

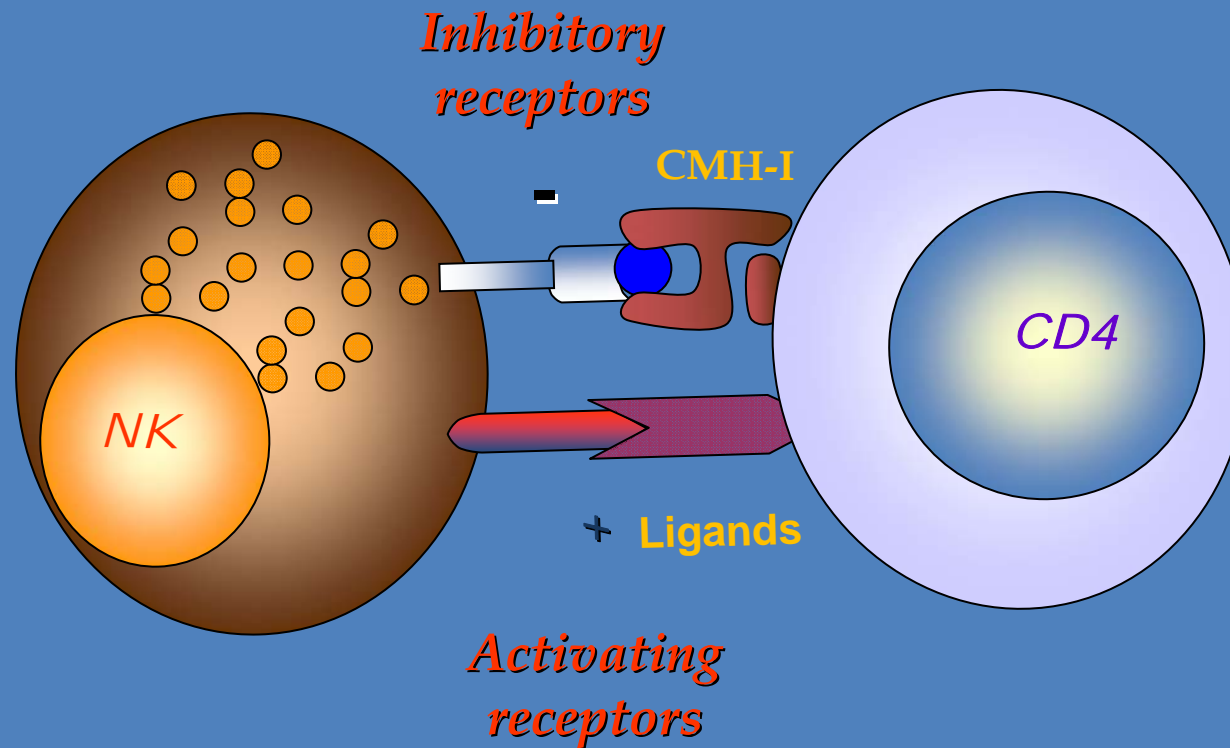
# HIV escape from natural killer cytotoxicity: Nef inhibits NKp44L expression on HIV-infected CD4<sup>+</sup> T cells.

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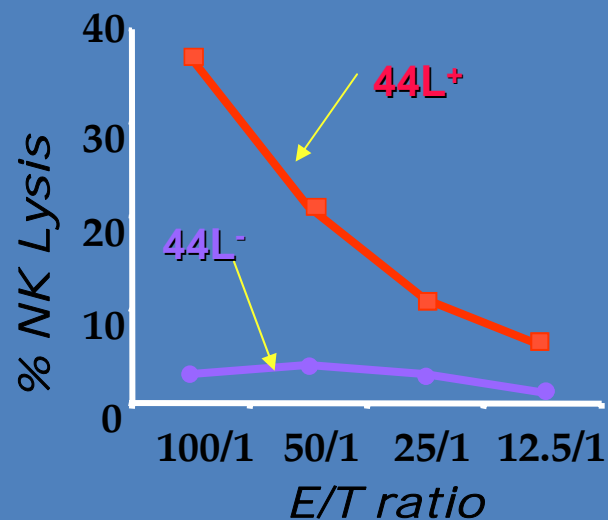
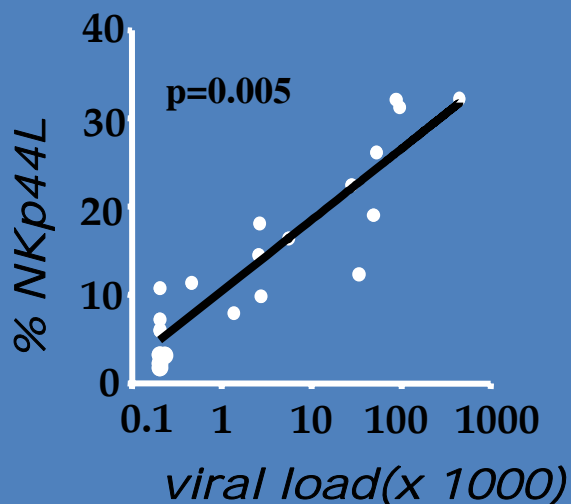
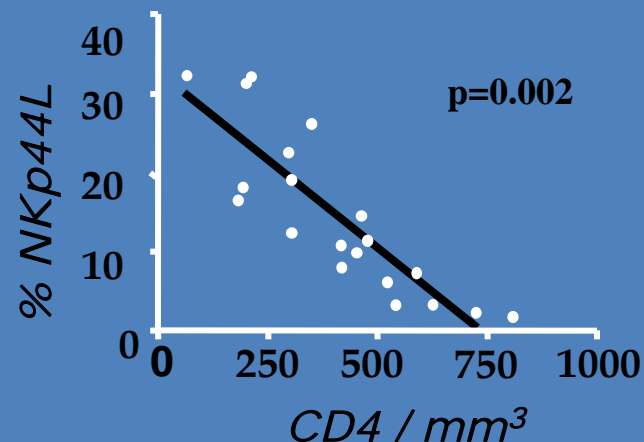
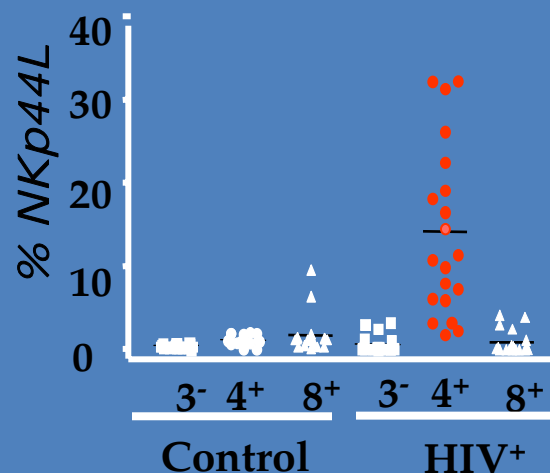
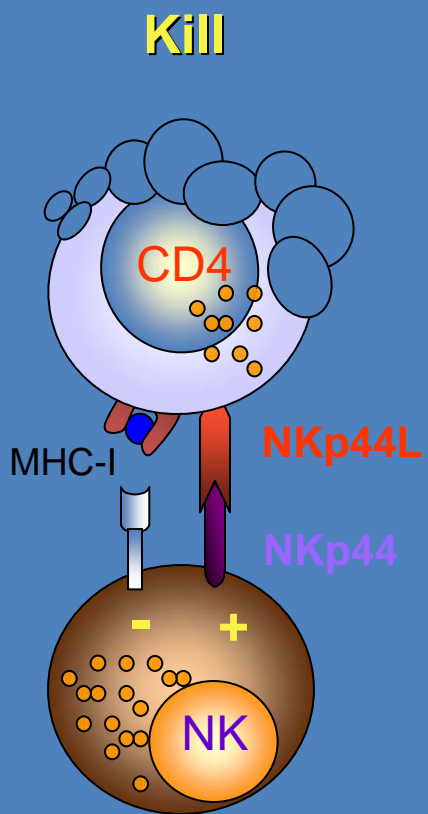


# A Role for NK cells in the CD4 T depletion ?



Role of the NCR : NKp30, NKp44 and NKp46

# Background : NKp44L expression by CD4<sup>+</sup> T cells from HIV-infected patients

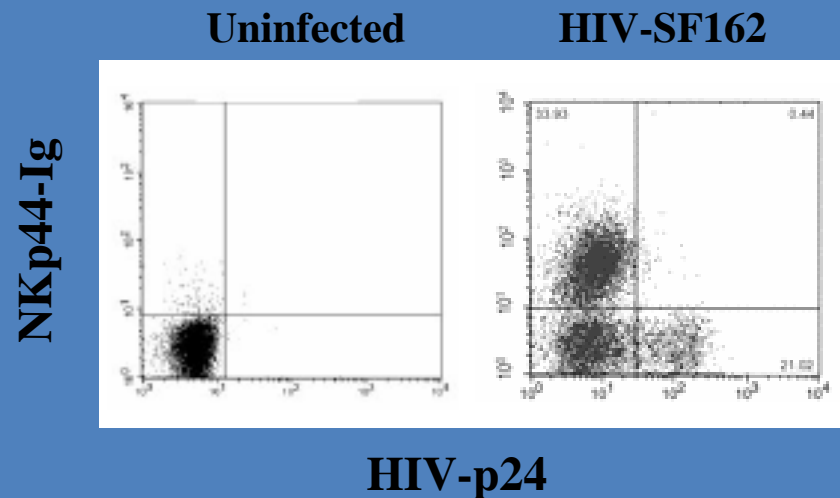


# NK cells and HIV-infected CD4<sup>+</sup> T cells

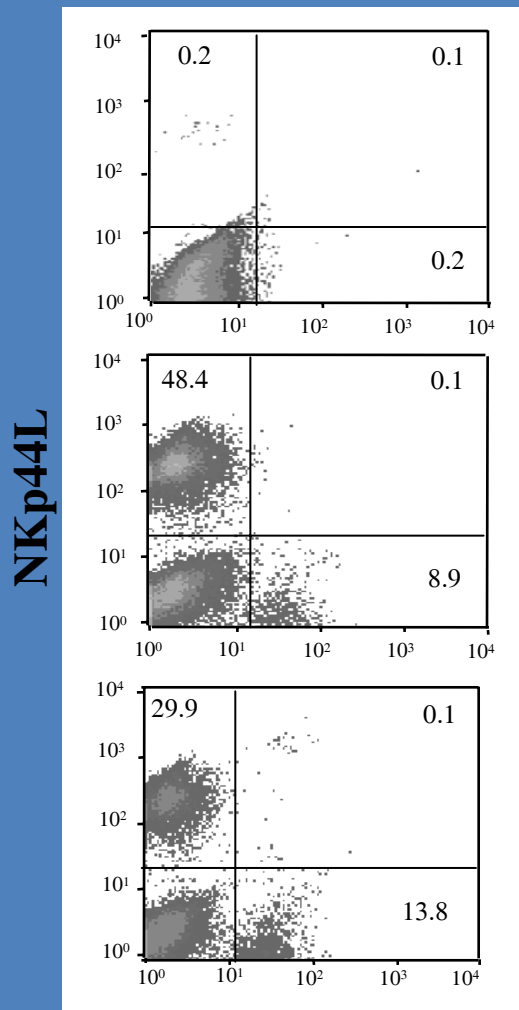
**Cohen et al:** The selective down-regulation of class-I major histocompatibility complex proteins by HIV-1 protects HIV-infected cells from NK cells. *Immunity* 1999, 10:661-671

**Bonaparte et al:** Inability of natural killer cells to destroy autologous HIV-infected T lymphocytes. *AIDS* 2003, 17:487-494

**Ward et al:** HIV modulates the expression of ligands important in triggering natural killer cell cytotoxic responses on infected primary T-cell blasts. *Blood* 2007, 110:1207-1214



# Inhibition of NKp44L expression in CD4<sup>+</sup> T cells infected by HIV-1 strains and viremic HIV-infection patients

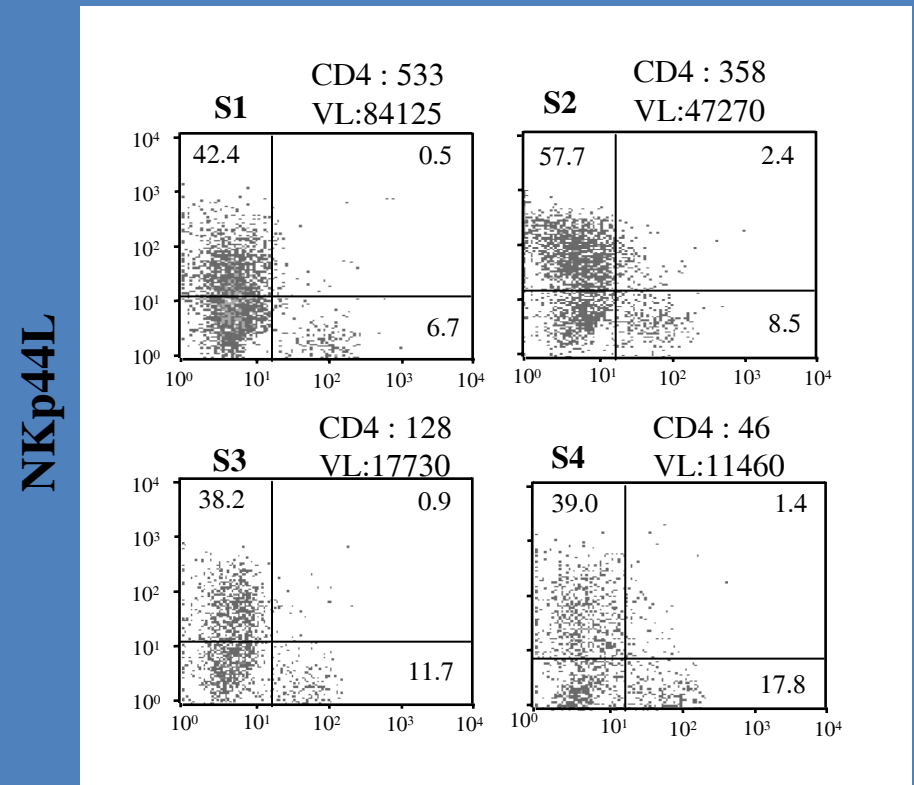


**Uninfected**

**HIV-AD8**

**HIV-NL4**

**HIV-p24**

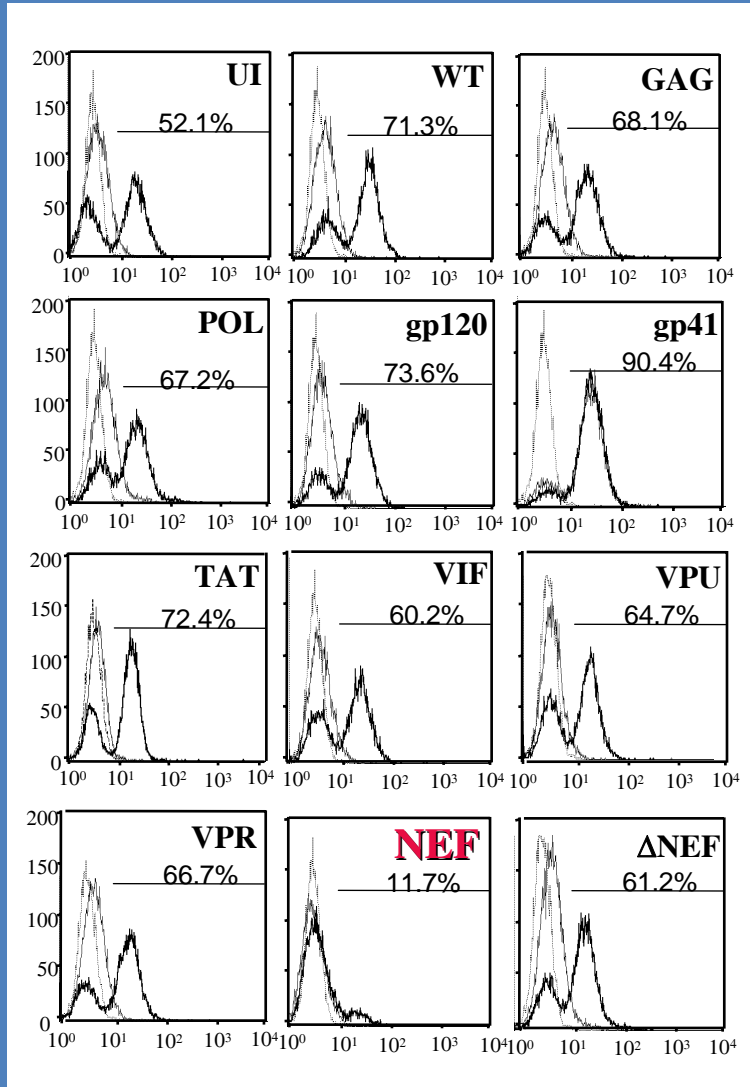


**NKp44L**

**HIV-p24**

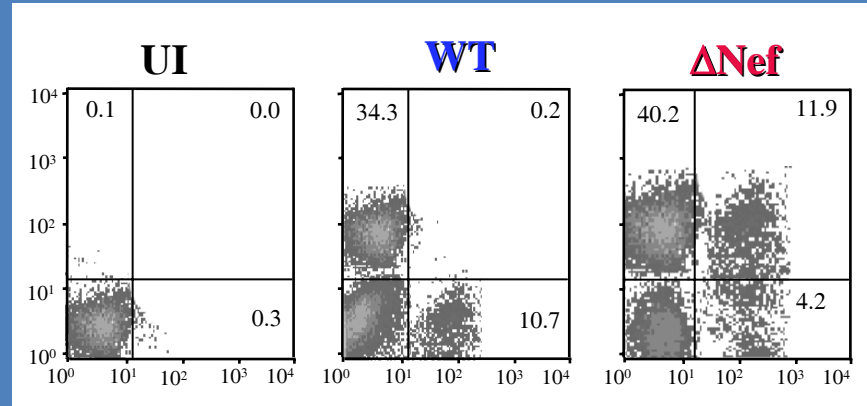
# Inhibition of NKp44L expression in CD4<sup>+</sup> T cells by **Nef**

Recombinant vaccinia viruses



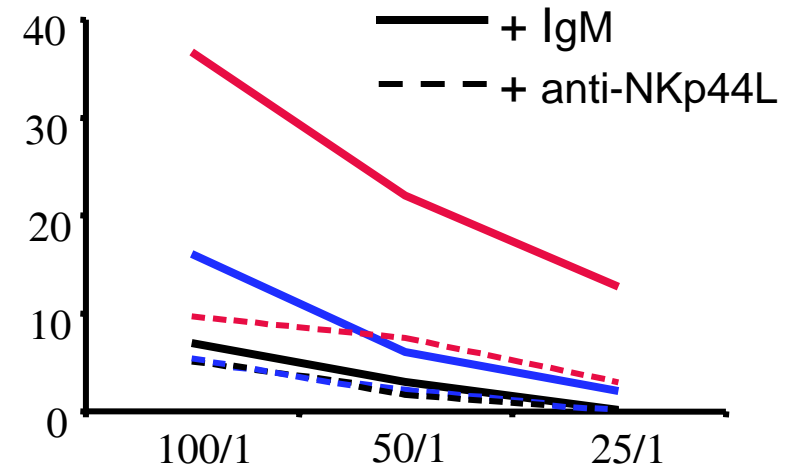
NKp44L

NKp44L



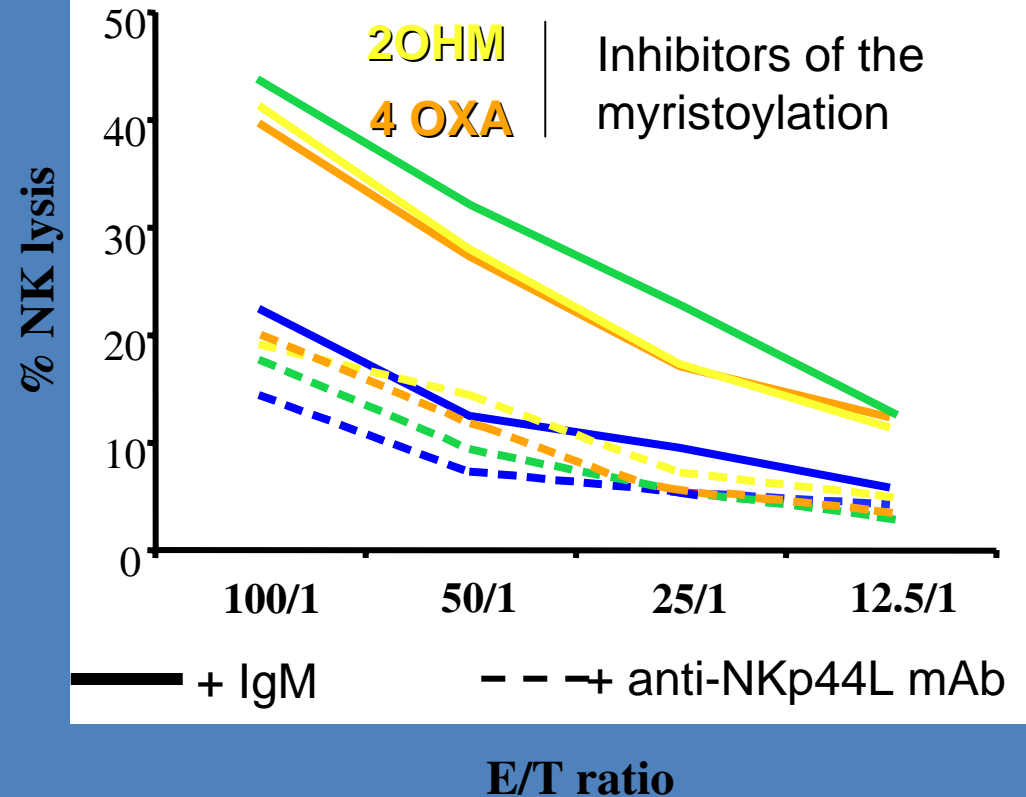
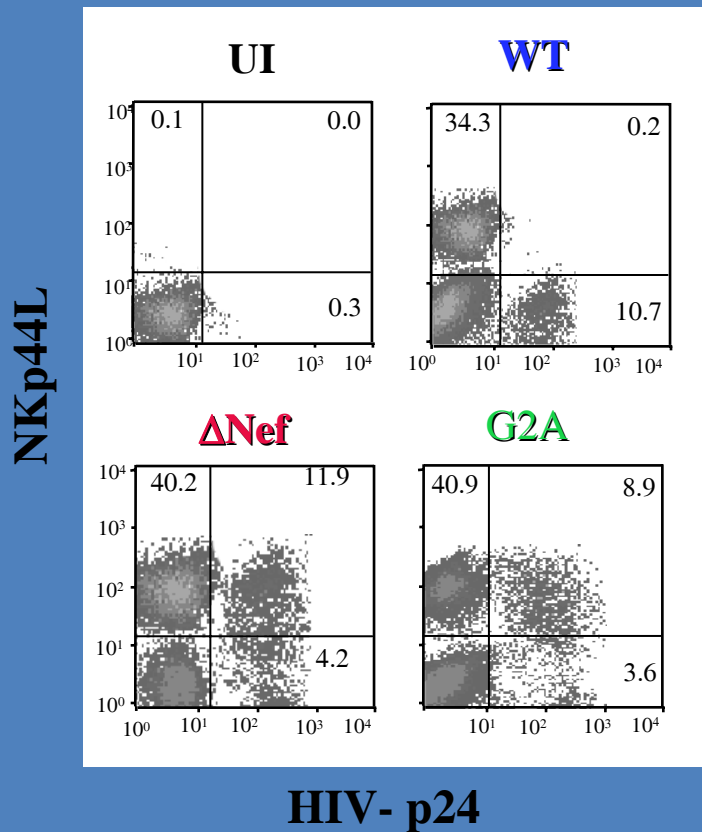
HIV-p24

% NK lysis



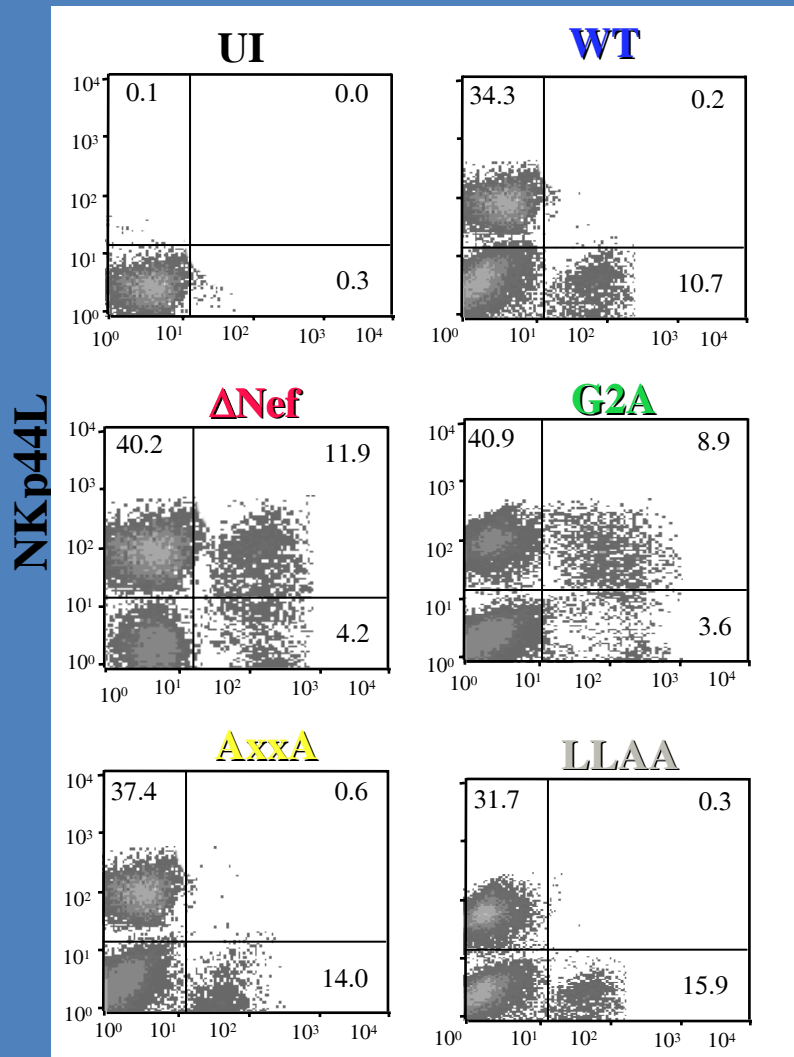
E/T ratio

# Effect of G2A Nef mutant on the NKp44L expression



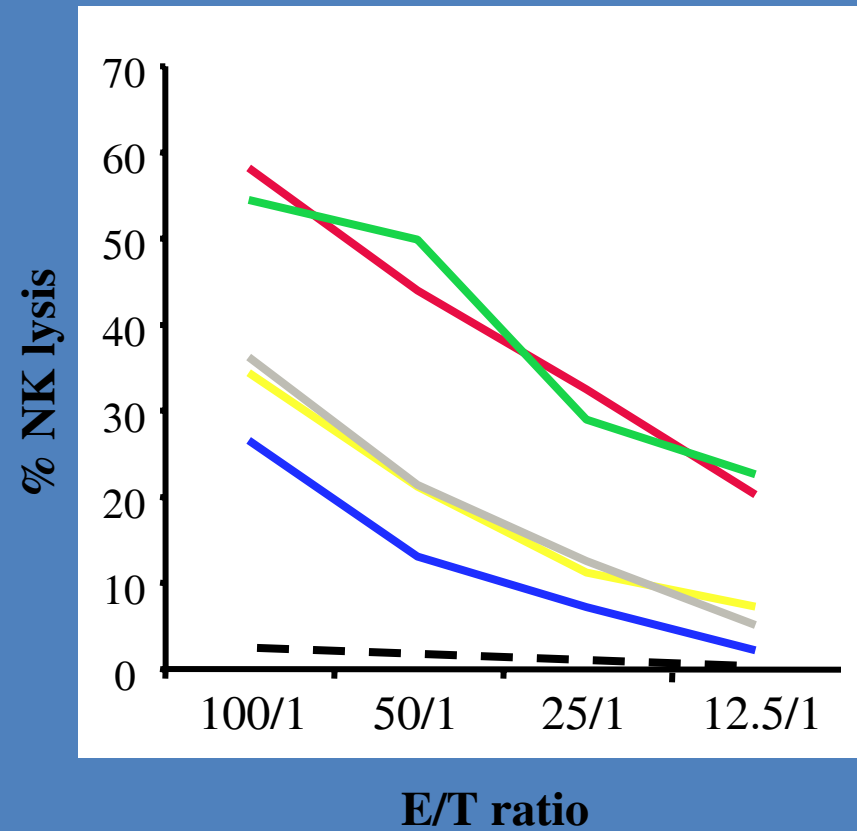
Mechanism of Nef is dependent of the **myristoylation**

# Effect of Nef mutants on NKp44L expression

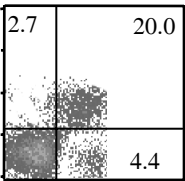
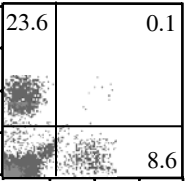
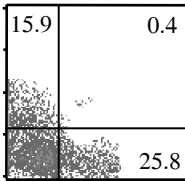
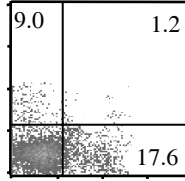


HIV- p24

Mechanism of Nef is independent of the classical pathways for  
**MHC-1** & **CD4** down-modulation



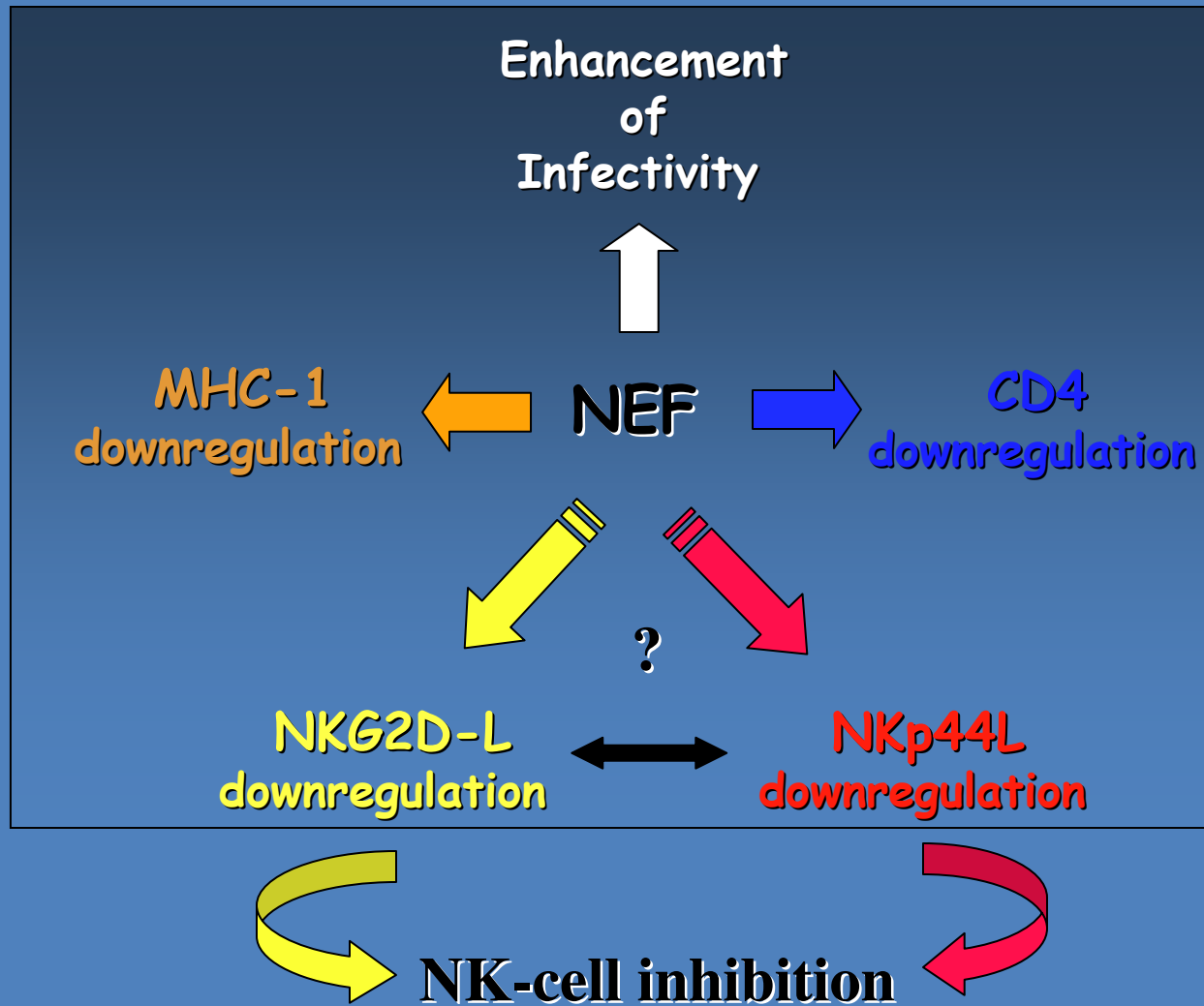
# Effect of Nef mutants on NKp44L expression on CD4<sup>+</sup> T cells from **LTNP** HIV-infected patients

patients	mutation	Reported functional consequences	
09.016	$\Delta$ 54-100	Non-functional Nef	
04.048	E62/63G	Loss of interaction with PACS crucial for MHC-I and CCR5 downregulation	
04.008	C55S/A56P	Non-functional cleavage site by the viral protease	
11.003	$\Delta$ 155-160	Loss of degradation of CD4 and MHC-I via $\beta$ -cop	

NKp44L

HIV- p24

# Conclusion



# Acknowledgments

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