

Poster presentation

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## Isolated $\gamma\delta$ T cells express natural cytotoxicity receptors

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### Introduction

$\gamma\delta$  T cells account for up to ten percent of T lymphocytes in the peripheral blood of healthy donors. They can be activated by cytokines like interleukin(IL)-2 and IL-15, express natural killer (NK) cell markers such as NKG2D and show cytotoxic activity against several tumor cells. Natural cytotoxicity receptors (NKp30, NKp44 and NKp46) have so far been regarded as specific NK receptors. Resting NK cells express NKp30 and NKp46 whereas NKp44 is expressed by activated NK cells only. To date, only two  $\gamma\delta$  T cell clones expressing NKp44 have been described. There is no description of polyclonal  $\gamma\delta$  T cells expressing natural cytotoxicity receptors.

The aim of the presented study was to evaluate the expression of activating NK cell markers including NKp30, NKp44 and NKp46 on isolated  $\gamma\delta$  T cells, since these may play a role in the cytotoxic activity of  $\gamma\delta$  T cells.

### Methods

$\gamma\delta$  T cells were isolated from healthy donors to a purity of >90% by magnetic activated cell sorting and cultured in the presence of anti-CD3, IL-15 and high dose IL-2. On days 0, one and seven the expression of activation markers including NKG2D and natural cytotoxicity receptors on  $\gamma\delta$  T cells were evaluated immunophenotypically. For further confirmation, RT-PCR was performed on a light cycler for mRNA of  $\beta$ -actin, NKp44 and DAP 12, the signal transduction molecule of NKp44.

### Results

On day 0 there was little expression of NK cell marker NKG2D on isolated polyclonal  $\gamma\delta$  T cells. Expression of NKG2D was up to 85 % after one day of stimulation with

cytokines IL-2 and IL-15 and did not change significantly during further culture. On day one of culture there was a slight expression of NKp30 and NKp46 ( $14 \pm 9$  % and  $18 \pm 11$  %,  $n = 4$ ), which decreased rapidly after 7 days of culture ( $3 \pm 2$  % for NKp30 and  $2 \pm 1$  % for NKp46). Although there was no expression of NKp44 on day one of activation with cytokines, on day 7 a surface expression of up to 26 % could be determined ( $n = 22$ , mean  $8 \pm 7$  %).

In contrast isolated CD4<sup>+</sup> and CD8<sup>+</sup>  $\alpha/\beta$  T cells were consistently negative for surface expression of NKp44 after culture with high dose IL-2 and IL-15. These results could be confirmed by detection of NKp44 and DAP12 mRNA by RT-PCR from RNA from  $\gamma\delta$  T cells but not from  $\alpha/\beta$  T cells.

### Summary and conclusion

To our knowledge this is the first description of natural cytotoxicity receptors on polyclonal  $\gamma\delta$  T cells. NK cell markers are known to play an important role in the cytotoxic activity of  $\gamma\delta$  T cells. NKp44 has so far only been described on two  $\gamma\delta$  T cell clones, however, in these, an activating role could also be determined (Cantoni *et al.*, *J Exp Med*, 1999). From our results we conclude, that natural cytotoxicity receptors are not only expressed by NK cells but also by isolated  $\gamma\delta$  T cells. In further studies the role of these receptors in the cytotoxic activity of  $\gamma\delta$  T cells should be evaluated.