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IFN-? regulation

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Keywords

NFAT-1 inhibition, NFAT-1 knockout mice, T cells, transcriptional IFN-? regulation

Context

This study follows on from previous work by the same group using nuclear factor of activated T cells (NFAT)-1 knockout mice. Their previous observation was that T cells from NFAT-1 knockout mice have a strong bias to differentiate into Th2 cells, thus producing increased levels of IL-4 relative to T cells from $NFAT^{+/+}$ littermates. They have noted also that naive $NFAT^{-/-}$ T cells produced less IFN-? than naive $NFAT^{+/+}$ T cells. However, because the latter could be due to overexpression of IL-4 they created a double-deficient $NFAT^{-/-}$ $IL4^{-/-}$ line. In this study, they show that, in the absence of endogenous production of IL-4, $CD4^{+}$ T cells lacking NFAT display a cell-intrinsic defect in IFN-? production.

Significant findings

Throughout this study, the authors compare T cells from $NFAT^{+/+}$ $IL\text{-}4^{-/-}$ and $NFAT^{-/-}$ $IL\text{-}4^{-/-}$ mice. The NFAT-deficient mice exhibit reduced production of IFN-? at both the mRNA and protein levels. These results are strengthened by data from $NFAT^{-/-}$ mice displaying reduced resistance to infection by *Leishmania major* due to lack of sufficient IFN-?. In the C1.7W2 murine T-cell clone a similar reduction in IFN-? production is imposed by direct inhibition of NFAT-1 with the specific inhibitor VIVIT. The possible effect of increased GATA-3 and Maf production, both of which downregulate IFN-? expression, was excluded as no difference in the expression of these transcription factors in $NFAT^{-/-}$ $IL\text{-}4^{-/-}$ and $NFAT^{+/+}$ $IL\text{-}4^{-/-}$ T cells was observed.

Comments

In general, most of the data included in this study are very intriguing, plausible and well-presented. However, the methods used to manipulate and stimulate the T cells for each experiment are not entirely straightforward and clear, making it difficult to define the exact conditions under which each set of data are obtained. Nevertheless, the data provide good evidence that IFN-? production in T cells is regulated by NFAT-1, most likely at the level of gene transcription.

Methods

T-cell culture, ELISA, ribonuclease protection assay, northern and western blotting, knockout mice, transfections

Additional information

References

1. Kiani A, Garcia-Cozar FJ, Habermann I, Laforsch S, Aebischer T, Ehninger G, Rao A: Regulation of interferon-? gene expression by nuclear factor of activated T cells. Blood. 2001, 98: 1480-1488.