HIV escape from natural killer cytotoxicity: Nef inhibits NKp44L expression on HIV-infected CD4\(^+\) 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+ T cells from HIV-infected patients

Vieillard et al (Proc Natl Acad Sci USA 2005)
NK cells and HIV-infected CD4+ T cells


Inhibition of NKp44L expression in CD4+ T cells infected by HIV-1 strains and viremic HIV-infection patients

Fausther-Bovendo et al. (AIDS 2009)
Inhibition of NKp44L expression in CD4+ T cells by Nef

Recombinant vaccinia viruses

HIV-p24

E/T ratio

% NK lysis
Effect of G2A Nef mutant on the NKp44L expression

Mechanism of Nef is dependent on the myristoylation
Effect of Nef mutants on NKp44L expression

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

HIV- p24

E/T ratio

% NK lysis

100/1 50/1 25/1 12.5/1
## Effect of Nef mutants on NKp44L expression on CD4+ T cells from LTNP HIV-infected patients

<table>
<thead>
<tr>
<th>patients</th>
<th>mutation</th>
<th>Reported functionnal consequences</th>
</tr>
</thead>
<tbody>
<tr>
<td>09.016</td>
<td>Δ54-100</td>
<td>Non-functional Nef</td>
</tr>
<tr>
<td>04.048</td>
<td>E62/63G</td>
<td>Loss of interaction with PACS crucial for MHC-I and CCR5 downregulation</td>
</tr>
<tr>
<td>04.008</td>
<td>C55S/A56P</td>
<td>Non-functional clivage site by the viral protease</td>
</tr>
<tr>
<td>11.003</td>
<td>Δ155-160</td>
<td>Loss of degradation of CD4 and MHC-I via β–cop</td>
</tr>
</tbody>
</table>
Conclusion

Enhancement of Infectivity

- MHC-1 downregulation
- NEF
- ?
- NKG2D-L downregulation
- NKp44L downregulation

NK-cell inhibition
Acknowledgments

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