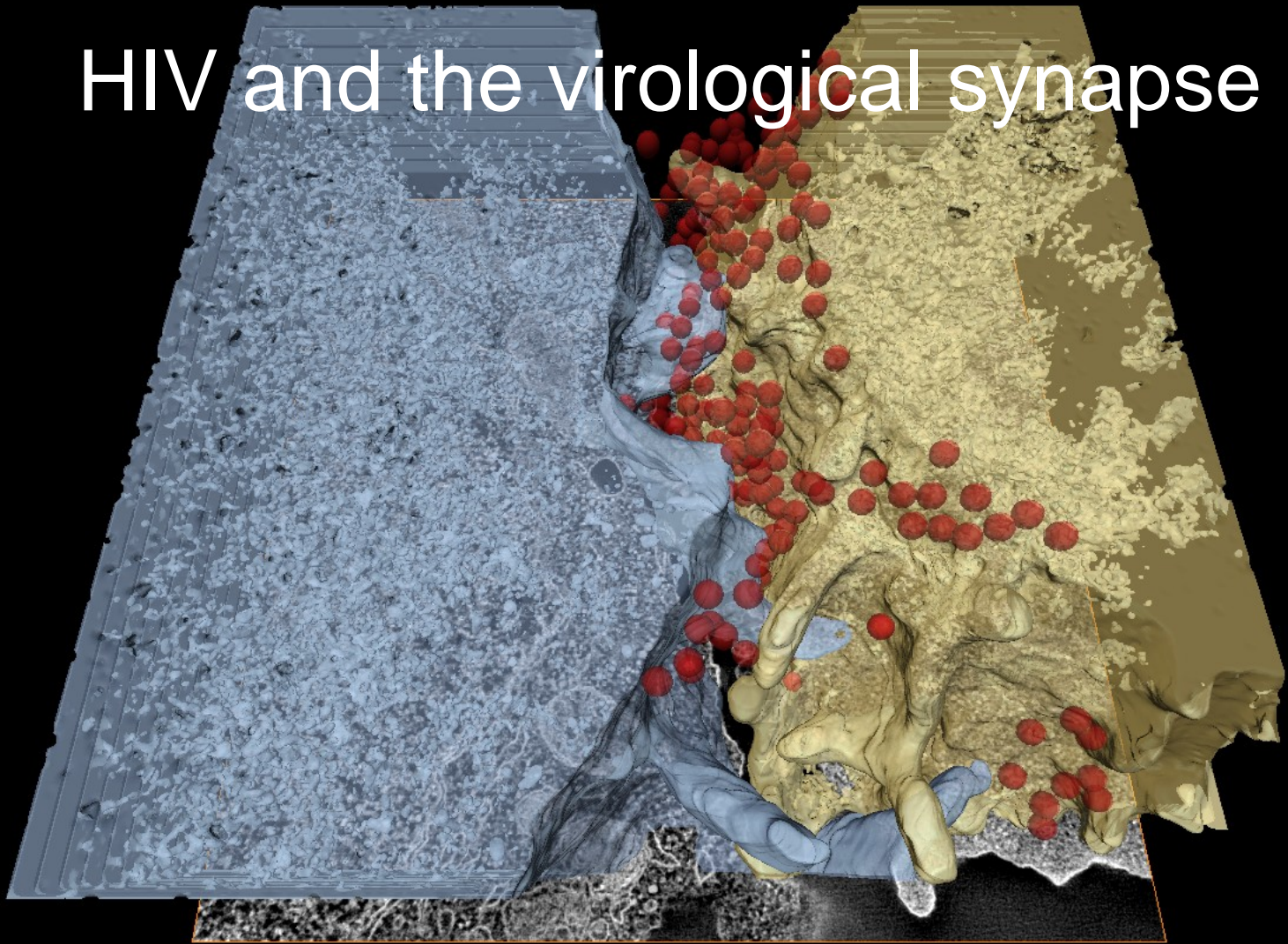


# HIV and the virological synapse



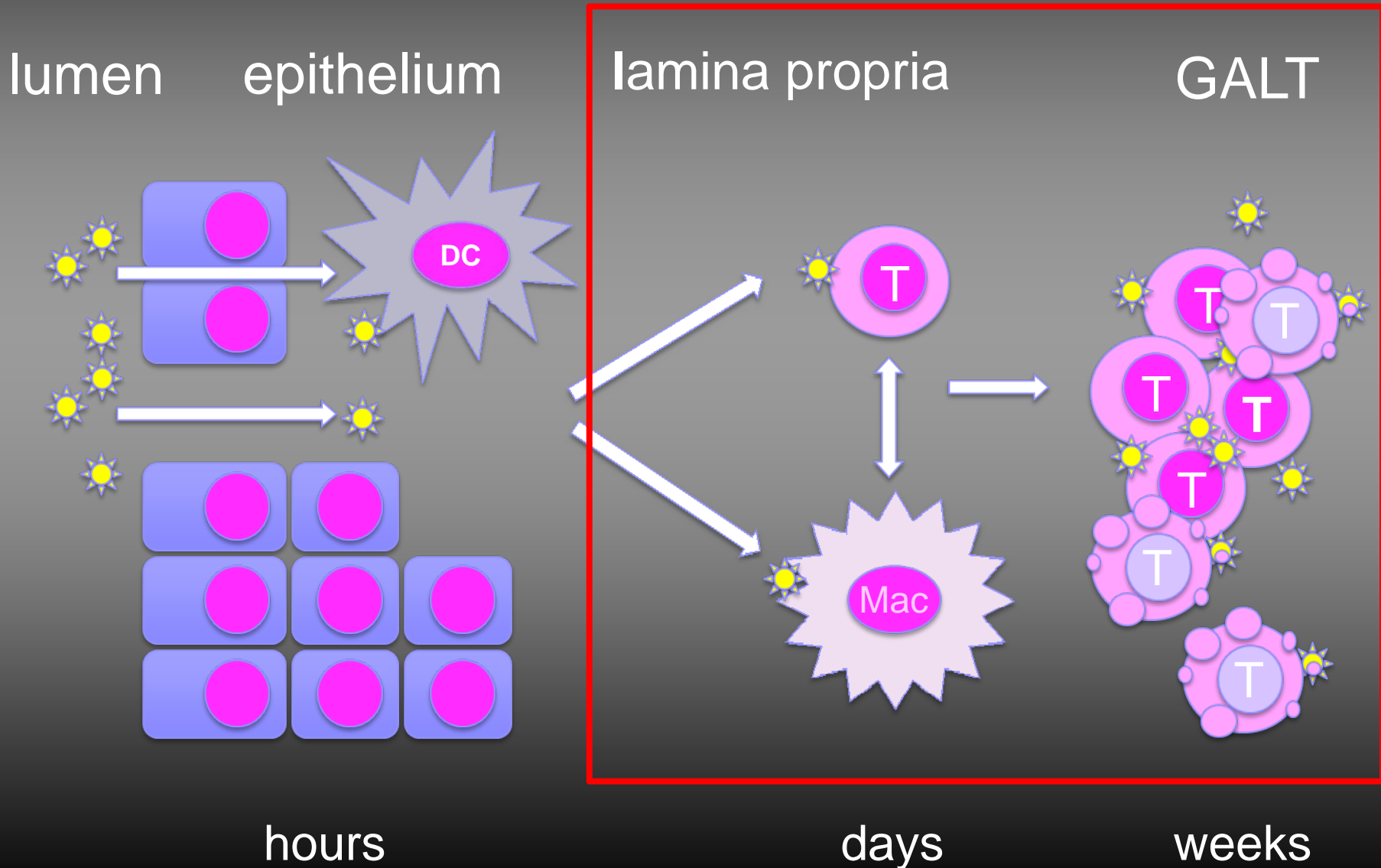
Quentin Sattentau

The Sir William Dunn School of Pathology University of Oxford

# The talk

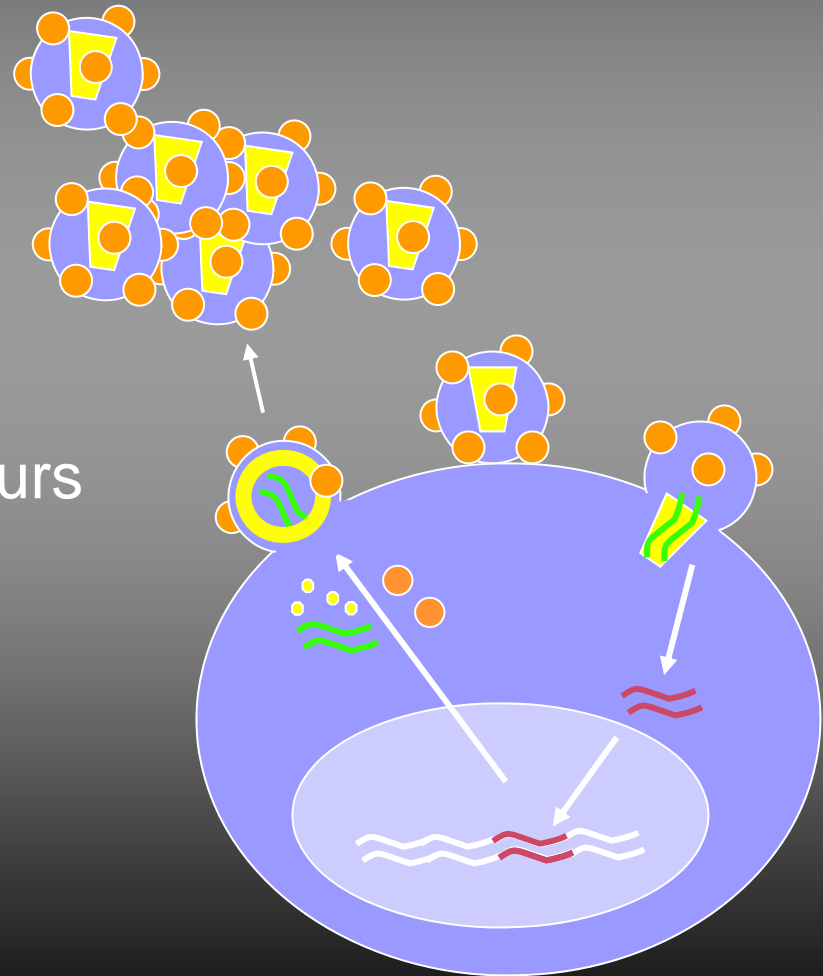
1. The HIV-1 T cell virological synapse
2. HIV-1-Macrophage-T cell interactions

# HIV-1 sexual transmission

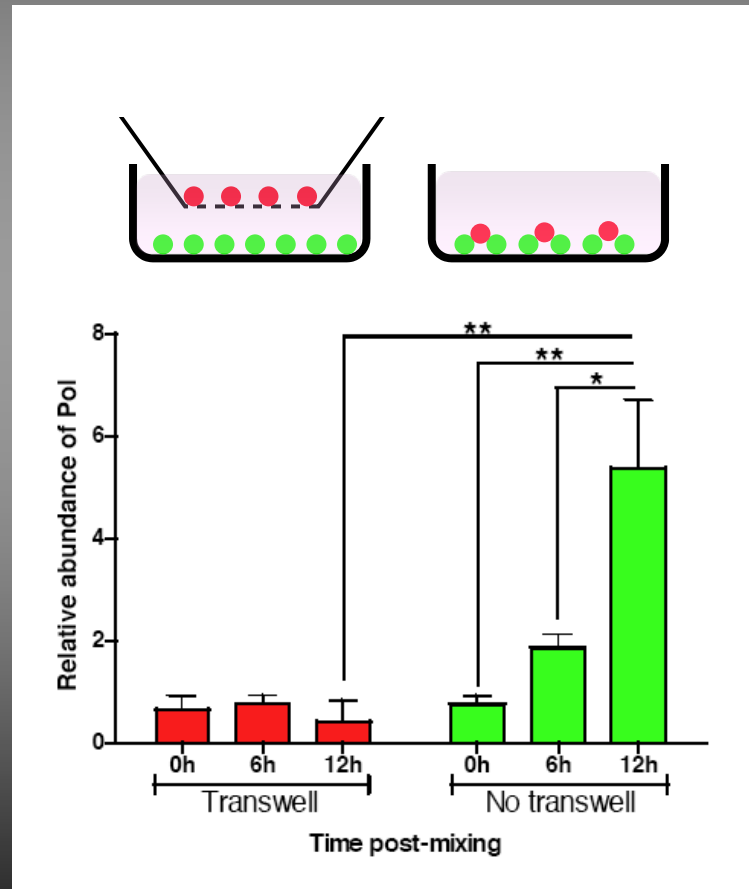


# The traditional paradigm of enveloped virus infection

HIV-1 cycle ~24 hours

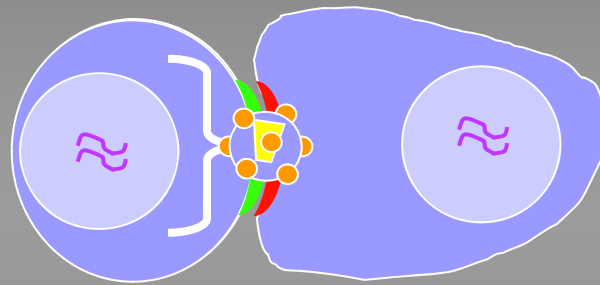


# Cell-cell spread of HIV-1 is more efficient than cell-free



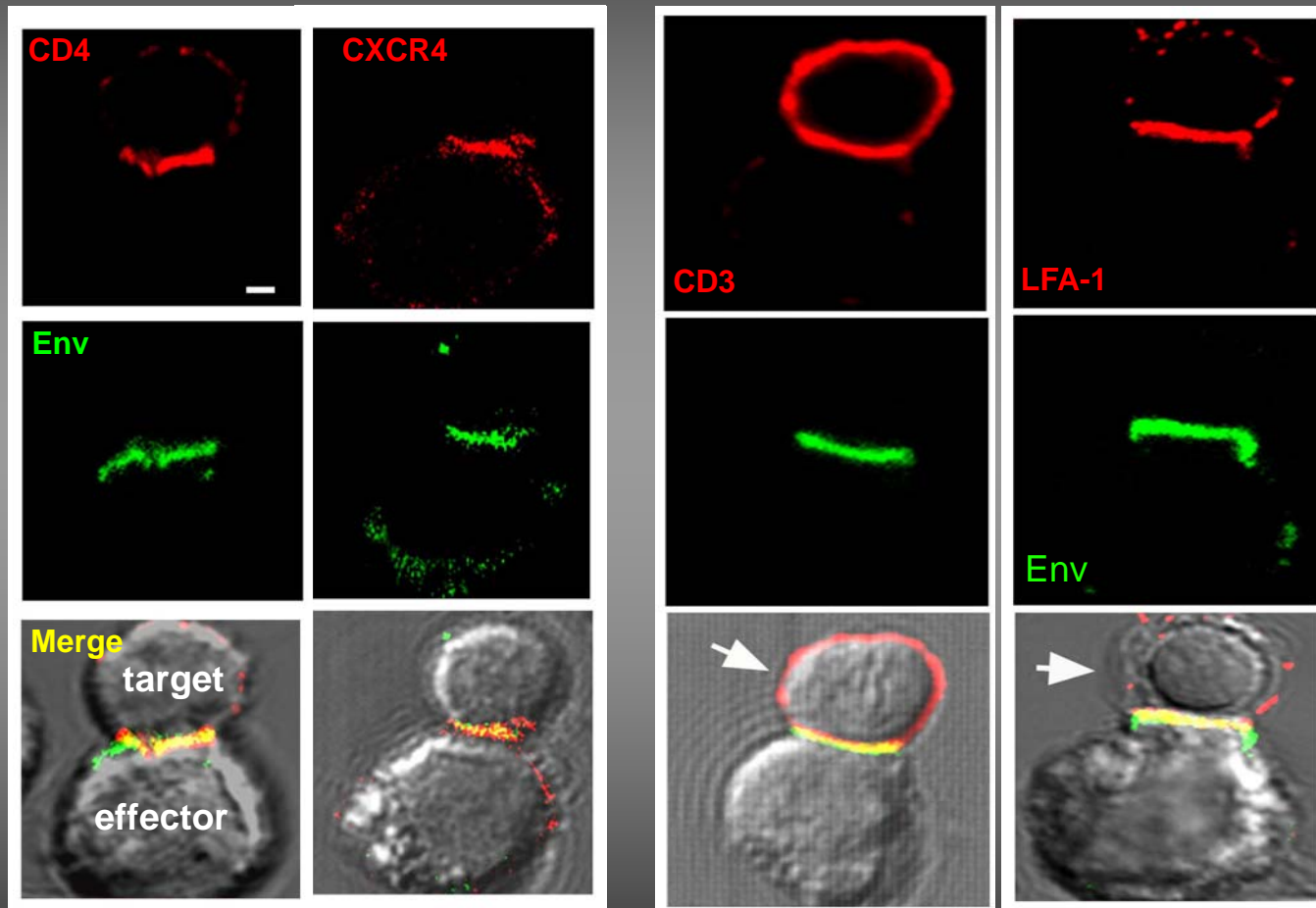
# Cell polarisation and synapses

Immunological synapse



**Hypothesis:** The virological synapse  
(Jolly and Sattentau 2002)

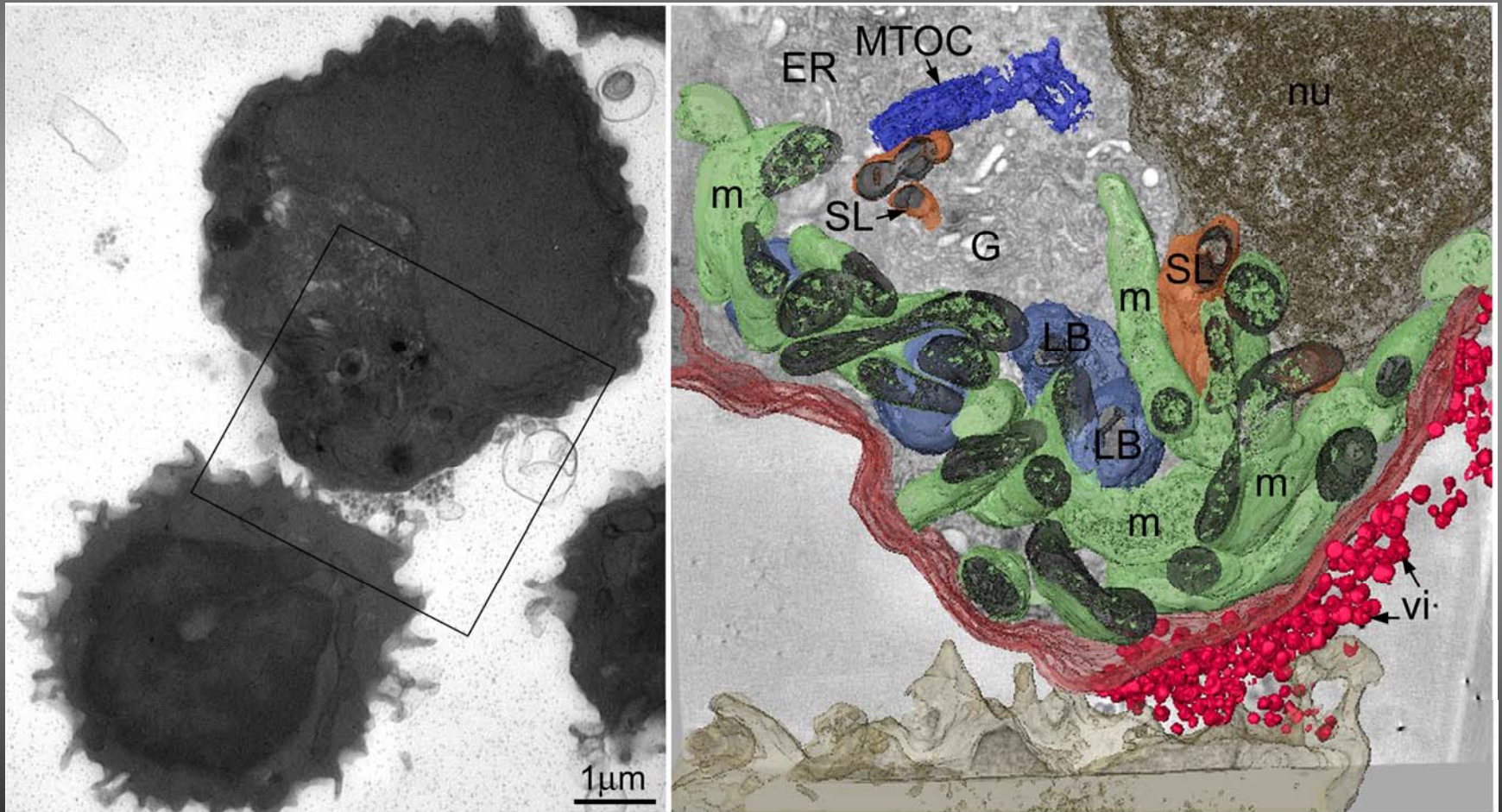
# The HIV-1 T cell-T cell synapse



Jolly et al JEM 2004

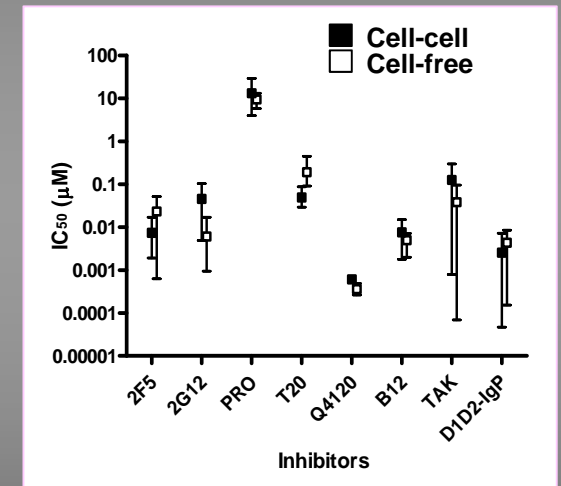
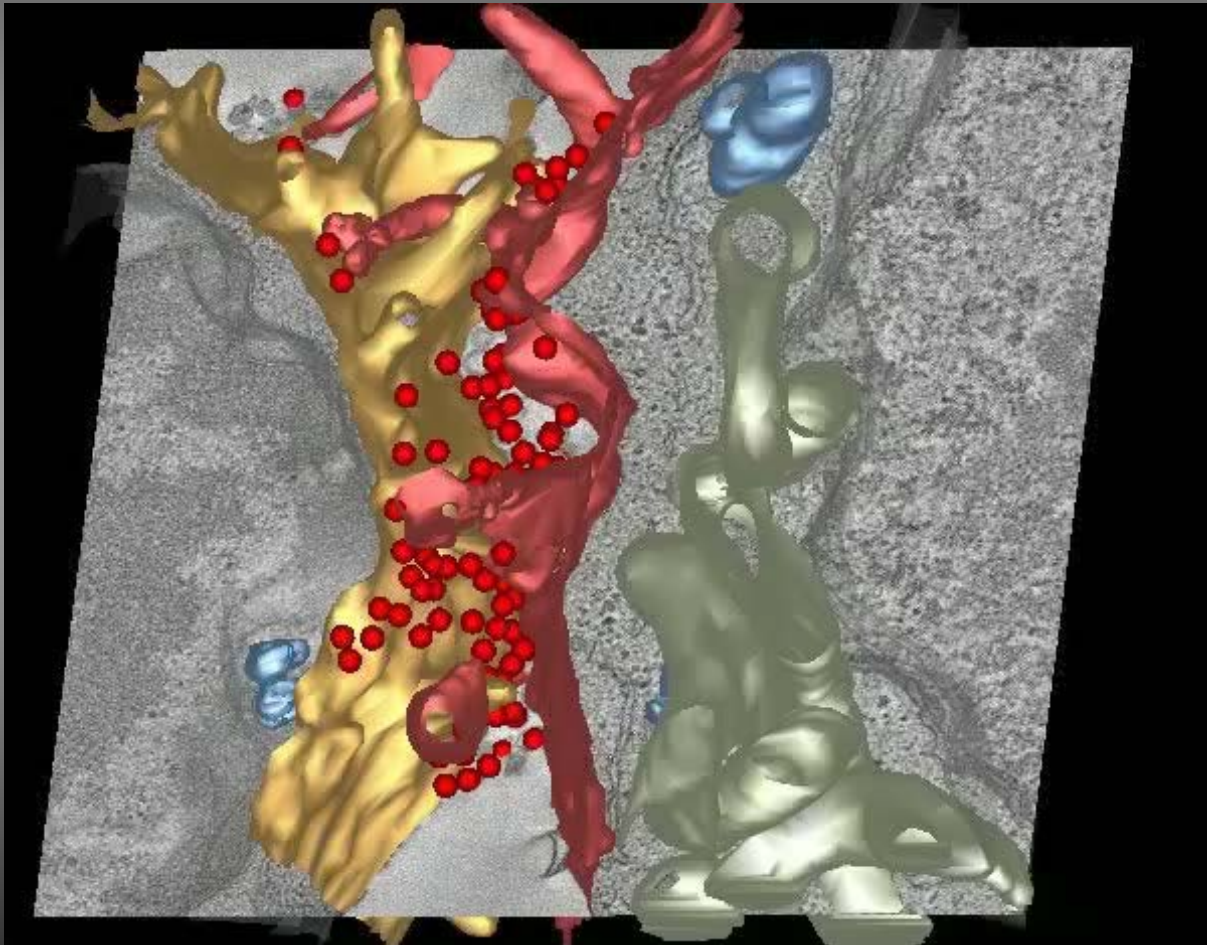


# Polarization of CD4+ T cell secretion at the virological synapse





# Architecture of the virological synapse



Martin et al  
JVI 2010

# The synapse family

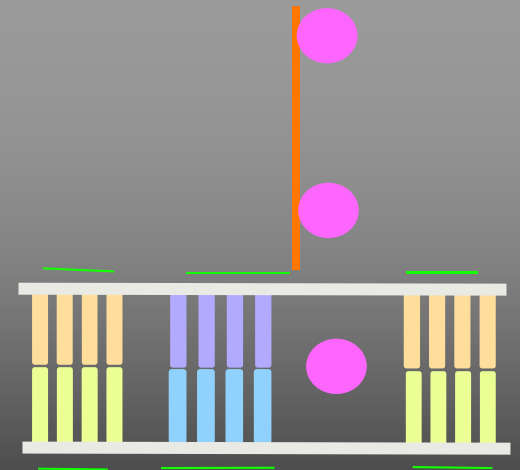
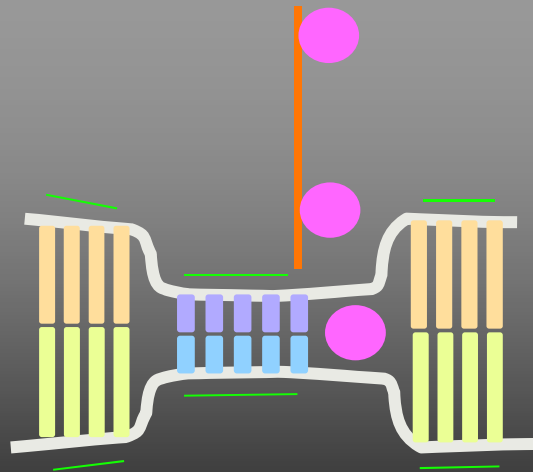
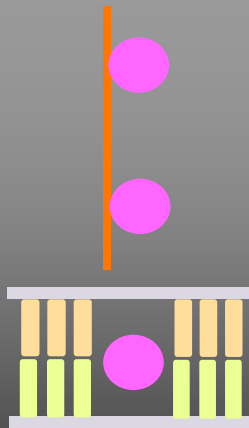
PRE-SYNAPTIC

---

Neural

Immunological

Virological



---

POST-SYNAPTIC

# Macrophages, T cells and HIV

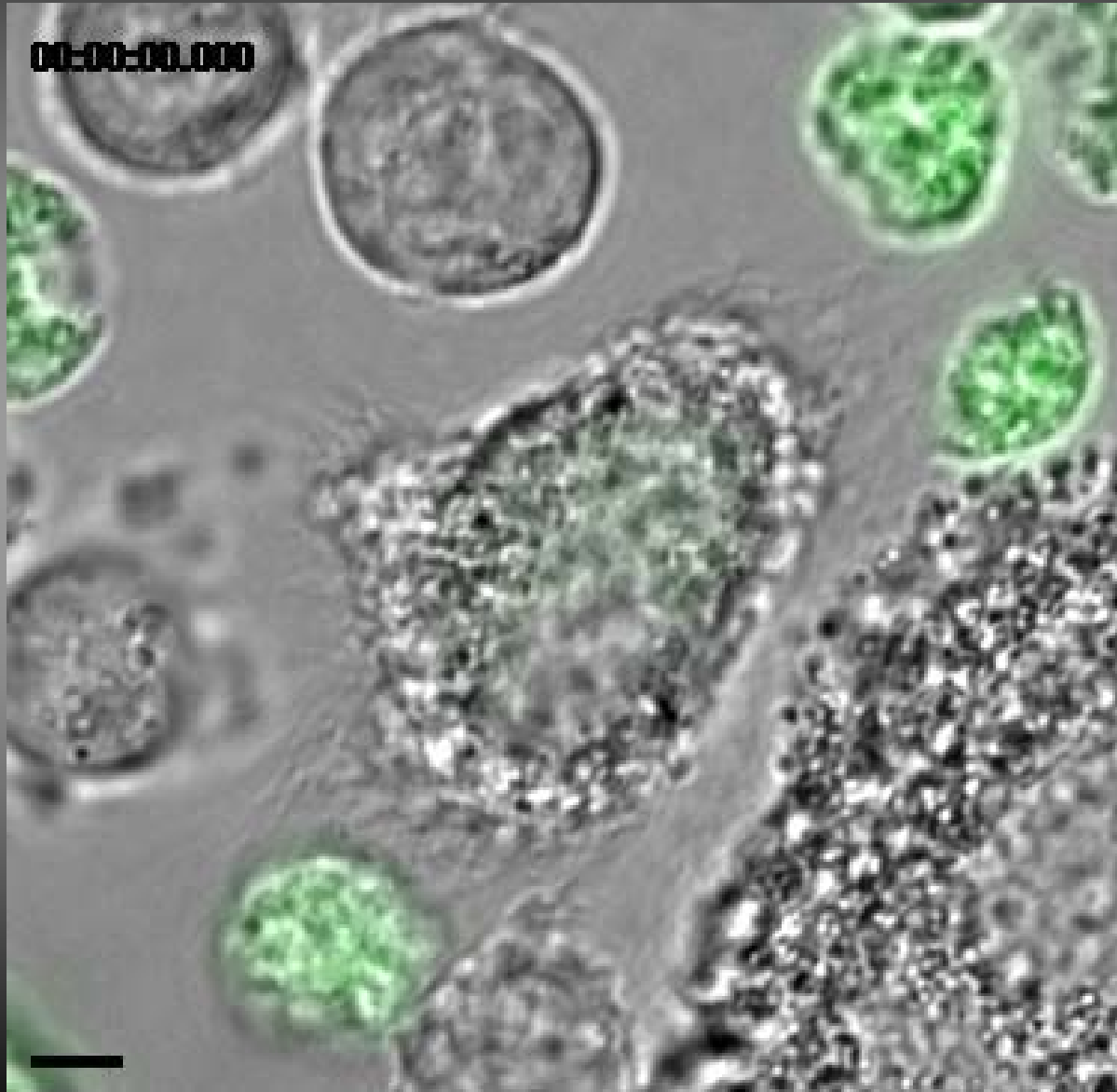
# HIV infection of macrophages

Macrophages are infected early, live long, and become 'viral reservoirs'

Infected macrophages contribute to viral pathogenesis in the mucosae and brain

But how are macrophages infected?

# Macrophage uptake of HIV-1+ T cells



HIV-1-GFP

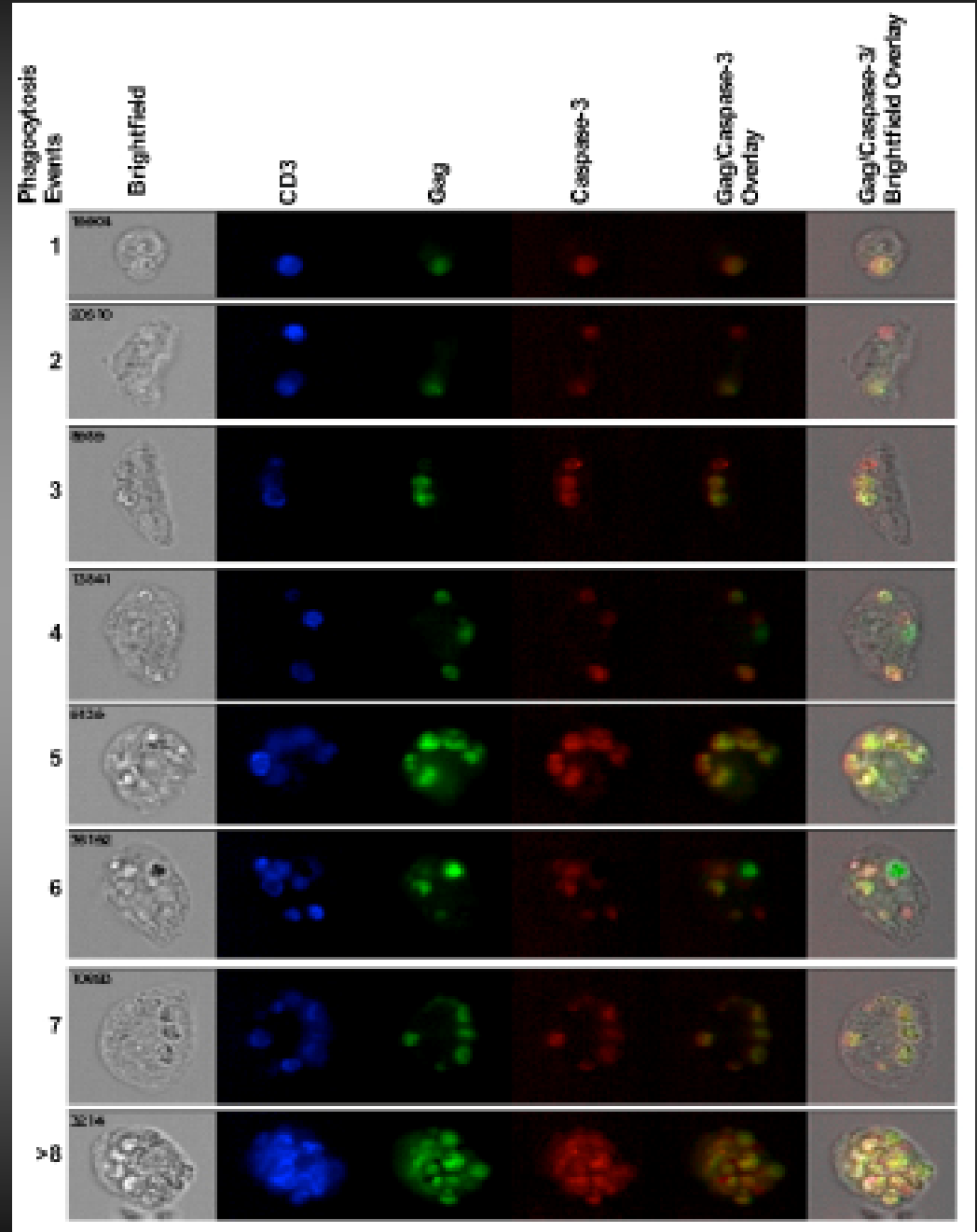


# Macrophage uptake of HIV-1+ T cells by multispectral flow cytometry (Imagestream™)

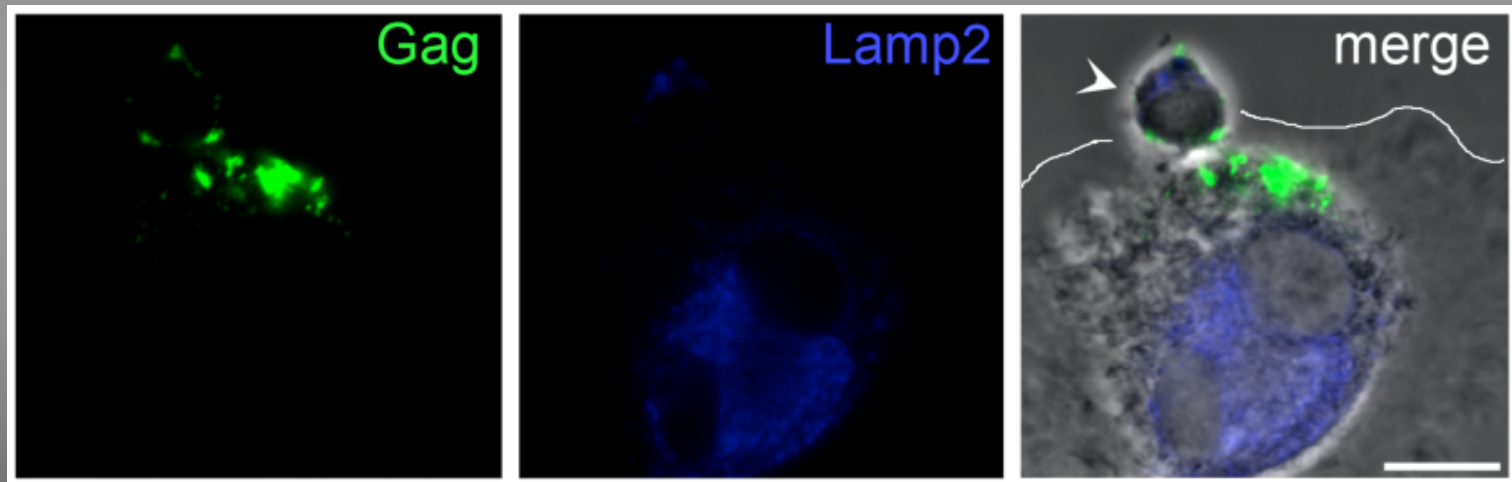
CD3 = T cell

Gag p24 = HIV-1

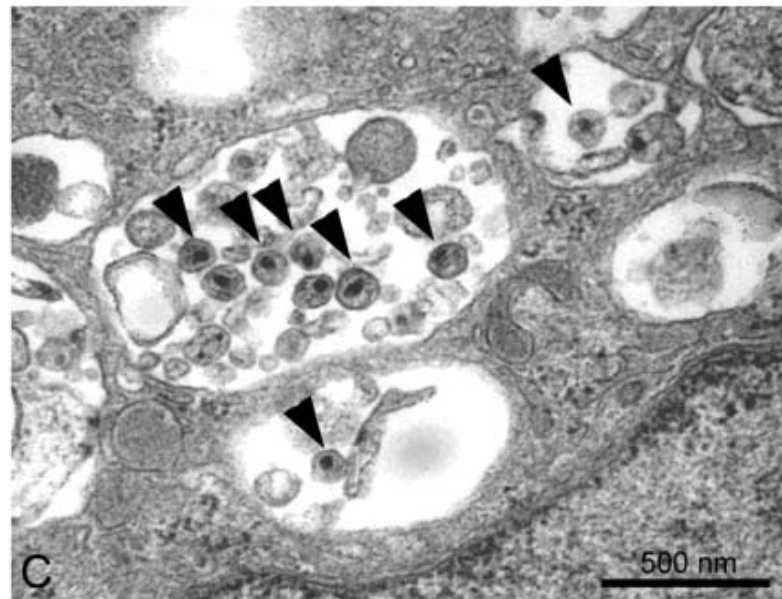
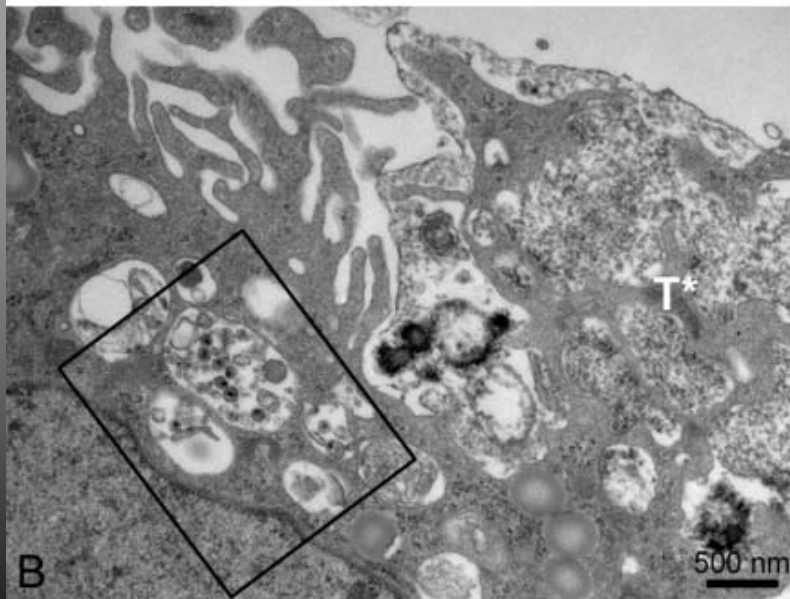
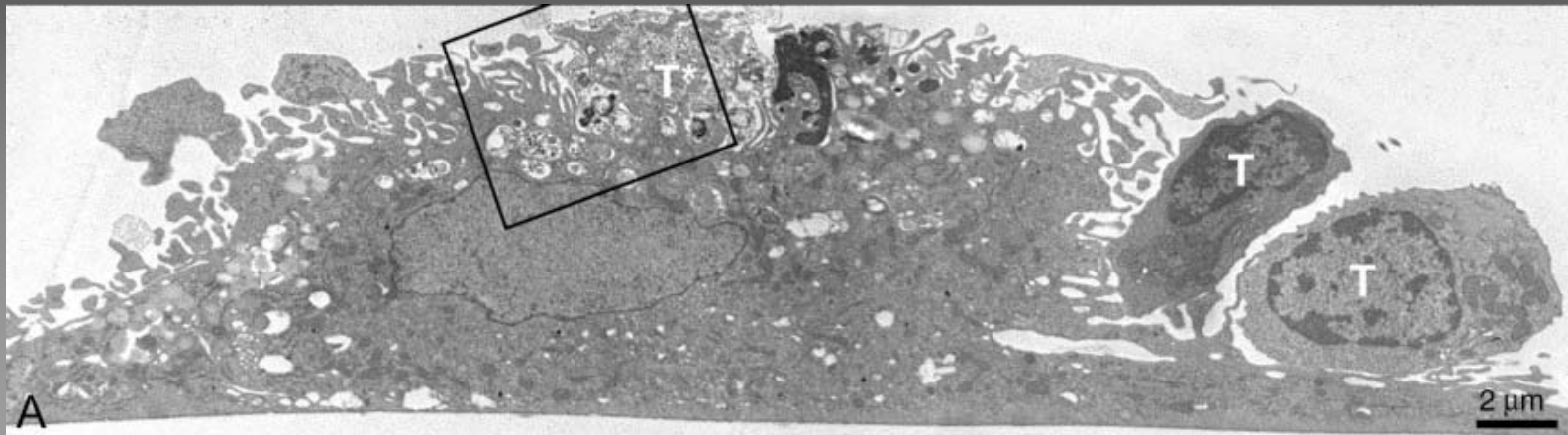
Caspase-3 = apoptosis



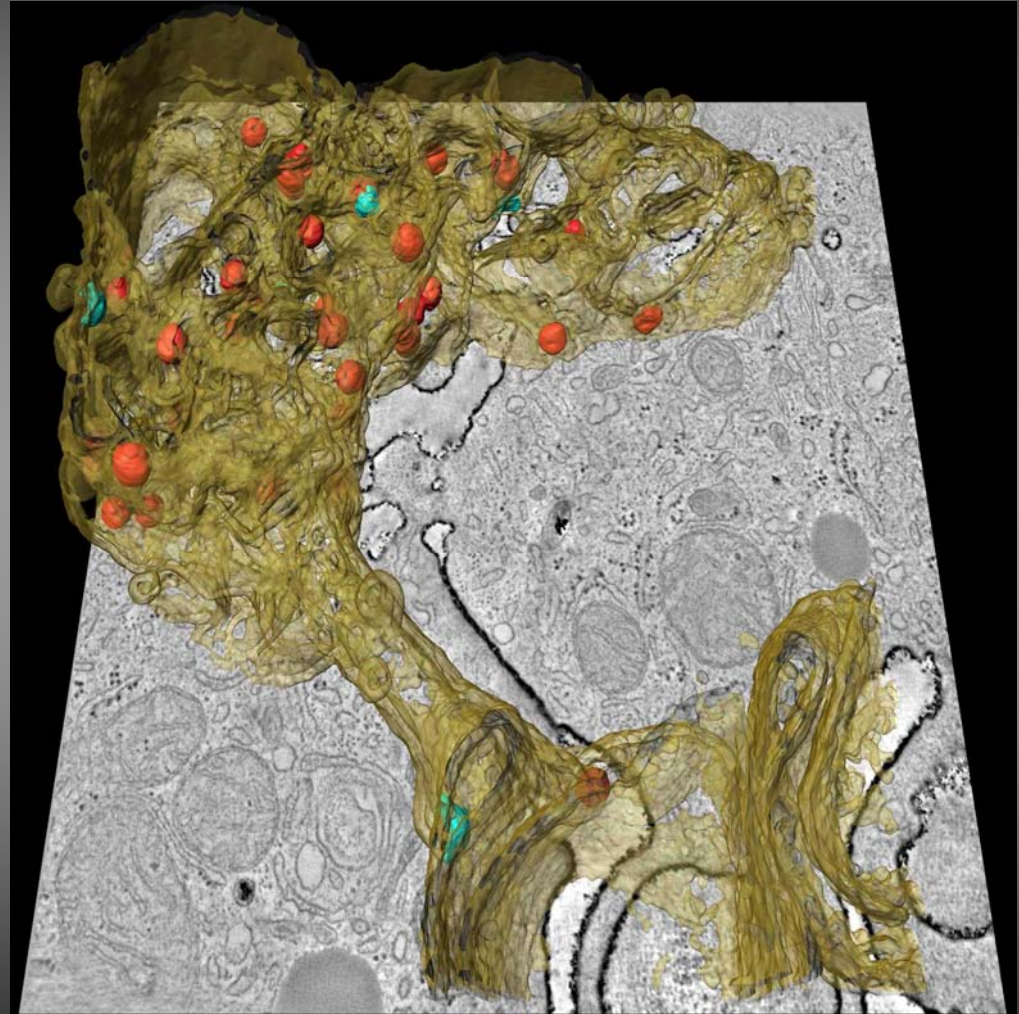
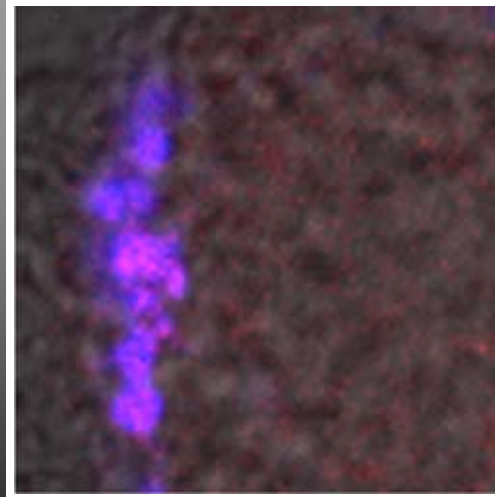
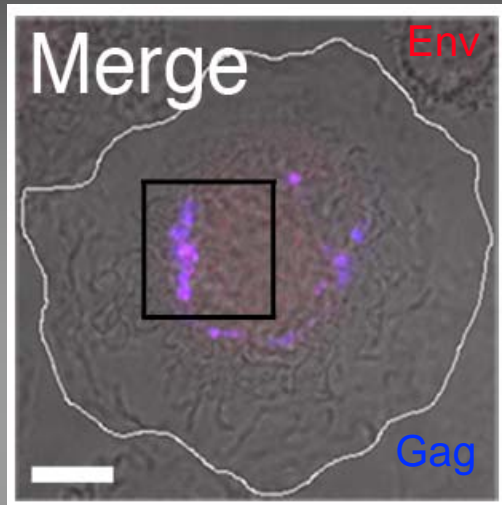
# Viral escape from degradation?



# Macrophage engulfment of HIV+ T cells

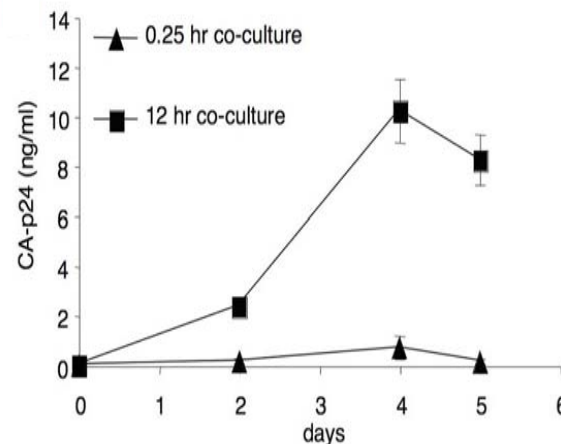
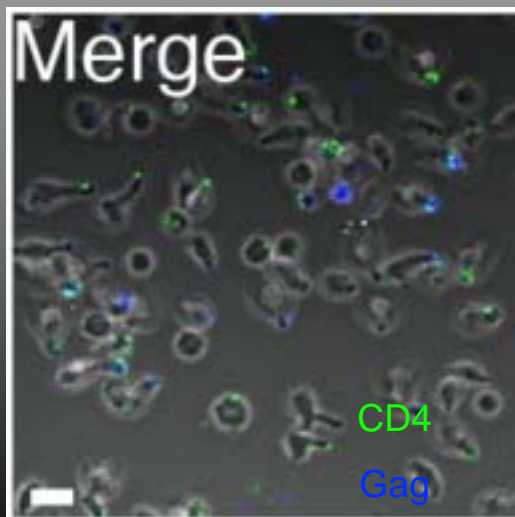
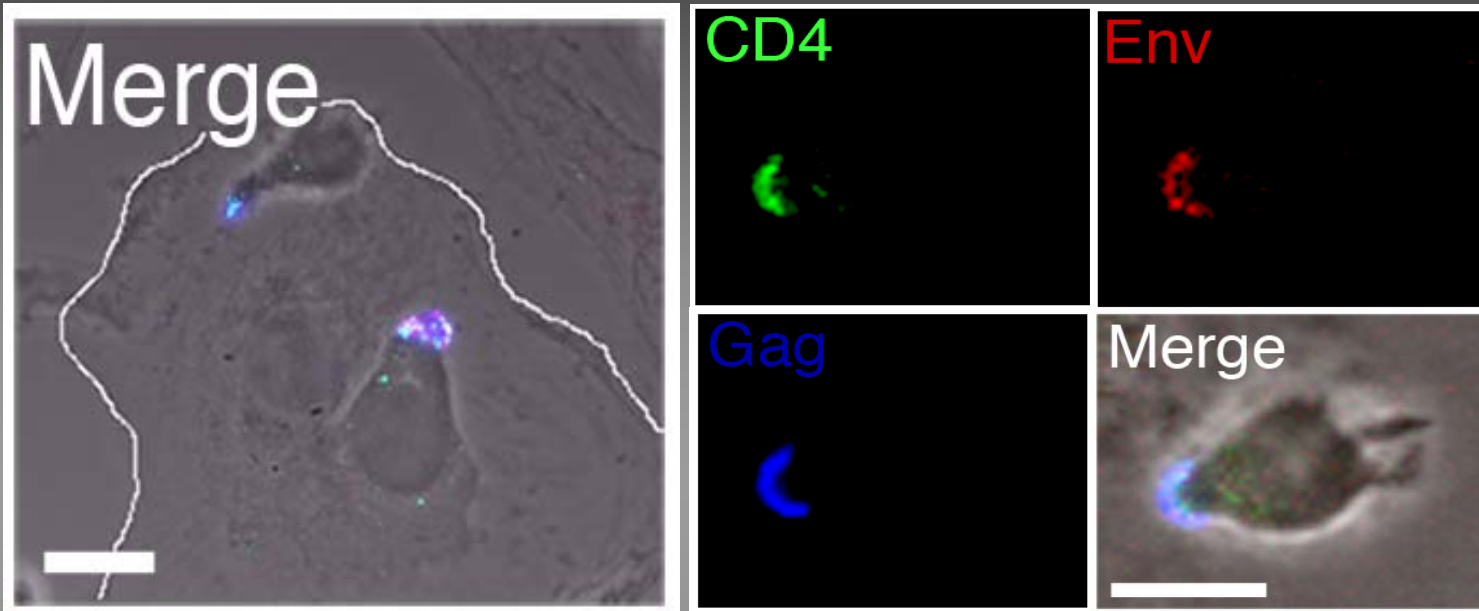


# Macrophage – virus compartment



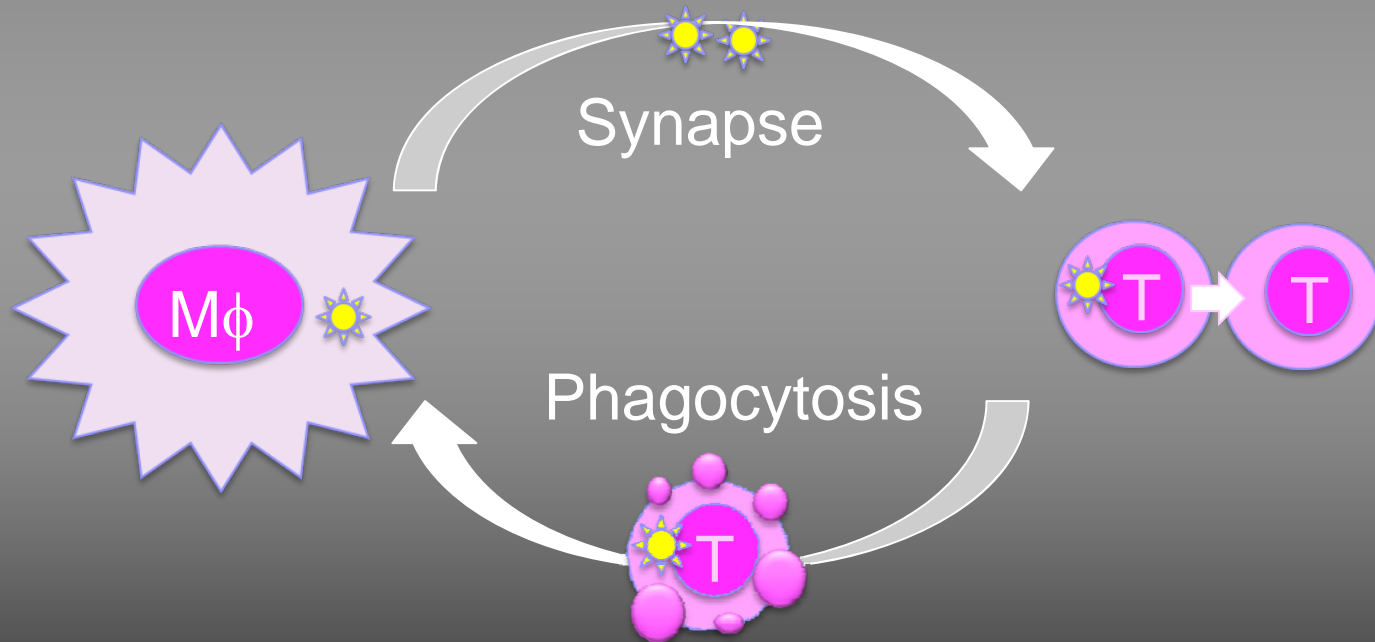
Welsch et al JVI 2011

# Macrophage - T cell synapse





# Working model for macrophage-T cell HIV-1 infection



# Acknowledgements

## Oxford

Fedde Groot  
Becky Russell  
Amy Baxter  
Chris Duncan  
Mike Shaw  
Chris Willberg  
Clair Jolly  
Ivonne Mitar

## Heidelberg

Sonja Welsch  
John Briggs



Leading science for better health