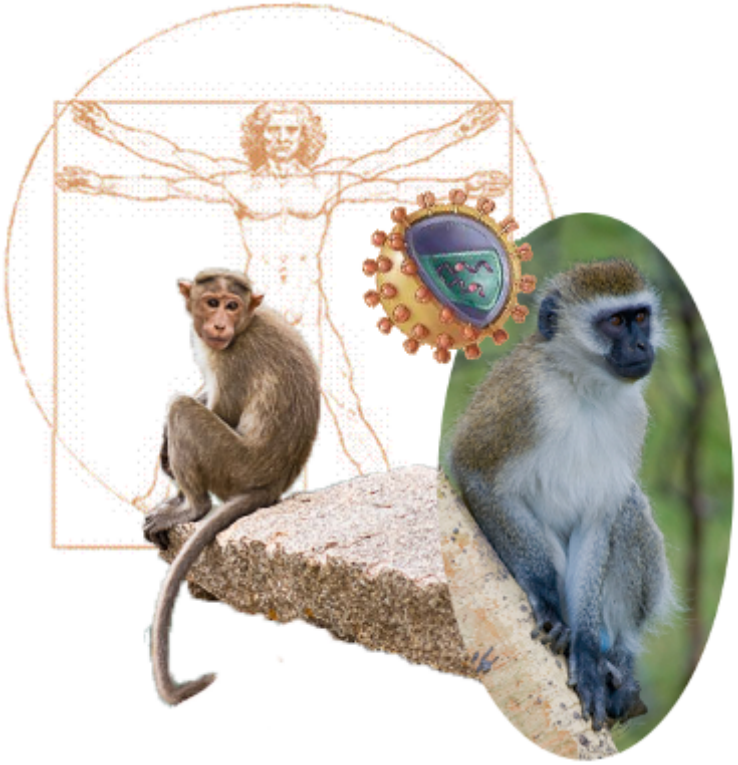
NK cell and viral dynamics within lymph nodes during pathogenic and non pathogenic SIV infection

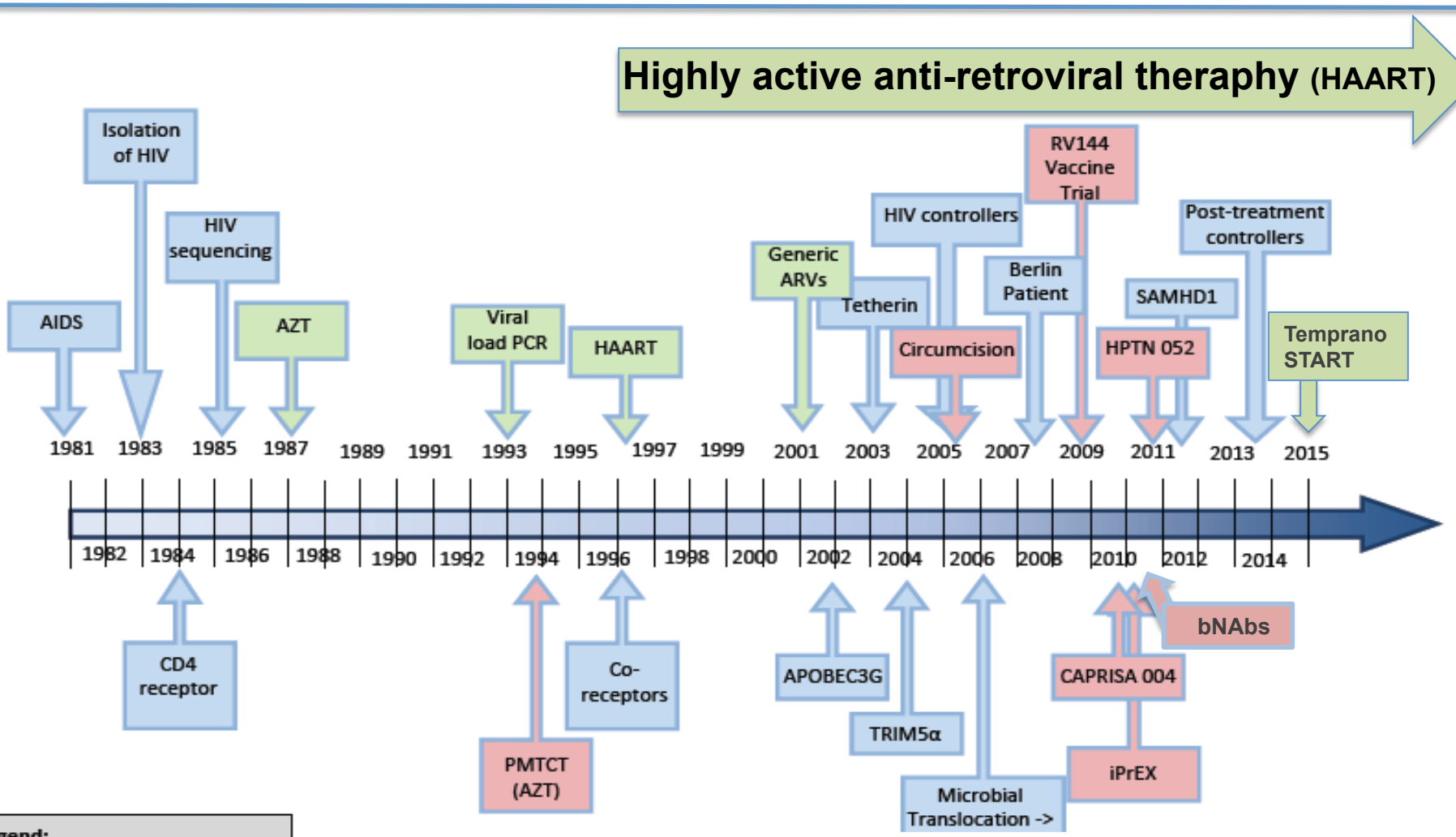
Les Pensières – Fondation Mérieux Conference Center - May 2016



Unité « HIV, Inflammation and Persistence »
Virology Department
Institut Pasteur, Paris, France

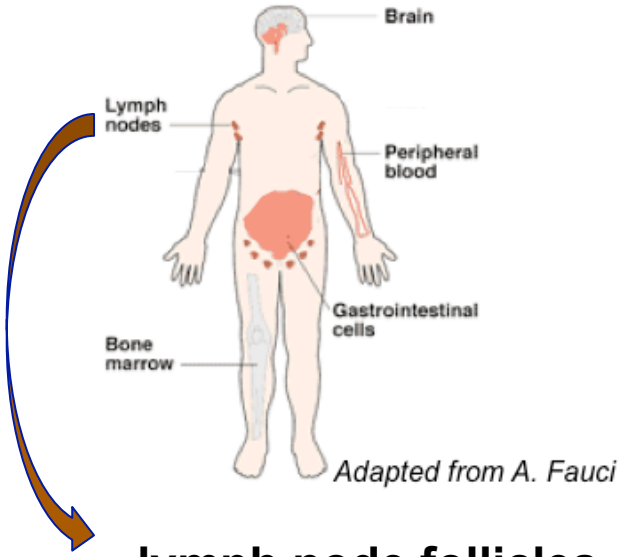
Institut Pasteur

More than 30 years of HIV Science
Rapid progress but still no vaccine and no cure



Adapted from Barré-Sinoussi F. & M. Müller-Trutwin. ***IAS News Letter****. 2002. 20:4-6.*

HIV persistence in lymph node follicles



lymph node follicles

T_{FH} cells

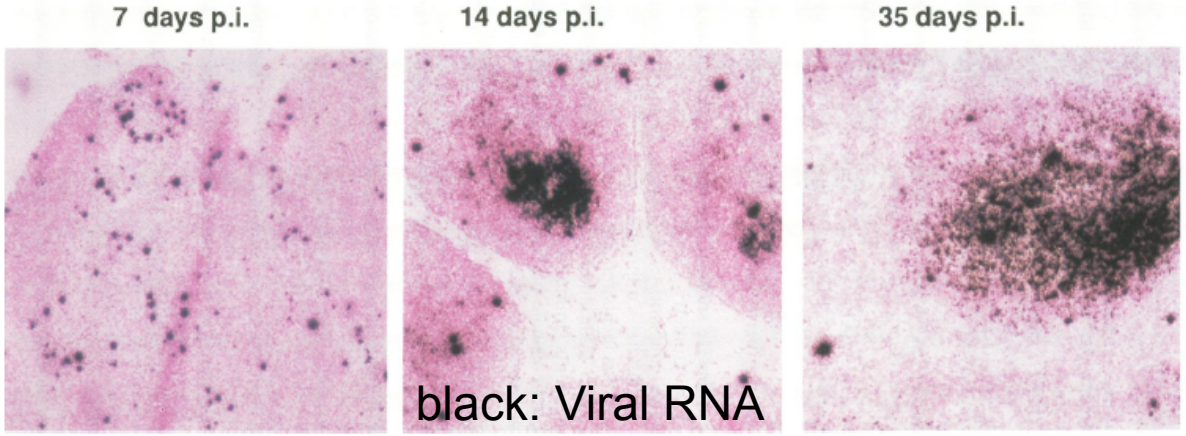
Lindqvist, M. *et al.. J. Clin. Invest.* (2012).
Brenchley, J.M. *et al. Blood* (2012).
Petrovas, C. *et al.J. Clin. Invest.* (2012).
Perreau, M. *et al.. J. Exp. Med.* (2013).

American Journal of Pathology, Vol. 144, No. 6, June 1994

Early Stages of Simian Immunodeficiency Virus Infection in Lymph Nodes

Evidence for High Viral Load and Successive Populations of Target Cells

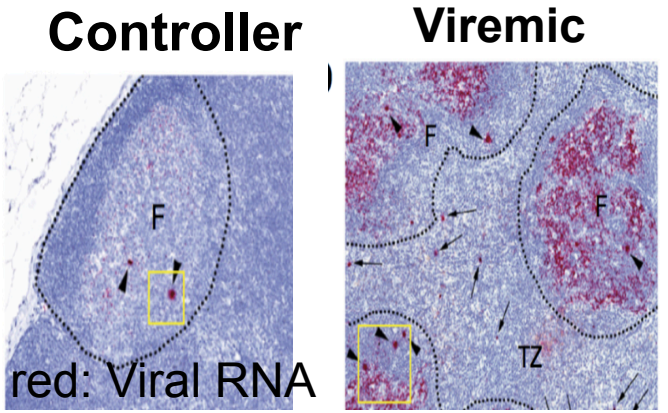
Chakrabarti L. et al



B cell follicle sanctuary permits persistent productive simian immunodeficiency virus infection in elite controllers

Yoshinori Fukazawa[1,2], Richard Lum[1,2], Afam A Okoye[1,2], Haesun Park[1,2], Kenta Matsuda[3], Jin Young Bae[1,2], Shoko I Hagen[1,2], Rebecca Shoemaker[4], Claire Deleage[4], Carissa Lucero[4], David Morcock[4], Tonya Swanson[1,2], Alfred W Legasse[1,2], Michael K Axthelm[1,2], Joseph Hesselgesser[5], Romas Geleziunas[5], Vanessa M Hirsch[3], Paul T Edlefsen[6], Michael Piatak, Jr[4], Jacob D Estes[4], Jeffrey D Lifson[4] & Louis J Picker[1,2]

Nat Med 2015



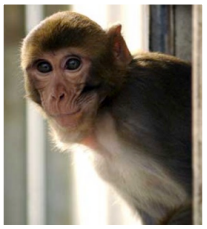
African NHP
Natural hosts of SIV
Non pathogenic infection

African green monkey (AGM)

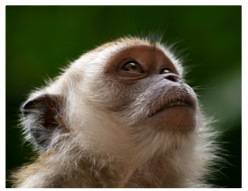
Sooty Mangabey

SIV

Asian NHP
Experimental hosts of SIV
pathogenic outcome



Rhesus macaque



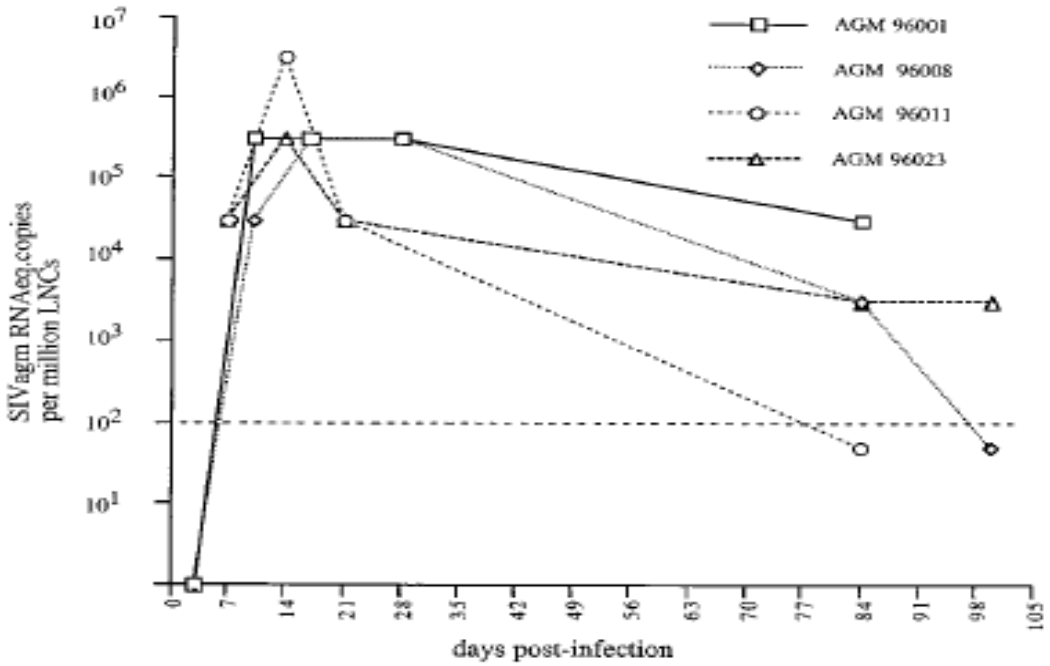
Cynomolgus macaque

Pigtailed macaque

	Natural host	Human/MAC
Chronic inflammation	-	+++
Viral mutation rate	+++	+++
Viremia (blood)	+++	+++
Viral load in gut	+++	+++

Paiardini & Müller-Trutwin, Immunol Rev, 2013

Rapid control of SIVagm replication in lymph nodes in AGM



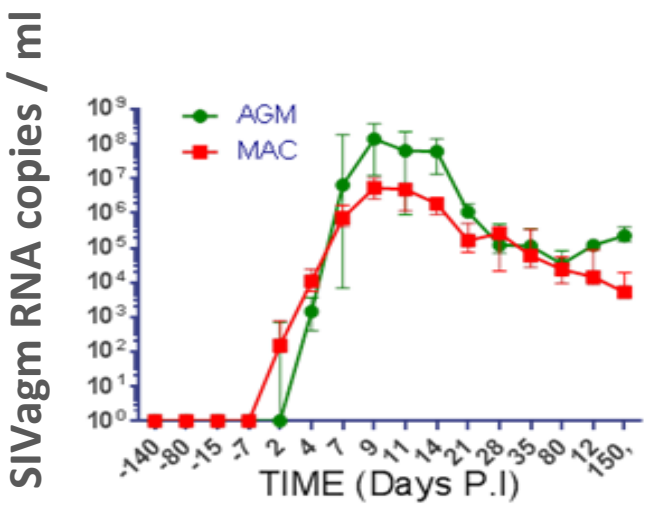
Diop et al, JVI, 2000

SIVagm, SIVmac : similar high replication levels during acute infection but opposite profiles in blood and lymph nodes in chronic infection

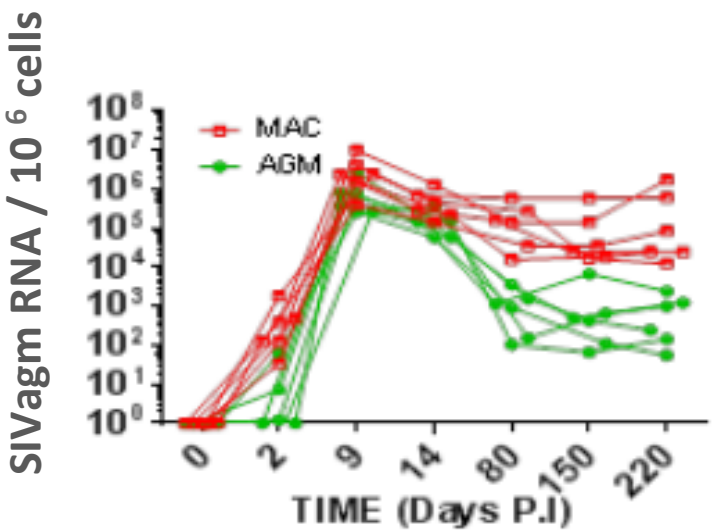
6 AGM (sabaeus), $SIVagm.sab_{92018}$, high dose IV
6 MAC (cynomolgus), $SIVmac_{251}$, high dose IV

→ Blood samplings
Lymph node biopsies

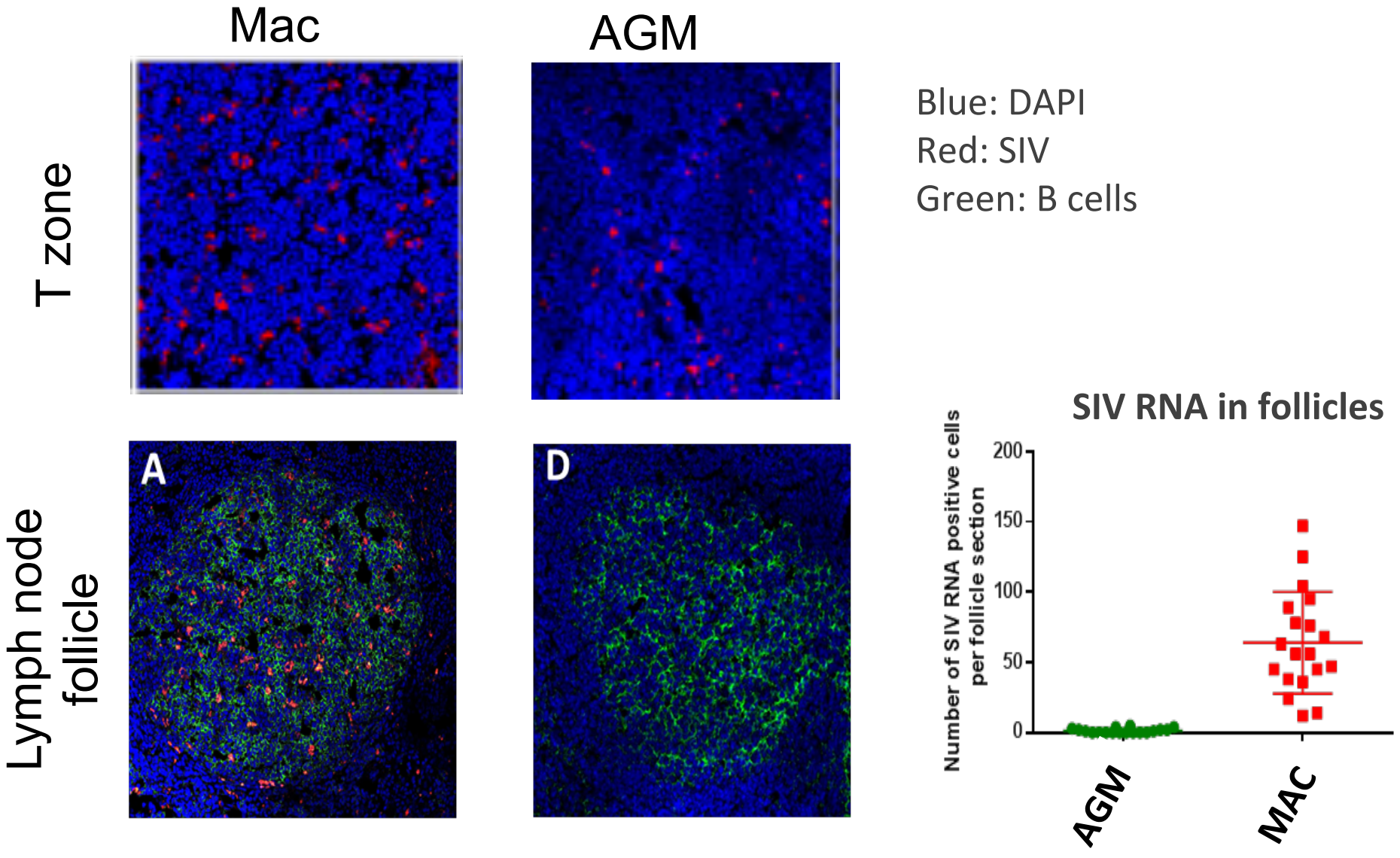
Blood



Lymph nodes



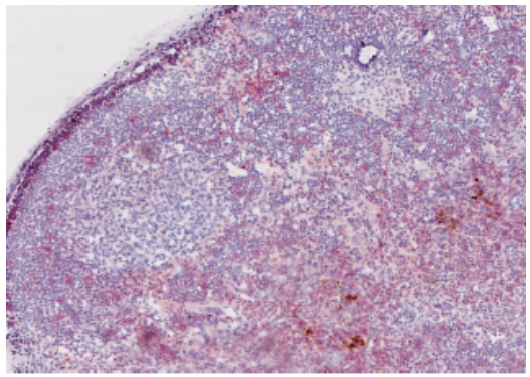
Chronic SIVagm infection in AGM: Strong control of viral replication in T zone and no virus in follicles



AGM/SIV: no evidence for $CD8^+$ T cells in lymph node follicles

CD8

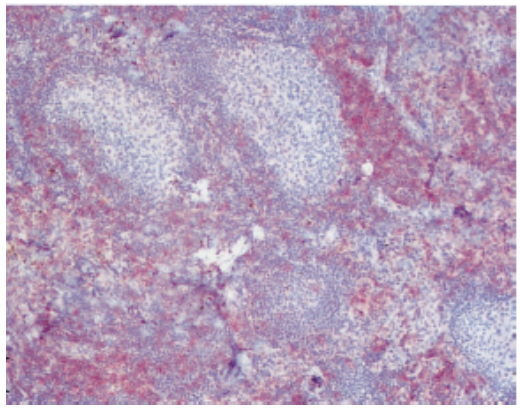
SIV-

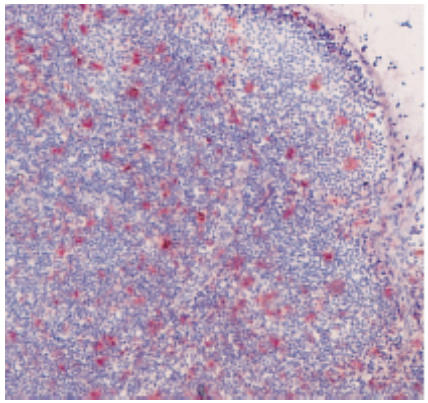


Diop et al, JVI, 2000

macrophages

SIV+





Blood cytokine profiles during HIV/SIV infections

Marker	AGM	HUMAN MAC
IL-15	++	++
IFN-α	++	+++
IP-10	+++	+++
MCP-1	+++	++
IFN-g	+	++
IL-18	+	+++
TNF-a	-	+
IL-8	-	+++
sTrail	-	+++
Il-6	-	+
IL-12	+	+
Mip-1a	-	++
MIP1-b	-	++
TGF-b	+	+++
IL-10	-	+
IP-10	-	+++
sCD14	-	+

Order of appearance in HIV and SIV infections

Jacquelin et al, JCI, 2009
Jacquelin et al, Plos Path 2014

OPEN ACCESS Freely available online 2014 PLOS | PATHOGENS

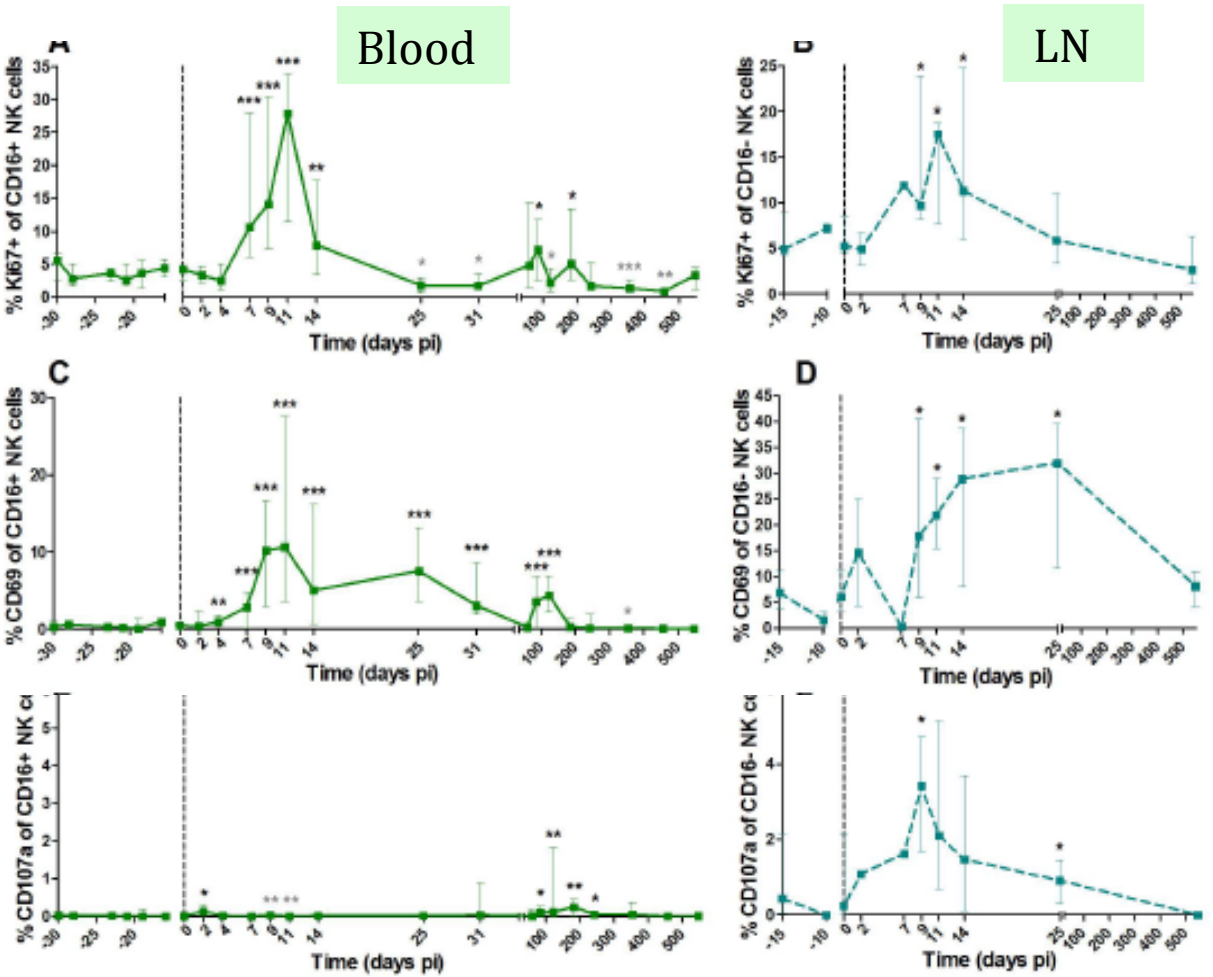
Innate Immune Responses and Rapid Control of Inflammation in African Green Monkeys Treated or Not with Interferon-Alpha during Primary SIVagm Infection

Béatrice Jacquelin[1], Gaël Petitjean[1], Désirée Kunkel[1], Anne-Sophie Liovat[1], Simon P. Jochems[1,2], Kenneth A. Rogers[3], Mickaël J. Ploquin[1], Yoann Madec[4], Françoise Barré-Sinoussi[1], Nathalie Dereuddre-Bosquet[5], Pierre Lebon[6], Roger Le Grand[5], François Villinger[3], Michaela Müller-Trutwin[1]*

NK cells Ki-67

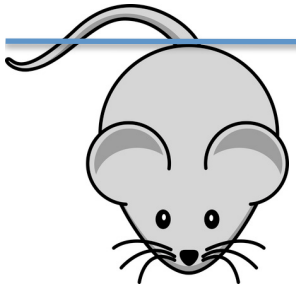
NK cells CD69

NK cells CD107a



Trafficking to lymph nodes ?

Tissue trafficking of NK cells



Rapidly recruited in a CCR7-independent, CXCR3-and CD62L-dependent manner to lymph nodes on stimulation by the injection of mature DCs

Martin-Fontecha A, Nat Immunol. 2004;5:1260-1265.

Early viral replication in lymph nodes provides HIV with a means by which to escape NK-cell-mediated control

*Rutger Luteijn[*1], Gaia Sciaranghella[*1], Jan van Lunzen[2], Anne Nolting[1], Anne-Sophie Dugast[1], Musie S. Ghebremichael[1,3,4], Marcus Altfeld[1] and Galit Alter[1]*

Eur. J. Immunol. 2011. 41: 2729–2740

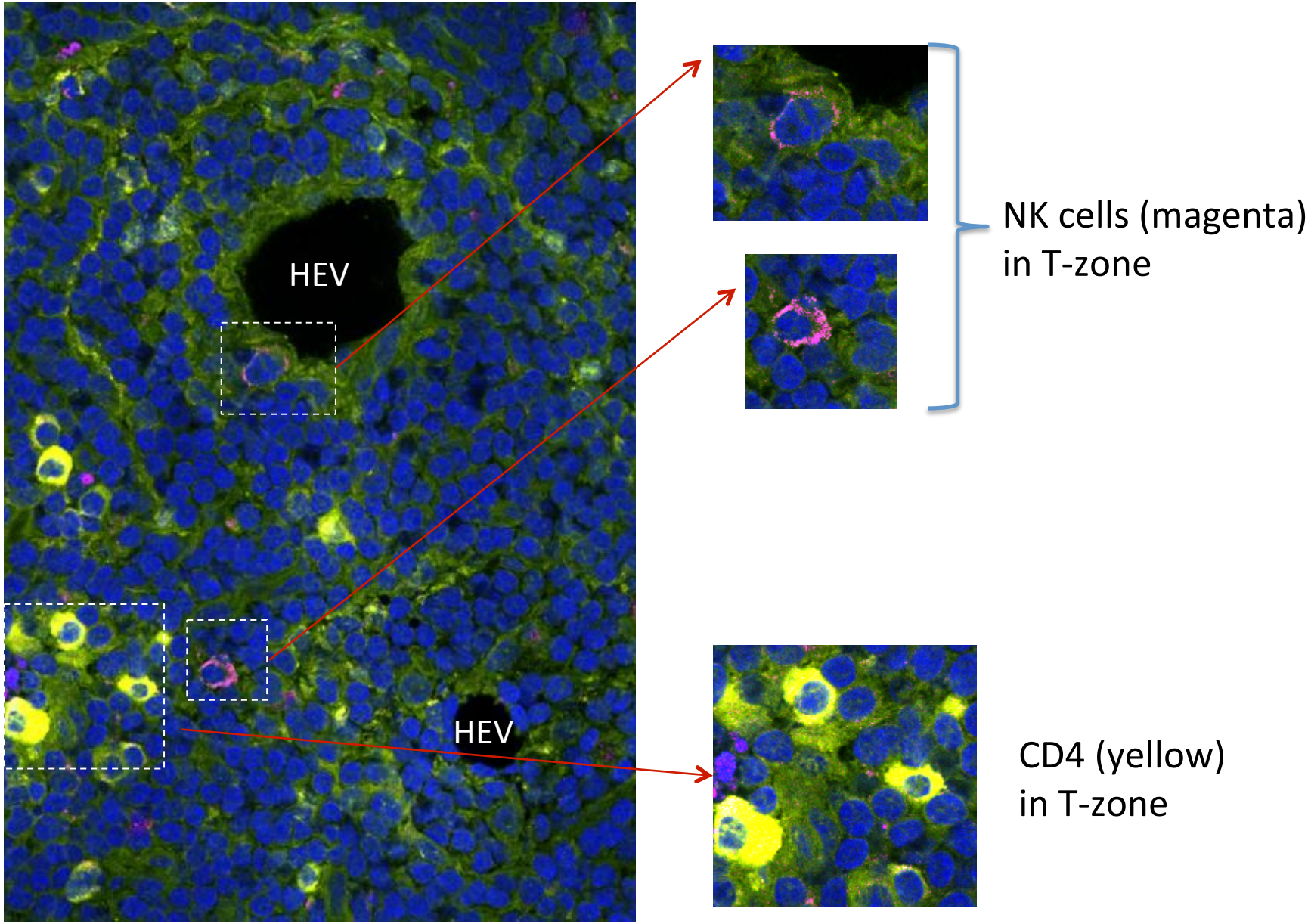
macaque

Simian Immunodeficiency Virus Infection Induces Expansion of $\alpha 4\beta 7^+$ and Cytotoxic $CD56^+$ NK Cells$^{\nabla}$

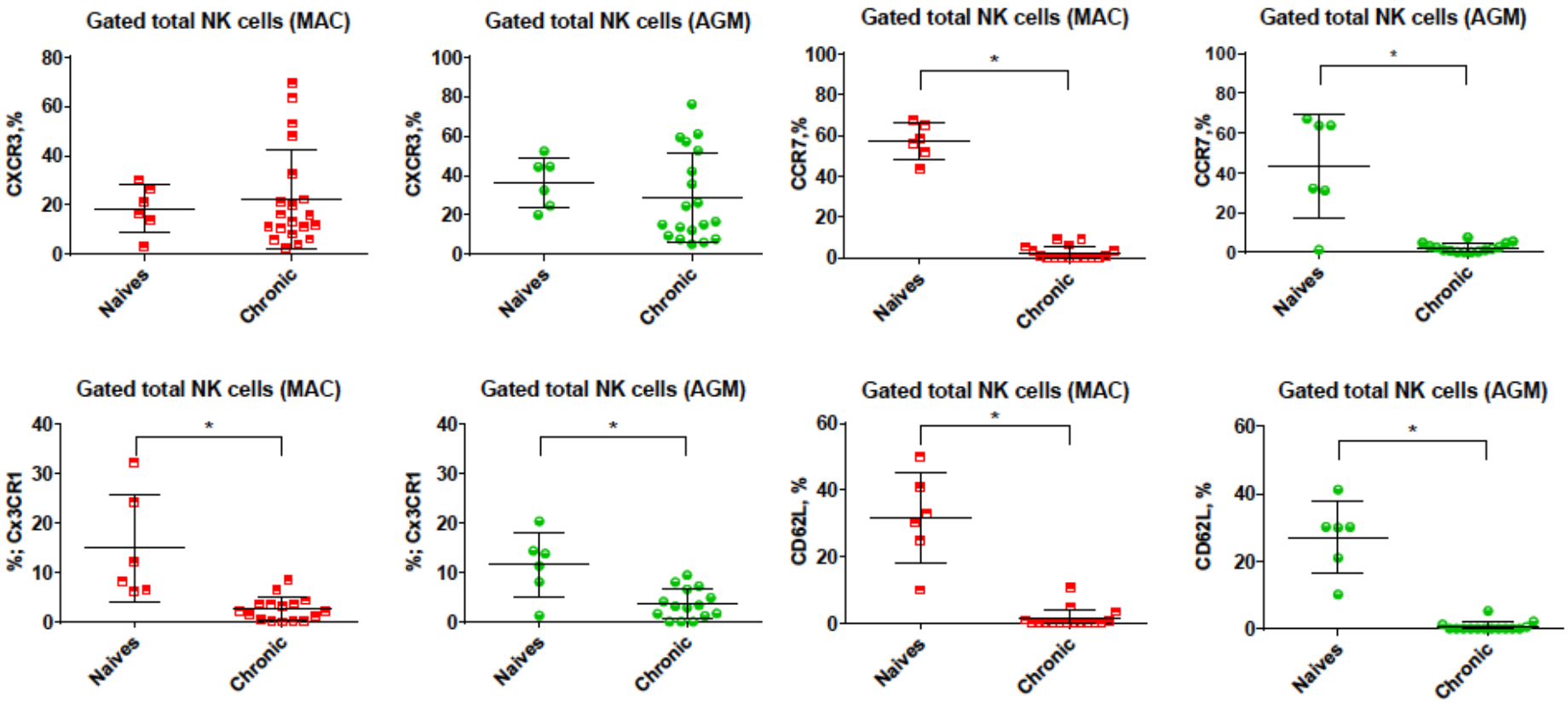
R. Keith Reeves,[1] Tristan I. Evans,[1] Jacqueline Gillis,[1] and R. Paul Johnson[1,2]*

J Virol. 2010 Sep;84(17):8959-63

Before SIV infection : most of NK cells in paracortex (MAC and AGM)



Frequent decrease of NK cells with lymph node homing markers Similar between pathogenic and non-pathogenic SIV infection



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Thank you