RETROVIROLOGY

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Towards a vaccine against AIDS

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Aim

The CD4 depletion in the chronic phase of HIV infection is mostly due to the loss of uninfected cells. We previously showed that this lost was related to the expression of NKp44L, a cellular ligand of the natural cytotoxicity receptor NKp44, which renders CD4 cells sensitive to NK killing. NKp44L is specially induced by the highly conserved 3S motif of the HIV-1 gp41 envelope protein. We also have shown that NKp44L is present on bystander non-infected CD4 cells, but absent from HIV-infected cells, through a Nef-dependent mechanism. In this study we sought to determine whether the loss of uninfected bystander CD4 cells could be prevented by a 3S therapeutic immunization in a macaque model chronically infected with SHIV162P3.

Methods

Ten cynomolgus macaques were chronically infected with SHIV162P3. Seven months after infection, the animals were primed/boosted in IFA with 3S-KLH or free KLH, as control. Lymphocyte samples and sera were periodically tested, while secondary lymphoid organs after euthanasia, at 7 months post-immunization.

Results

We discovered that immunization with 3S-KLH, significantly decreases of NKp44L expression on CD4 cells, and NK cells cytotoxicity against autologous CD4 cells, when compared to infected group with free KLH-immunization. Interestingly, the frequency of CD4 central memory T cells from immunized animals remains stable, while decreasing in the control group. Finally, in lymphoid organs, including spleen, lymph node and gut, a significant decrease of the cell-activation and the caspase-3 dependent apoptosis was observed in macaques immunized by 3S-KLH, as compared to control.

Discussion

These results emphasize the deleterious role of NK cells on CD4 depletion and demonstrate for the first time, its prevention by a therapeutic vaccine, which should also inhibits and/or delay disease evolution to AIDS.

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