

**FACTORS OF NATURAL
RESISTANCE TO HIV-1
INFECTION IN VIETNAMESE
EXPOSED UNINFECTED
INTRAVASCULAR DRUG USERS**

*PASTEUR INSTITUTE
HOCHIMINH CITY*

1996-1998

Study on HIV infection among IDUs in HCMC

464 IDUs : 362 HIV **INFECTED**
 102 HIV **UNINFECTED**

COMPARISON OF RISKY BEHAVIOURS

	HIV (-)	HIV(+)
Years IV drug	20.4 (2-32)	18.5(1-43)
<hr/>		
Mode		
IV	100 %	94%
AV	69%	61 %
<hr/>		
Place		
Shooting galery	51%	60 %
Home	84%	75 %
needle sharing	36%	36%
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Time/day	3 (1-6)	3 (1-10)

COMPARISON of PREVALENCE of BLOOD-TRANSMISSION INFECTIONS

	HIV (-)	HIV(+)
	%	%
HTLV	80	76
HCV	100	100
anti HBc	96	86
HBsAg	18	16
Toxoplasmosis IgM-IgG	6-2	3-9
Varicella-Zona IgM-IgG	2-98	1-99
CMV IgM-IgG	0-98	0-100
Herpes virus IgM-IgG	0-100	0-99
TPHA	29	27

**SOME IDUs REMAIN HIV-NEGATIVE
EVENTHOUGH STRONGLY EXPOSED TO HIV
*EUs (Exposed Uninfected)***

ARE THEY RESISTANT TO HIV INFECTION ?

OBJECTIVES

**RESEARCH OF NATURAL RESISTANCE TO HIV
INFECTION AMONG HIGHLY EXPOSED UNINFECTED
IDUs**

STUDY POPULATION

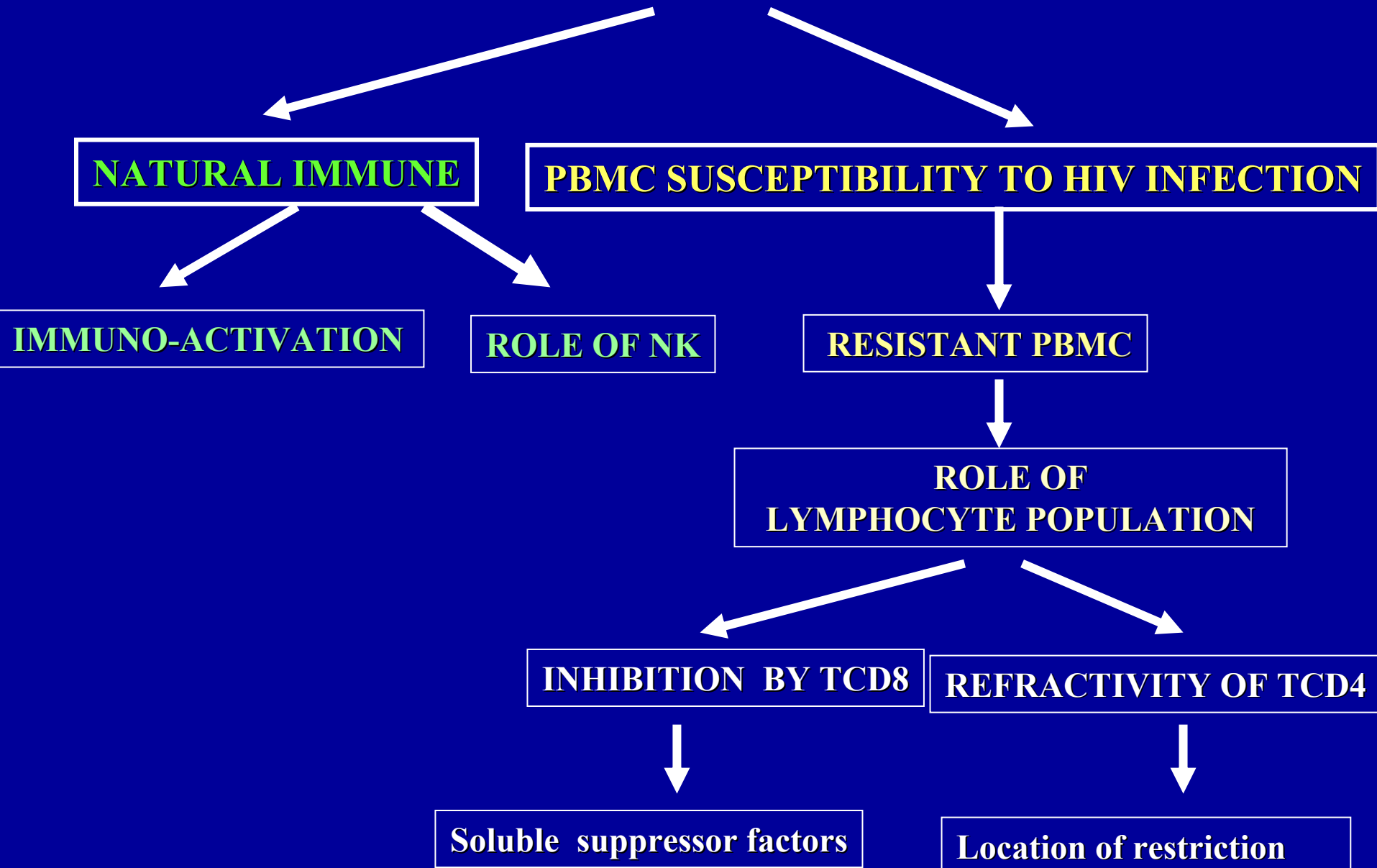
45 EUs

*Follow up during
1996-1998*

50 Controls

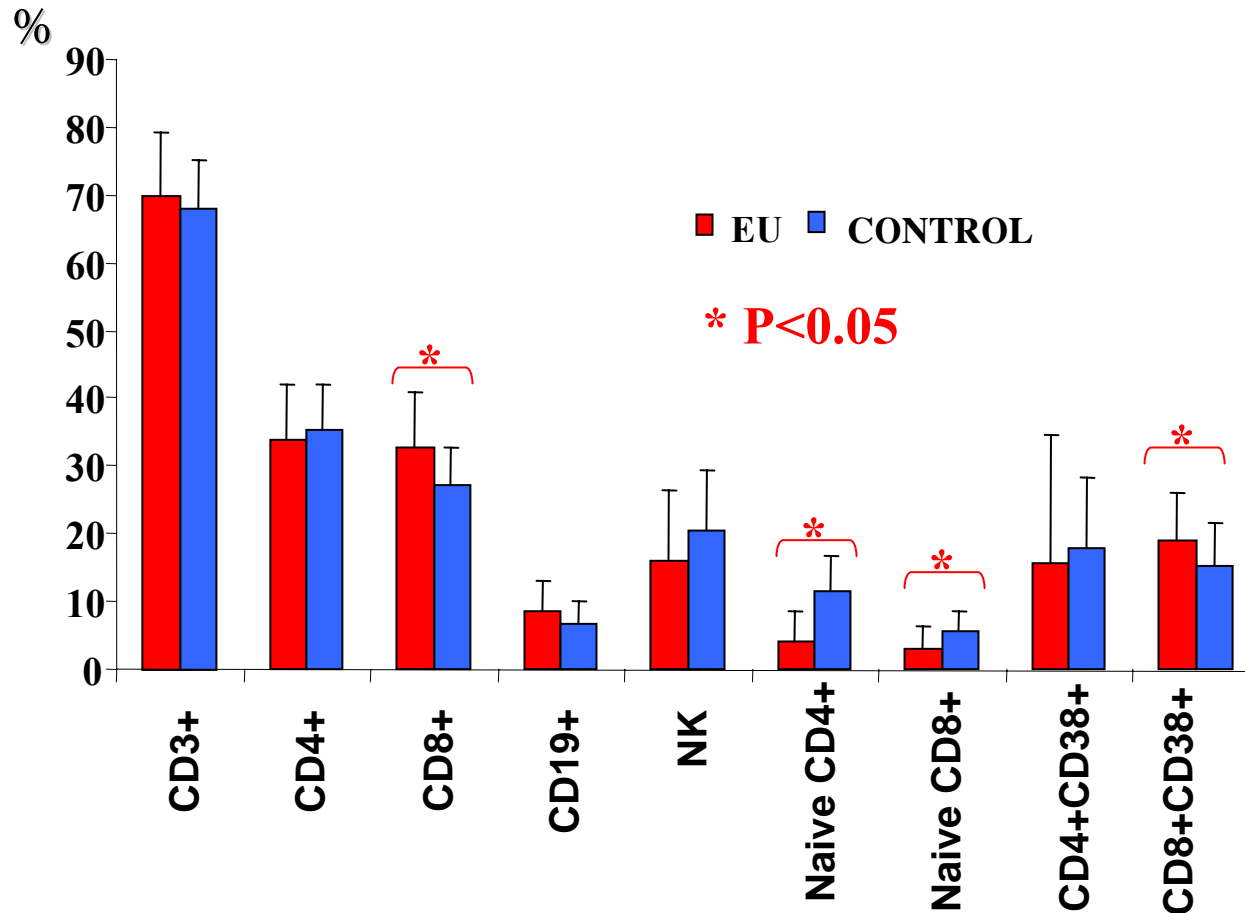
- Injecting drug (≥ 10 yrs)
 - Shooting galleries and/or needle sharing
 - HBV(+), HCV(+), HTLV(+)
 - **HIV-negative** by Serological & PCR diagnosis
- on samples collected during follow-up
- Low risk control : blood donors
 - HIV, HBV, HCV, HTLV : negative

FACTORS OF NATURE RESISTANCE TO HIV INFECTION



OBJECTIVE 1 : IMMUNO-ACTIVATION

Lymphocyte markers analyzed by FACS



Increasing of TCD8+ & memory T cell sub-populations in EUs

↙ *Peripheral immune activation in EUs*

CONCLUSION (1)

Increasing activation of immuno-system



ROLE OF NATURAL IMMUNE?

NK ACTIVATION ?

OBJECTIVE 2: NATURAL KILLER ACTIVITY

Subjects

- * 37 EU individuals
- * 28 Blood donors (CONTROLS)
- * 10 IDUs seroconverted during the follow-up
(*blood samples taken before & after seroconversion*)

NK cell cytokine production

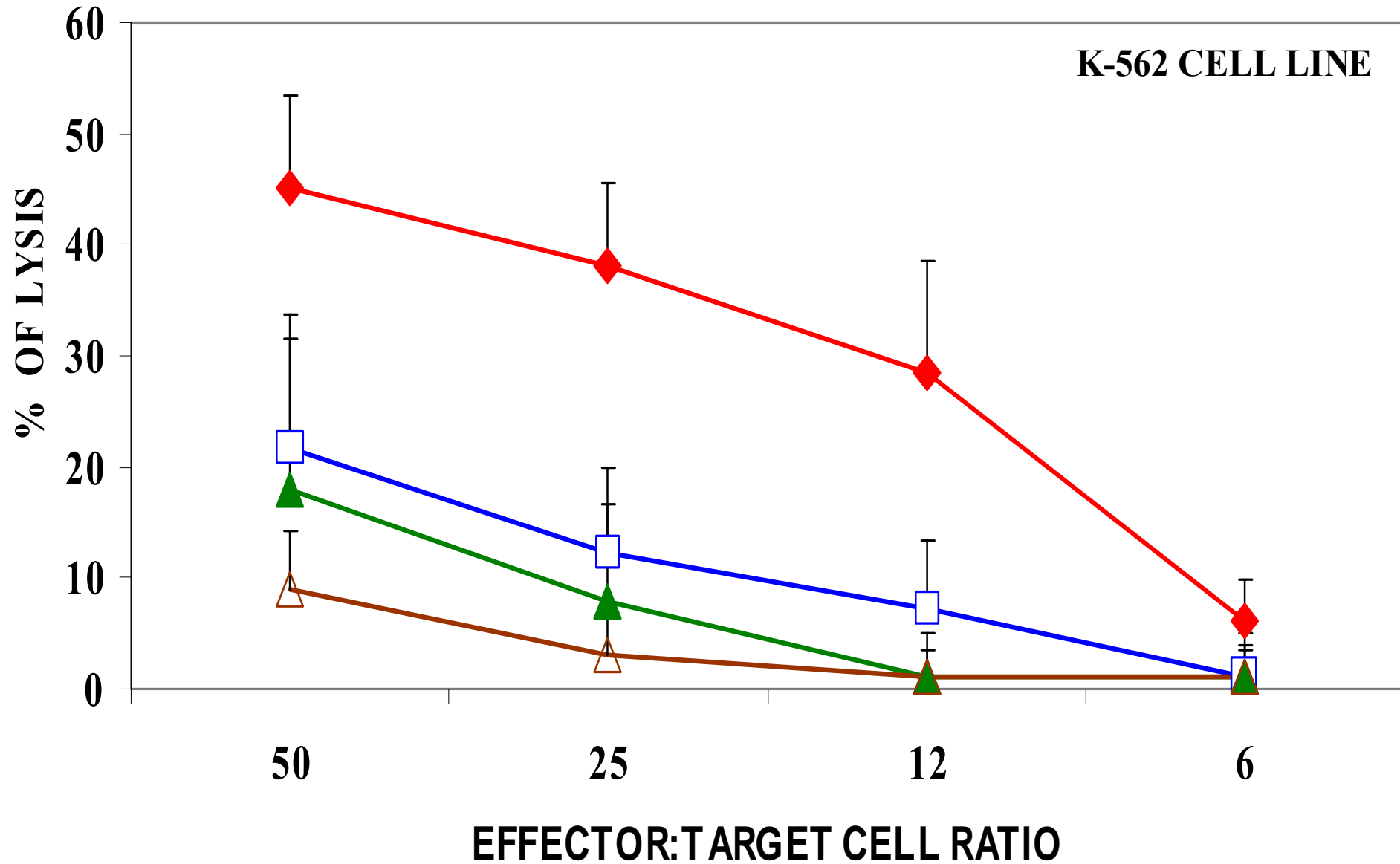
- * Intracellular staining , Flow cytometry analysis

NK cell cytotoxicity

- * Standard ⁵¹Cr-release assay (K562 target cells)

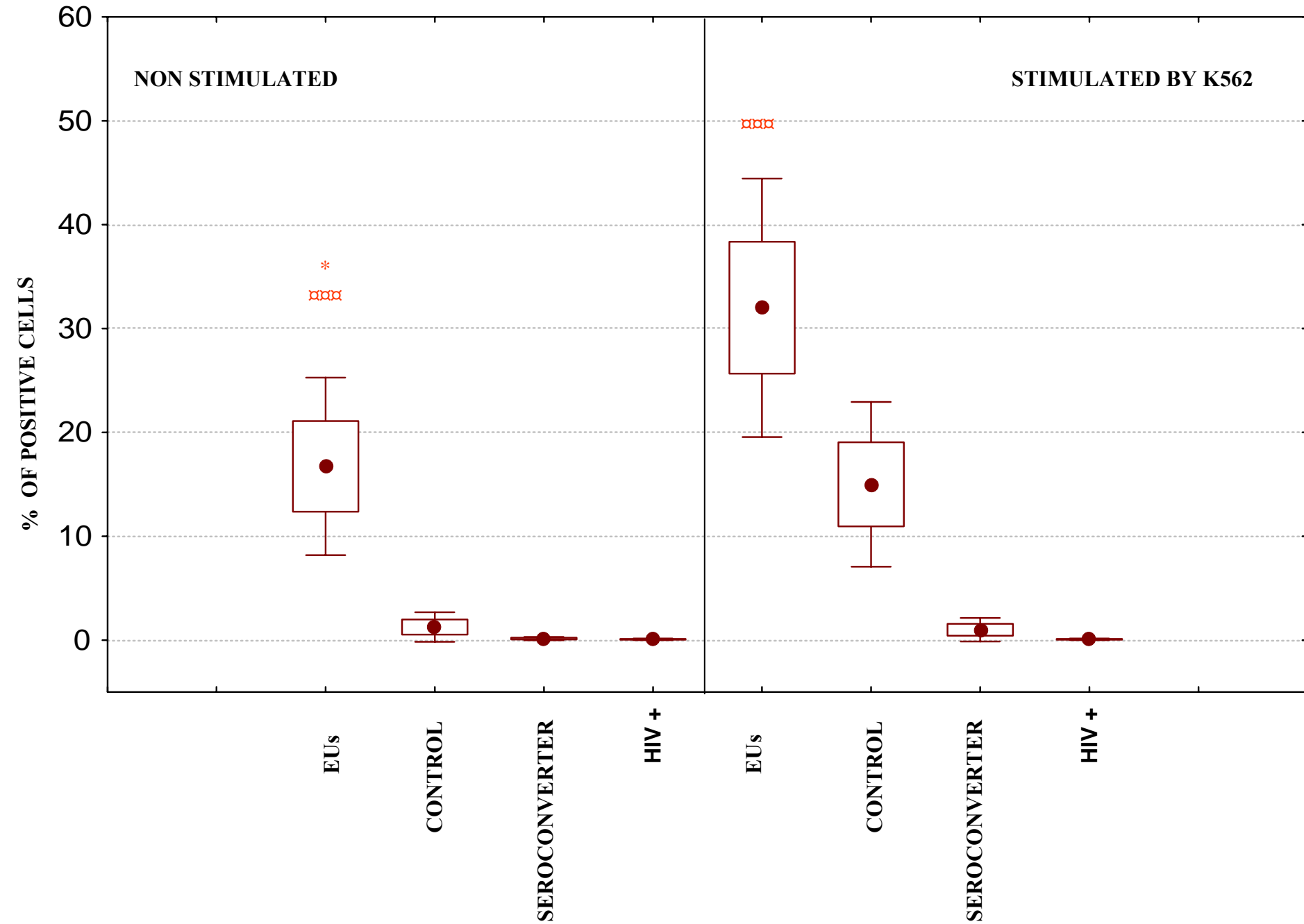
NK CYTOTOXIC ACTIVITY

K-562 CELL LINE

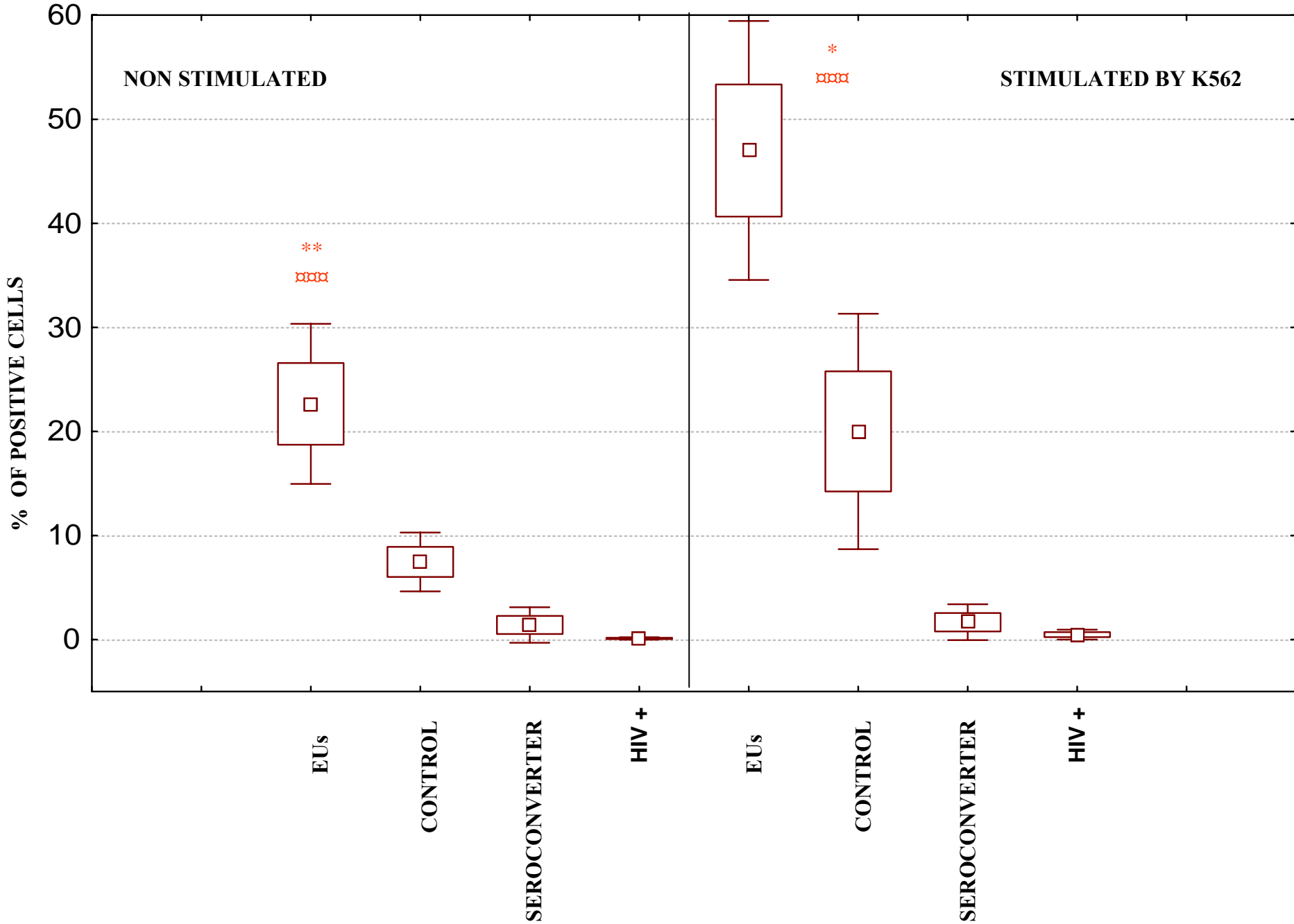


◆ EUS □ CONTROLS ▲ CONVERTERS △ HIV+

PRODUCTION OF IFN γ BY NK



PRODUCTION OF β CHIMIOKINE BY NK



CONCLUSION (2)

EU_s: Increasing NK cytotoxic and secretory activities

ॐ **Lysis** K562 target cells

ॐ **Production of cytokine**

ॐ **Activation of NK *in vivo*.**

OBJECTIVE 3

PBMC SUSCEPTIBILITY TO HIV-INFECTION

PHA-activated PBMC (EUs & Controls) infected by

3 HIV-1 isolates : - **Tropism R5 (BaL)**

- **Tropism X4 (NL4.3)**

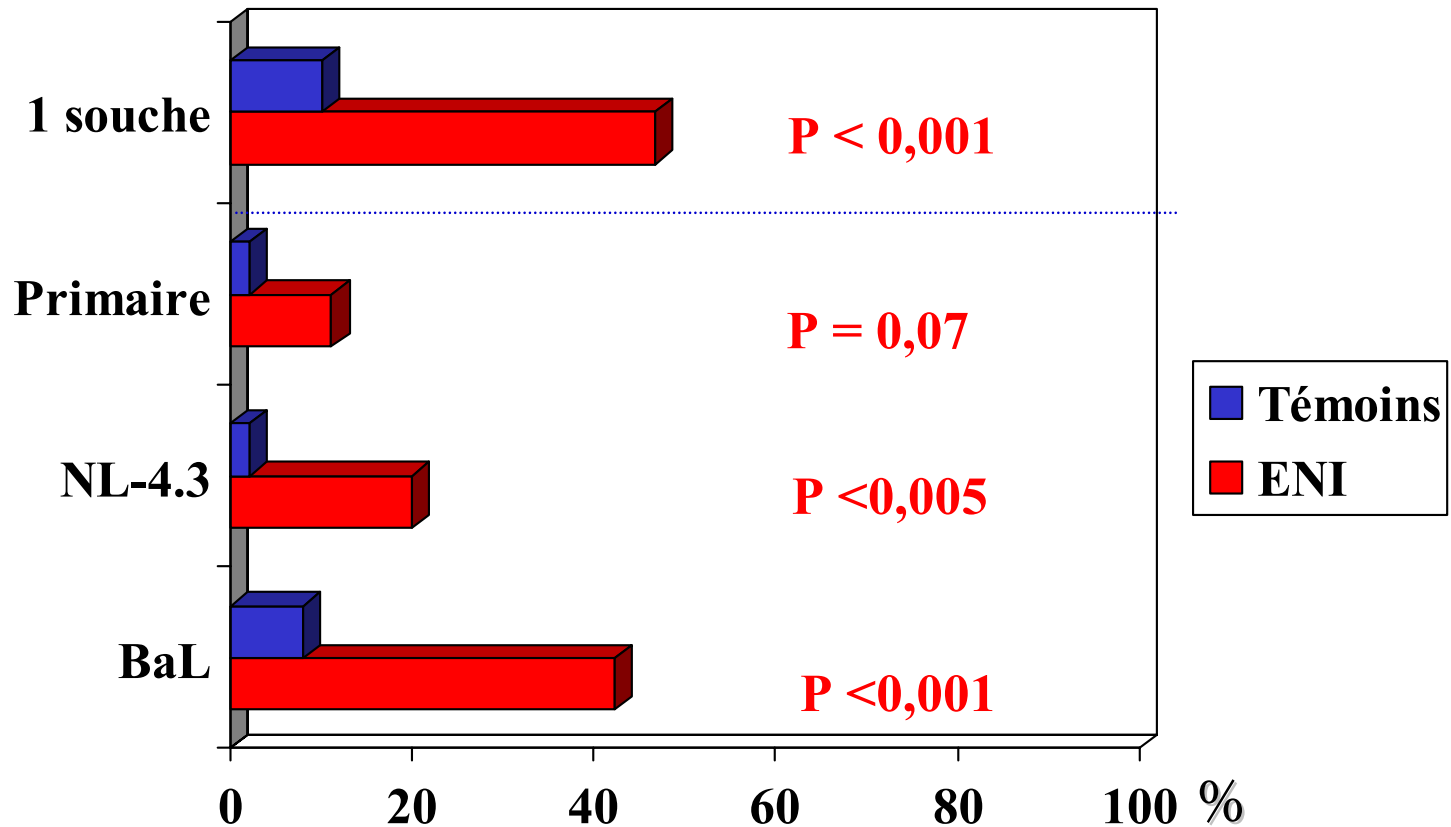
- **Primary vietnamese R5-X4 (W132)**



Reduced susceptibility of PBMC

> 1 log reduction in p24 production / standard PBMC

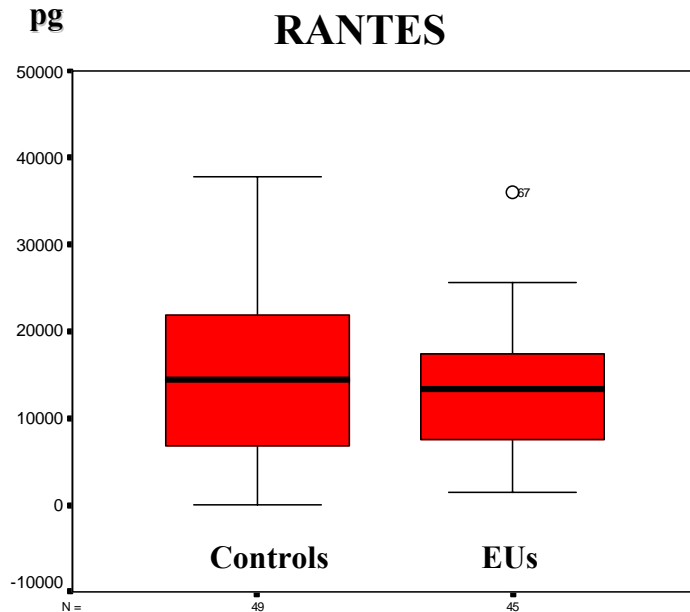
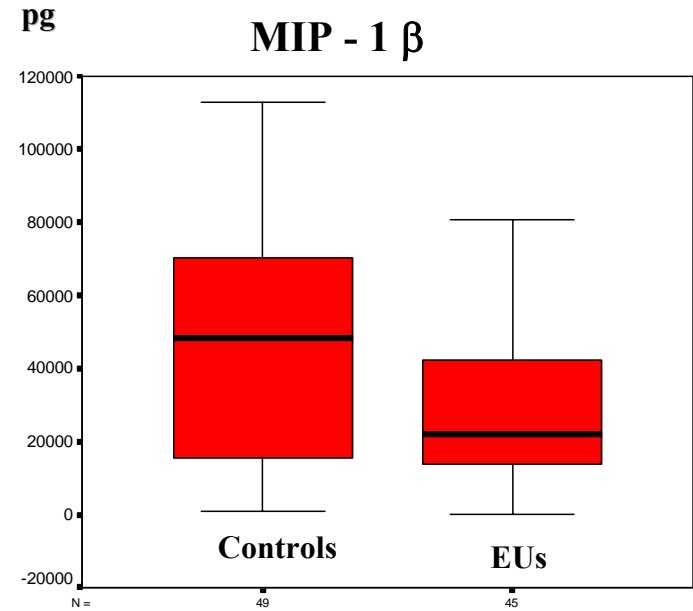
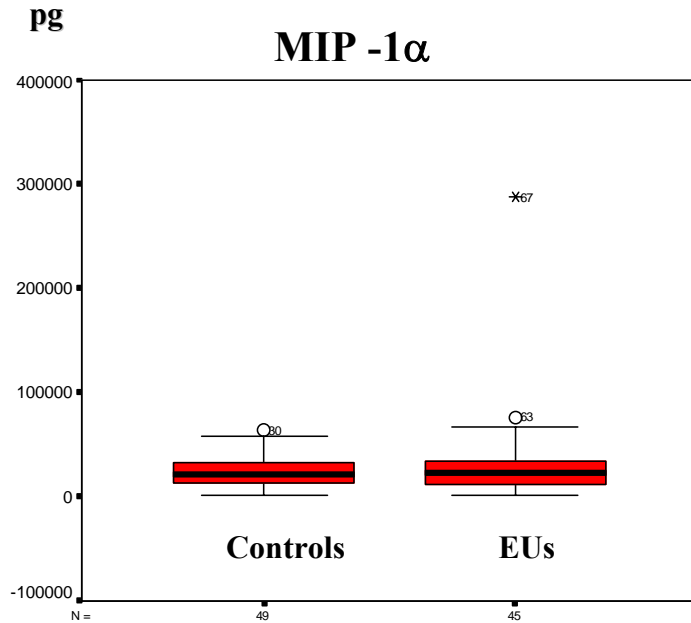
REDUCING SUBCEPTIBILITY OF PBMCs TO HIV-1 INFECTION



PBMCs of 46% EUs resistance to at least 1 virus

In most cases PBMCs were resistant to R5 HIV-1 BaL

BETA-CHEMIKINE PRODUCTION



**No statistical difference
between EUs and control groups
in the level of β -chemokine
secretion**

CONCLUSION (3)

**PBMC of some ENI resistance/ reducing susceptibility
to HIV-1 infection**

Non increasing β -chimiokines producing from PBMC



Inhibitory role of TCD8+?

Refractivity of TCD4 + ?

Other factors ?

RESISTANT PBMC TO HIV INFECTION

? Role of sub.population lymphocyte

CD4 + CD8 + virus

Inhibition by CD8+ cells

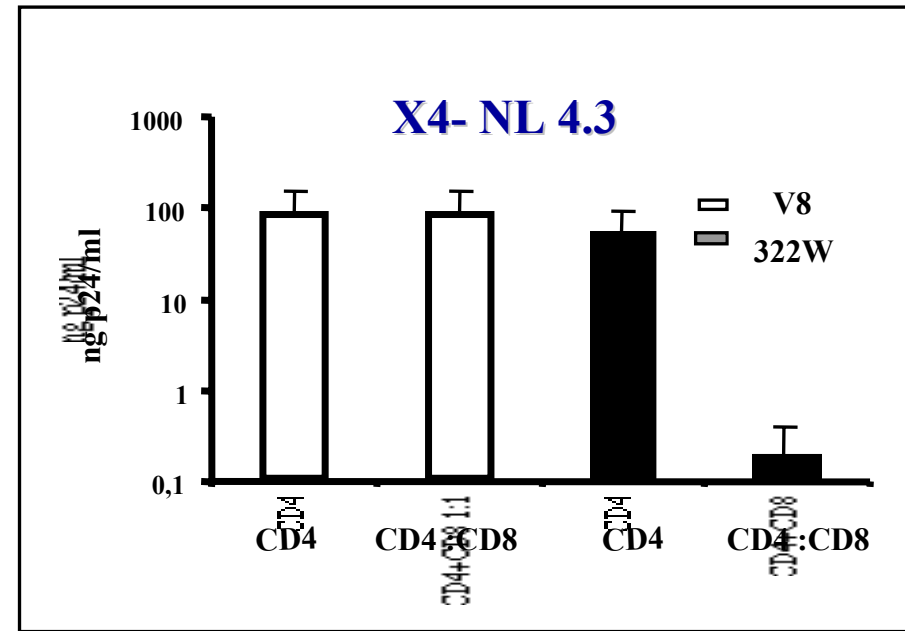
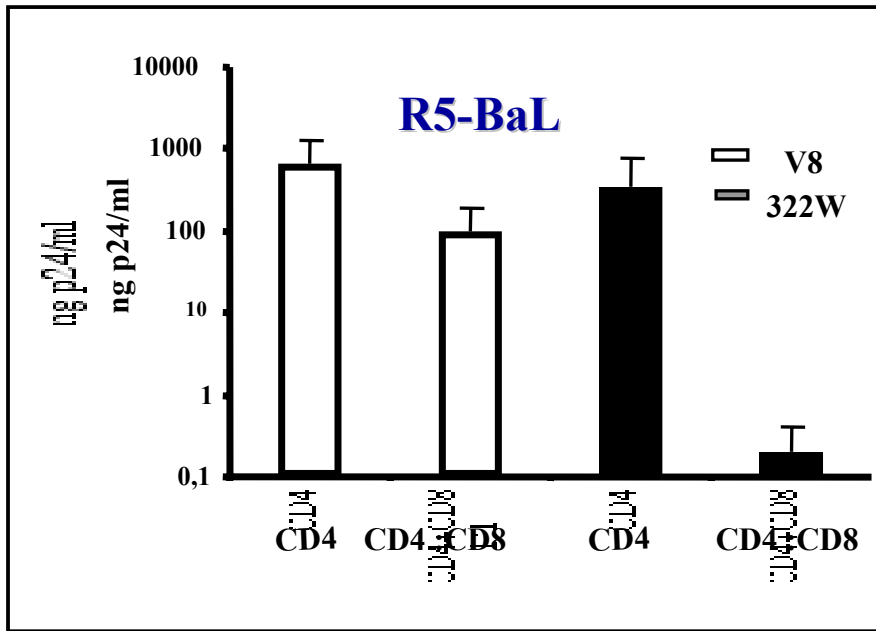
Soluble suppressive factors

CD4 + virus

Refractivity of CD4+cells

Location of restriction

CD8+ CELL SUPPRESSION OF HIV-1 INFECTION



Tropism independent CD8+ cell HIV-1 suppression

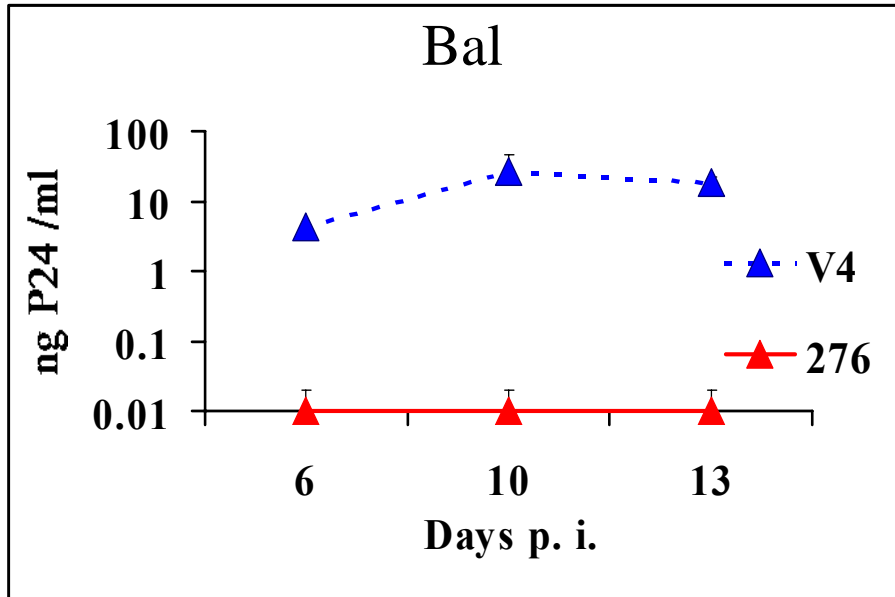
CONCLUSION (3.1)

ॐ T CD8 OF EU_s INHIBIT REPLICATION OF HIV-1

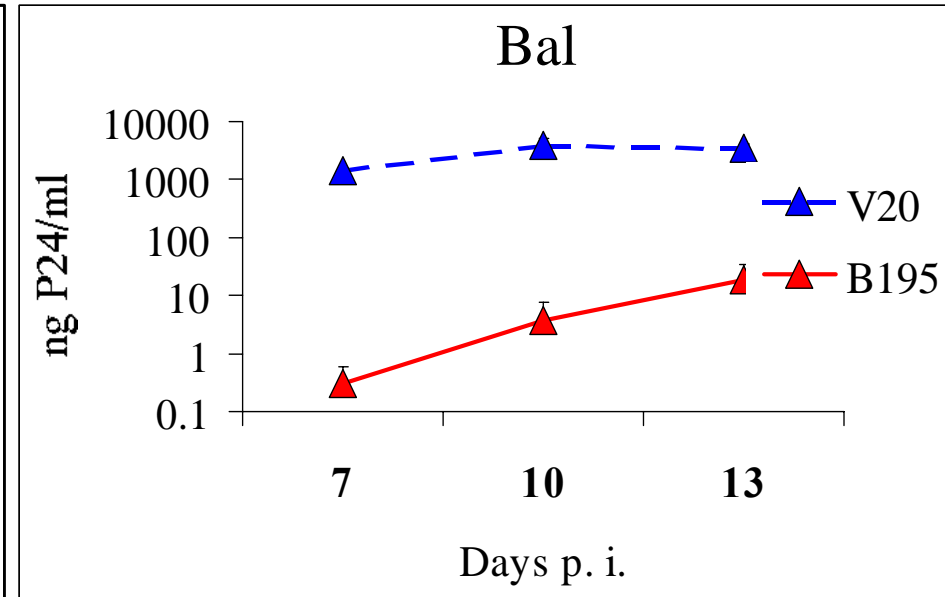
ॐ INHIBITATION TO BAL ISOLATE, AND POSSIBLE TO OTHER ISOLATES

TCD8 ==> INHIBITORY MECHANISM OF VIRUS ?

CD4+ CELL RESTRICTION OF HIV- REPLICATION



Resistant CD4 +



Reducing suceptibility CD4+

CONCLUSIONS

Resistance of Vietnamese EUs is associated with:

- 1. Increasing immuno-activation**
- 2. Increasing NK cytotoxicity and secretory activities**
- 3. Relative resistance of PBMC to HIV-1 infection**
 - viral suppression by CD8+ cells**
 - Replicative retraction of virus by CD4+ cells.**

PERSPECTIVES

- *CHARACTERISATION OF NK CELLS IN ASSOCIATING TO HIV-1 RESISTANCE*

- *CHARACTERISATION OF SOLUBLE SUPPRESSIVE FACTORS OF TCD8 CELLS*

- * *INHIBITORY MECHANISM OF TCD4 CELLS*

COLLABORATIVE TEAMS

- *Pasteur Institute HCMC*
- *Pasteur Institute Paris*
- *Binh Trieu Hospital*

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