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Poster presentation

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PI9-25. A vaccine model to prevent the depletion of uninfected bystander CD4 cells during HIV infection

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Background

The CD4 depletion in the chronic phase of HIV infection is mostly due to the loss of uninfected cells. We recently showed that the expression of NKp44L, a cellular ligand of an activating NK receptor was exclusively expressed on non-infected CD4 cells from HIV-infected patients. NKp44L is specially induced by the highly conserved 3S motif of the HIV-1 gp41 envelope protein. In this study we sought to determine whether the loss of uninfected bystander CD4 cells could be prevented by an anti-3S vaccine.

Methods

Ten cynomolgus macaques were primed/boosted in IFA with 3S-KLH or free KLH, as control. Sixteen weeks after the last immunization, all animals were challenged IV with the SHIV162P3. Peripheral and lymphoid lymphocyte samples were periodically tested.

Results

We discovered that 1) During HIV infection, uninfected CD4 cells exclusively express NKp44L; 2) In a macaque model of SHIV162P3 infection, a 3S-KLH immunization significantly decreases NKp44L expression on CD4 cells, NK cells cytotoxicity and apoptosis, when compared to infected control group immunized with free KLH. Interestingly, the CD4 cells level of immunized animals remains stable, while it decreased in the control group.

Conclusion

These results emphasize the deleterious role of NK cells on the depletion of uninfected bystander CD4 cells. They

also present new opportunities for HIV vaccine strategies, which should subsequently inhibits and/or delay the disease evolution to AIDS.