

Role of NK cells in HIV inhibition by antibodies

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HIV vaccination

■ Adaptative immune response

- cellular immunity : Cytotoxic T lymphocytes
- humoral immunity : neutralizing antibodies (NAbs)

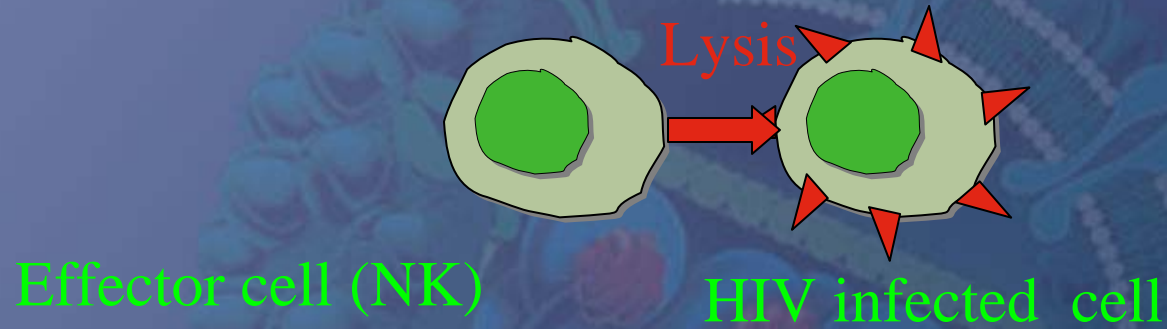
■ NK cells : link between innate and adaptative immunity

- NK cells participate in both cellular and humoral immunity by the induction of ADCC (antibody-dependent cellular cytotoxicity)
=> HIV-1 specific Abs binding to Fc γ RIII (CD16)

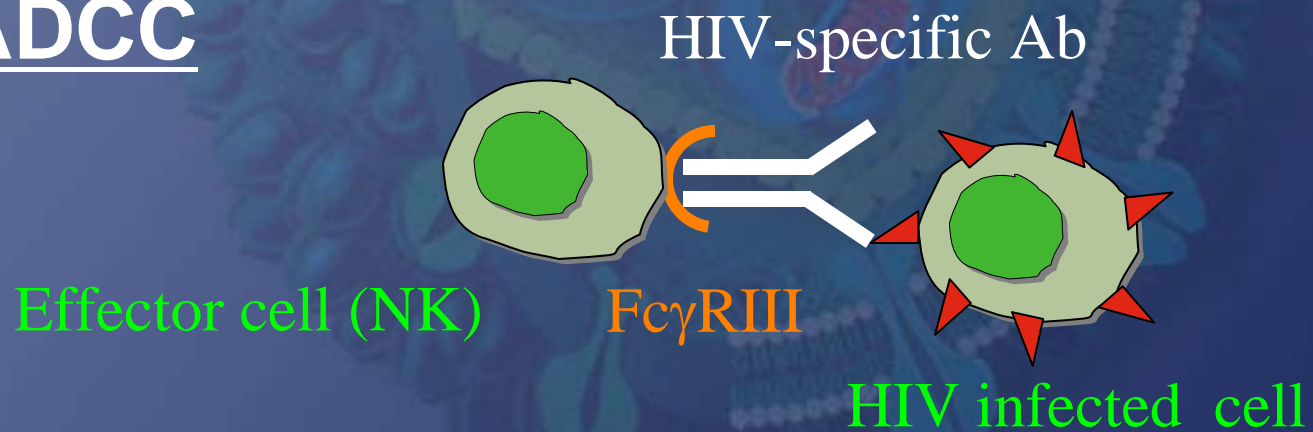


NK inhibition

Lysis



ADCC



Lysis of infected cells



Study of HIV-inhibitory Abs: Role of NK cells

- In HIV neutralization assay (conventional assay)
 - inhibition of HIV replication *in vitro*
 - target : PHA-stimulated PBMC (peripheral blood mononuclear cells)
 - presence of NK cells

AIM:

=> What is the contribution of NK cells in HIV inhibition by Abs in this assay ?



Experimental conditions

- neutralization assay :

One round of infection

Detection of intracellular Gag p24 by flow cytometry

IC90: 90% reduction of HIV-infected cells

- primary HIV target cells used:

(●) PHA-stimulated PBMC (conventional neutral. assay)

(●) PHA-stimulated PBMC depleted in CD56⁺ NK cells

(●) depleted PBMC + 50% of activated NK cells

(●) depleted PBMC + 10% of activated NK cells

(purified NK cells were activated with IL-2 for 2 days)

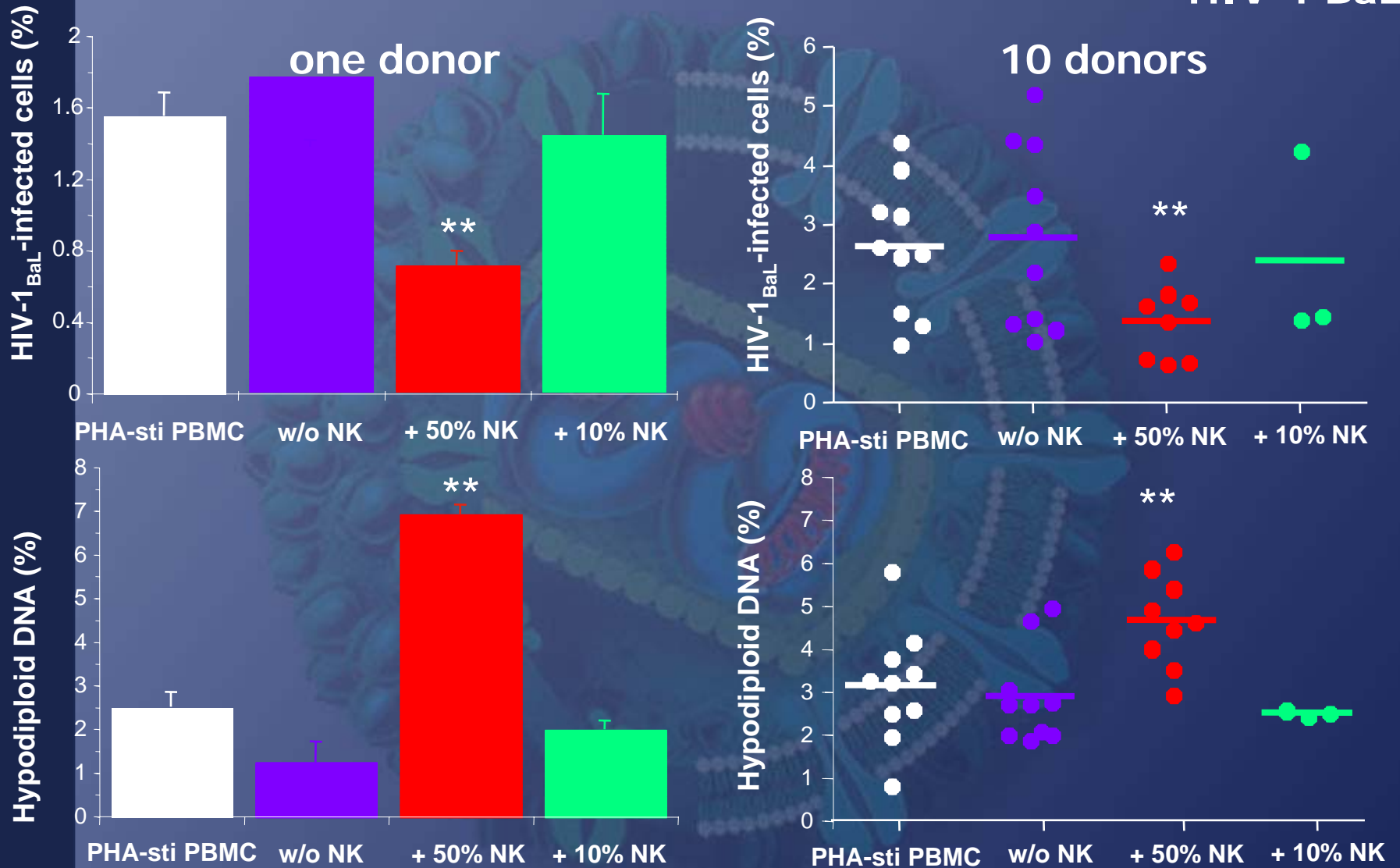
- HIV primary isolates :

R5 HIV-1 strains



Role of NK cells in the absence of Abs

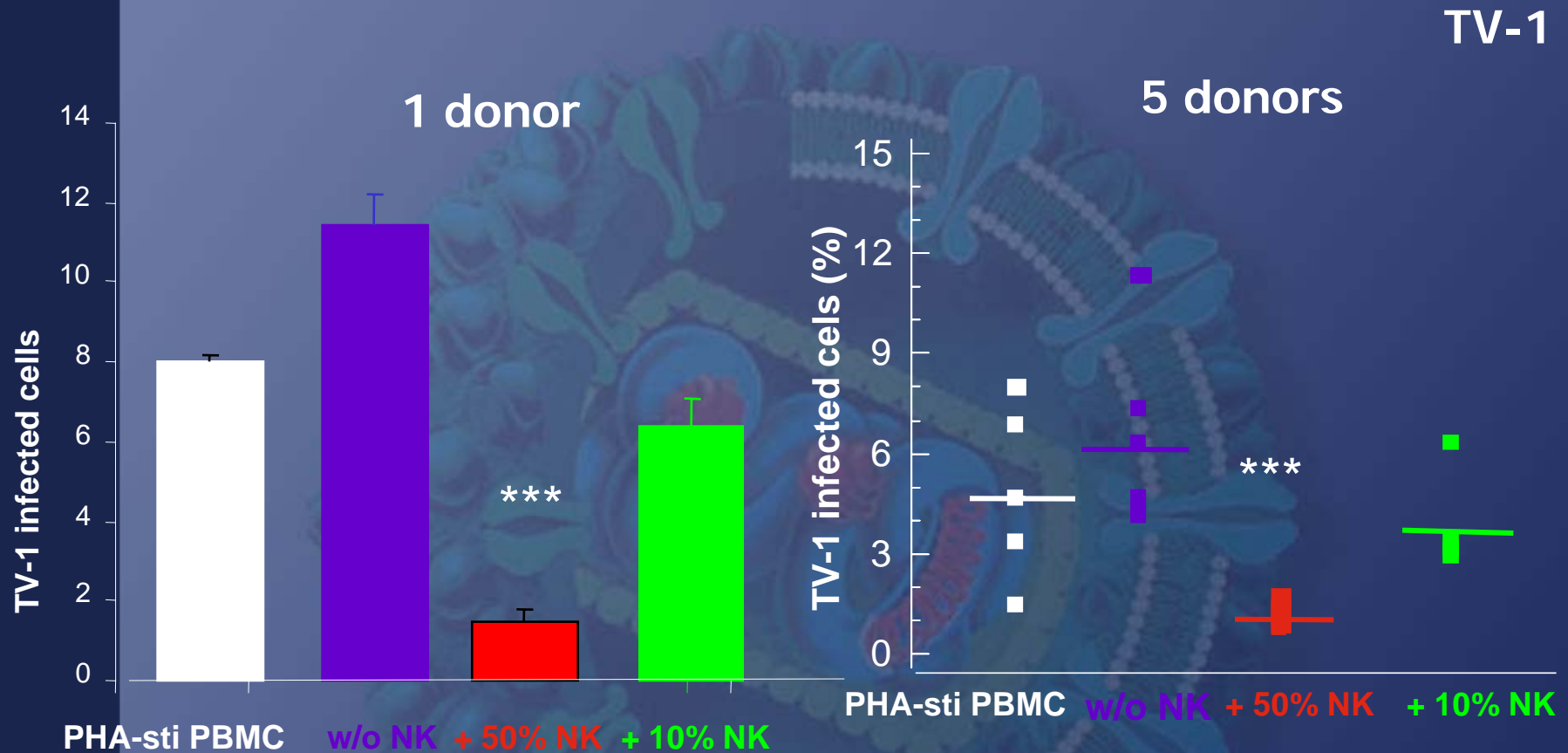
HIV-1 BaL



Detection of direct lysis of HIV-infected cells in presence of 50% NK



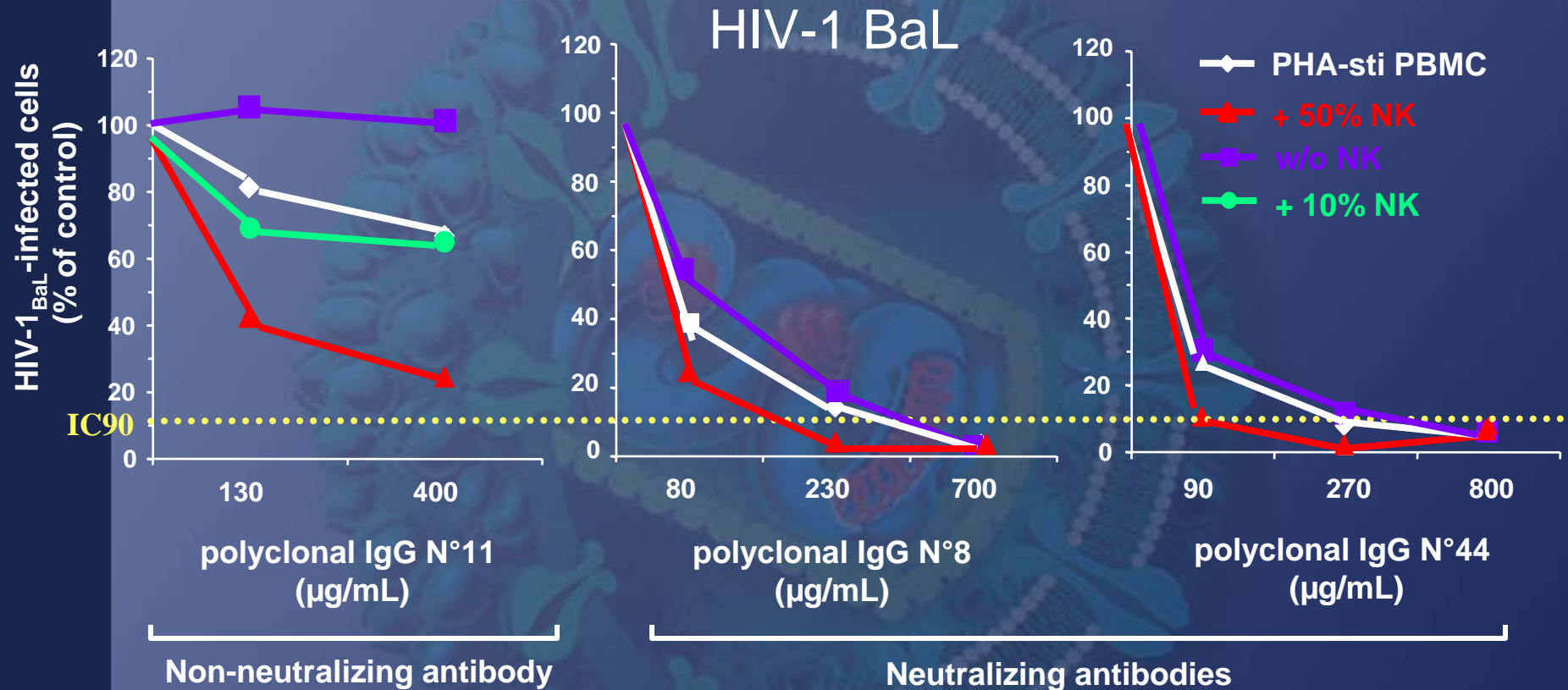
Role of NK cells in the absence of Abs



Detection of direct lysis of HIV-infected cells in presence of 50% NK, but inhibition of infected cells by NK is limited in PHA-stimulate PBMC.



Role of NK cells in the presence of polyclonal Abs



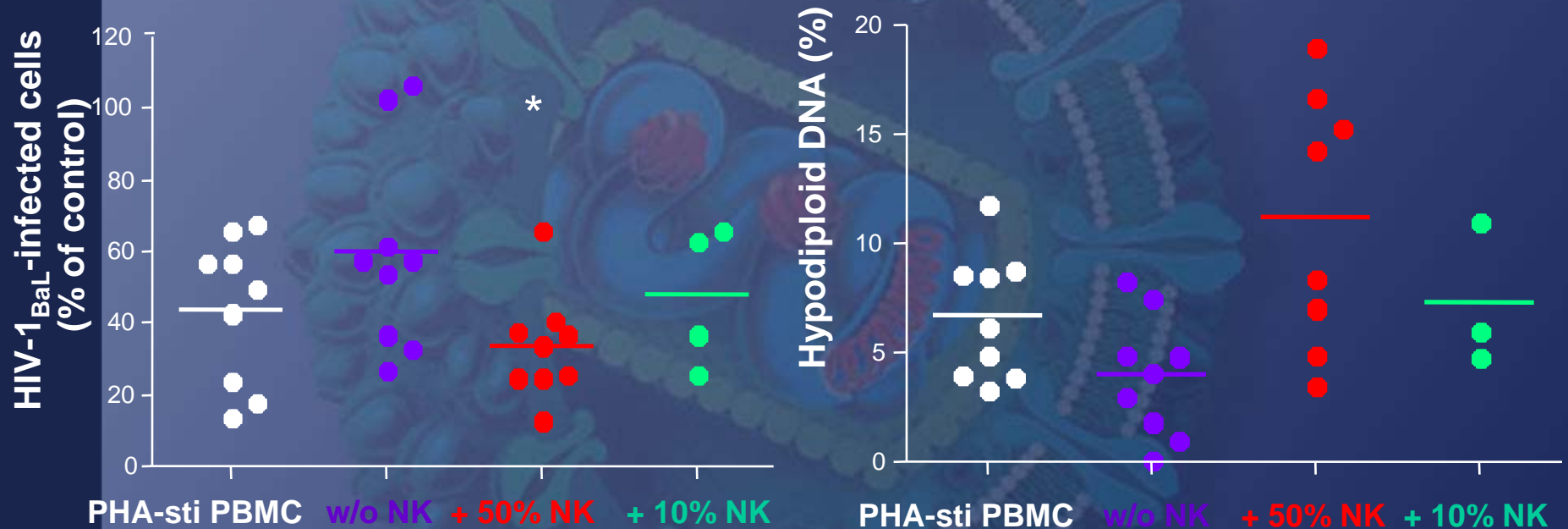
NK cells participate to HIV inhibition by Abs

- in presence of high percentage of NK cells
- is Ab concentration dependent



Role of NK cells in the presence of polyclonal Abs

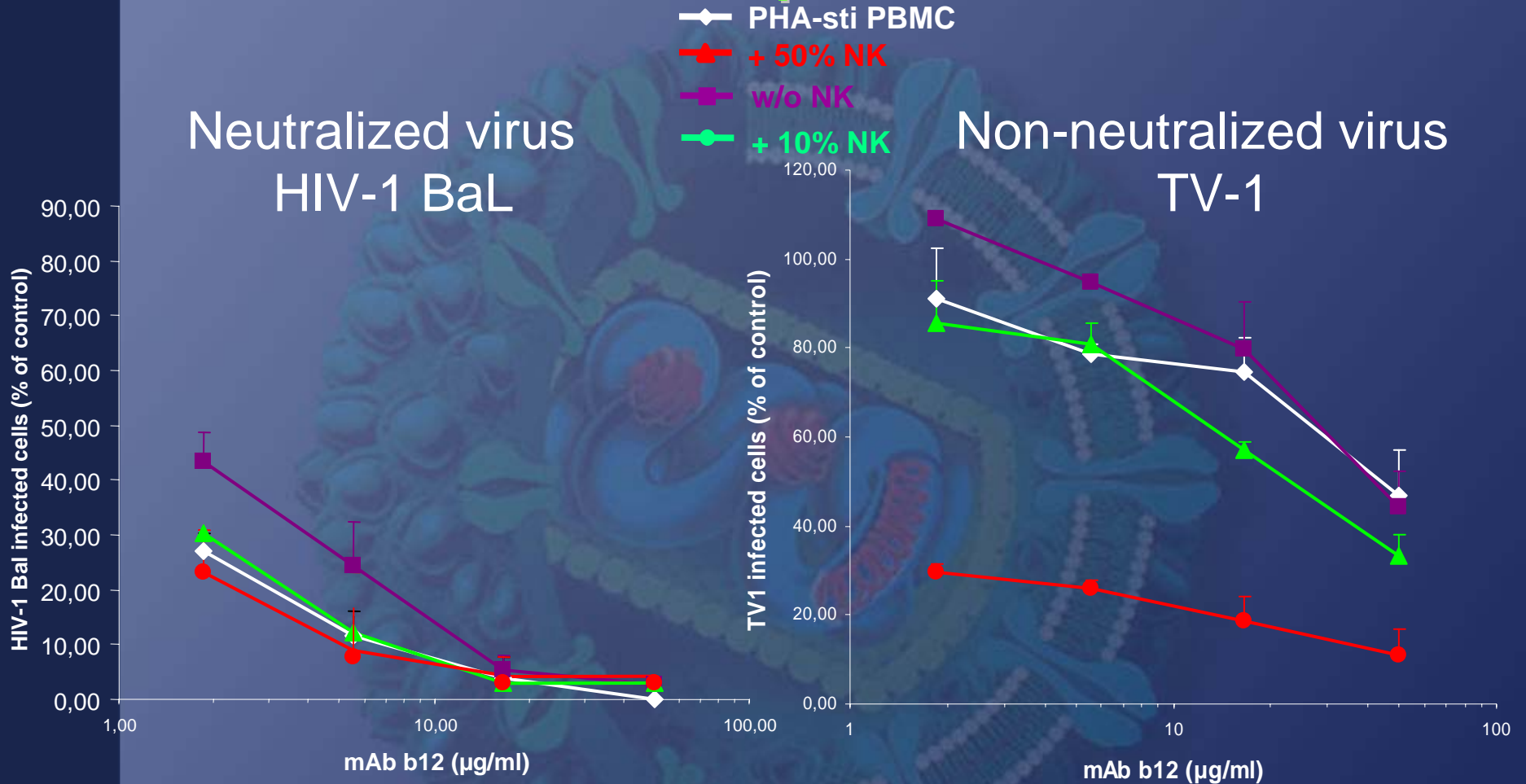
IgG N°11 at 400 µg/mL



-Significant inhibitory effect with 50% NK
-correlates with % hypodiploid DNA



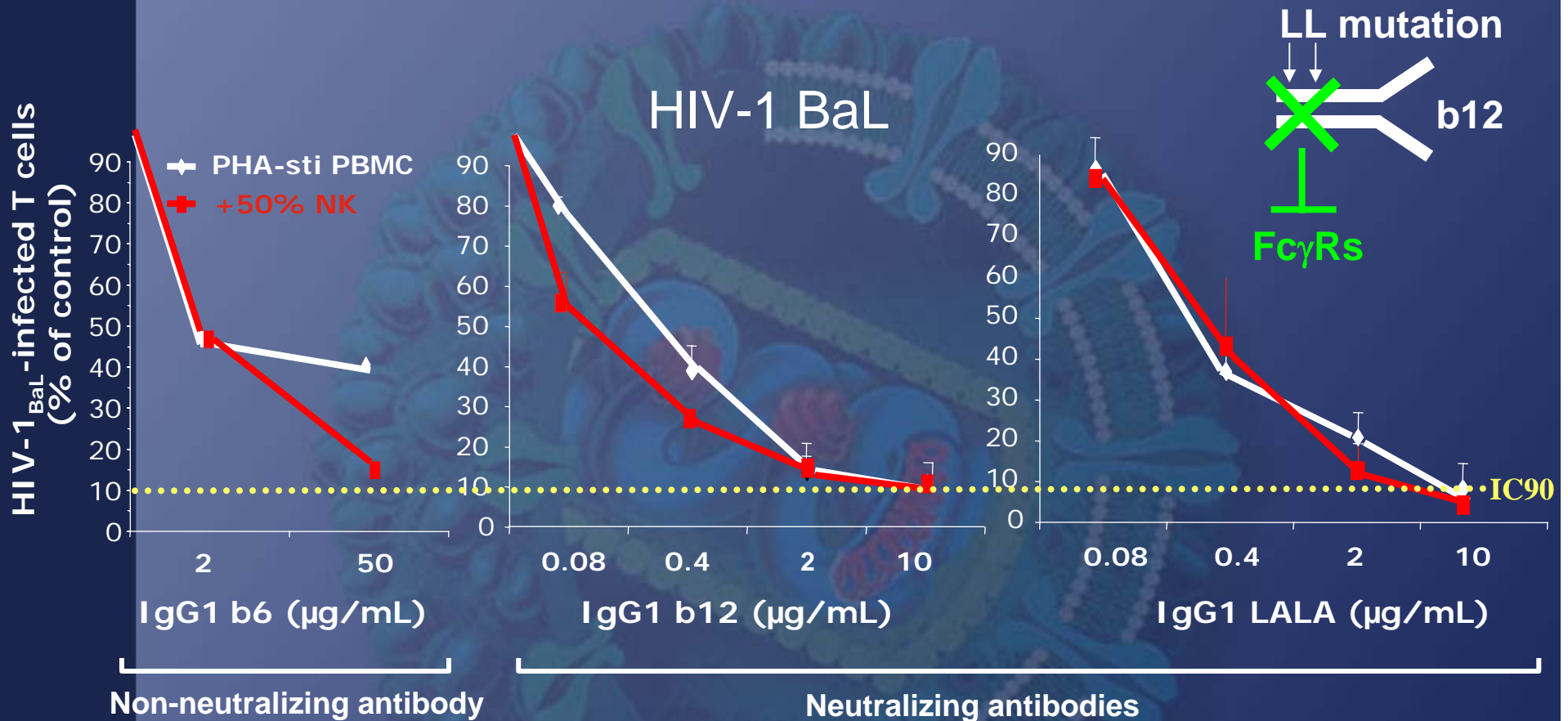
Role of NK cells in the presence of mAb b12



The contribution of NK cell in HIV inhibition in neutralizing assay is limited
NK cells, when present at high concentration, participate to HIV inhibition



Role of Fc γ R in NK inhibition by Abs

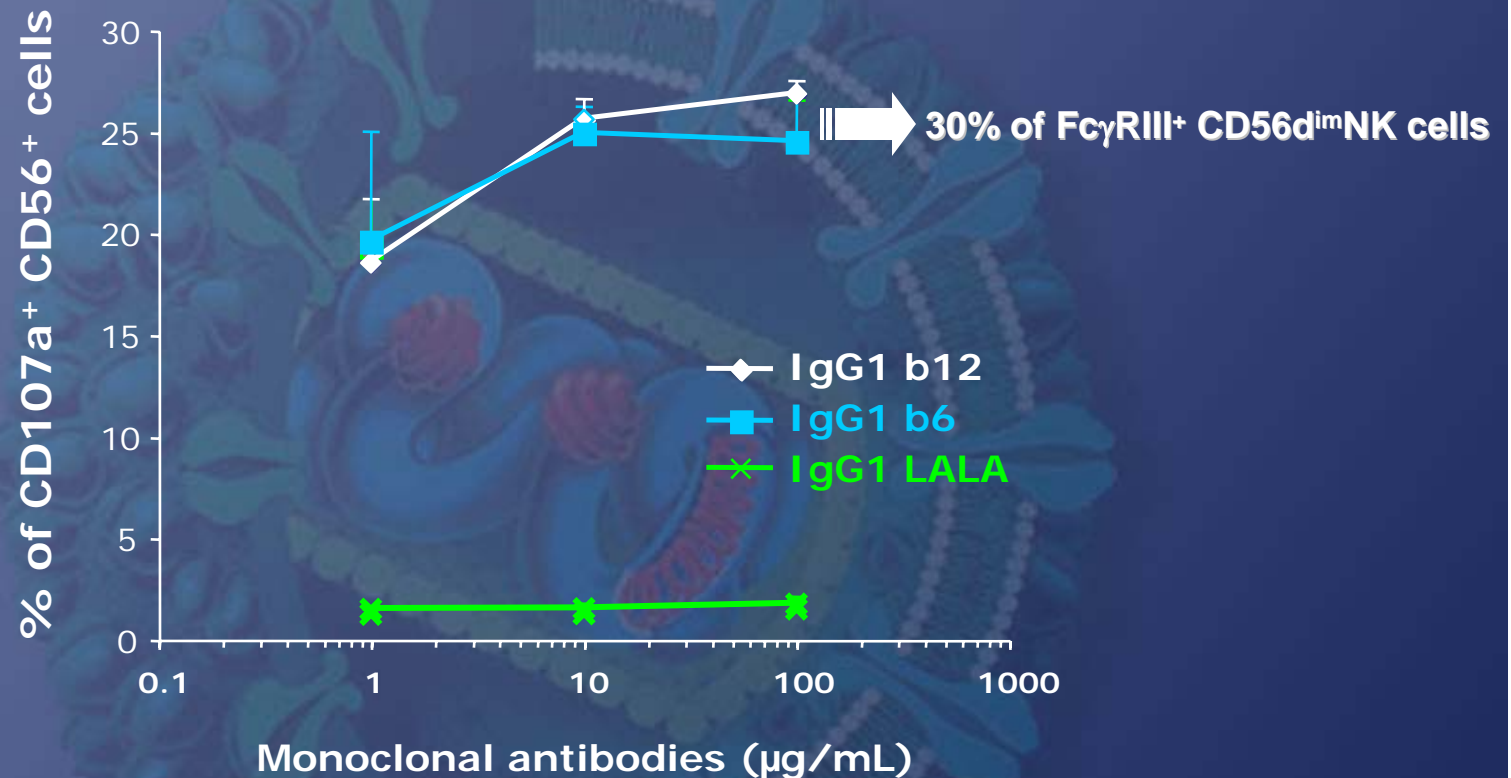


ADCC NK inhibitory activity involves Fc γ R

NK cells induce degranulation ?



Degranulation of NK cells in presence of Abs



Similar degranulation activities

for non-neutralizing Ab b6
for neutralizing Ab b12

No degranulation activities

for neutralizing Ab LALA



Conclusions

In the absence of Abs,

NK decrease HIV infected cells when present at 50% in PHA-stimulate PBMC.

In the presence of Abs,

- NK cells participate in HIV inhibition by inducing ADCC. However, this effect is only detected with high % of NK cells.
- In conventional neutralisation assay, NK inhibitory activity is very limited.

In the presence of both non-neutralizing and neutralizing Abs,

degranulation occurs ($=>$ ADCC)
and is concentration-dependent

In vivo?



Role of NK cells in HIV inhibition by antibodies

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