

Contrasting responses of DC and NK cells to IFN-I contribute to host resistance to viral infection

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Introduction

Type I interferons (IFN-I) are cytokines mediating potent direct antiviral activity and a multiplicity of immunoregulatory functions. IFN-I signal through the ubiquitous IFN- α receptor (IFNAR) which leads to signaling pathways that are cell-type specific. Despite their use in human therapies, the precise role of IFN-I in immune responses is not well characterized.

At day 1.5 after murine cytomegalovirus (MCMV) infection, plasmacytoid dendritic cells are the major source of IFN-I. Here we study the direct role of IFN-I in shaping dendritic cell (DC) and natural killer (NK) cell responses to MCMV infection *in vivo*.

Fig 1: cDC and pDC undergo a common transcriptional reprogramming at day 1.5 after MCMV infection.

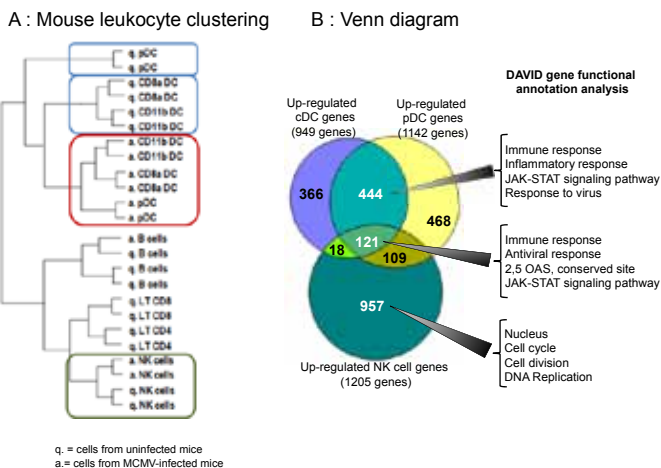


Fig 2: Contrasting roles of innate cytokine for the genetic reprogramming of DC subsets and NK cells during MCMV infection.

A: GSEA analysis of cytokine responsive genes expression in DC subsets and NK cells. B: Fold change of selected genes in DC and NK cells at 1.5 day after MCMV infection.

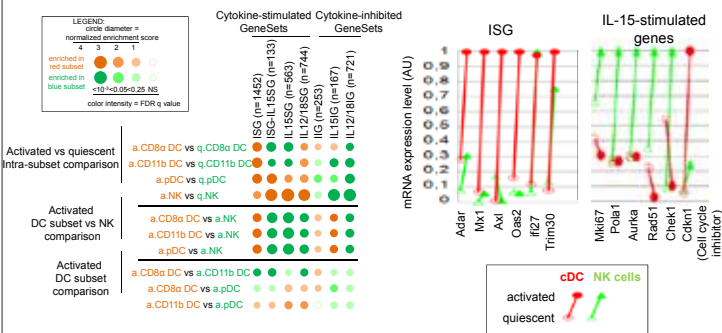


Fig 3: During MCMV infection DC subset versus NK cell genetic reprogramming occur in response to distinct signaling pathways.

A: Fold change of genes implicated in DC- and NK cell-signaling pathways.

B: Phosphorylation of STAT1 and STAT4 in chimera mice.

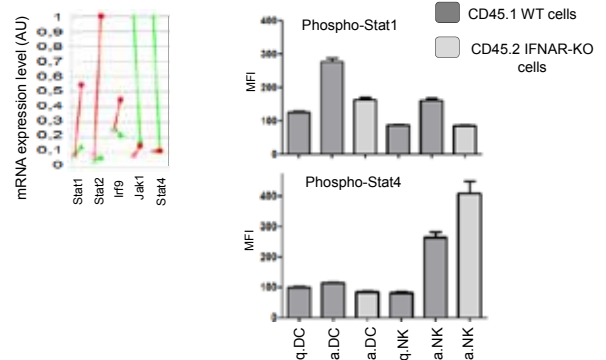
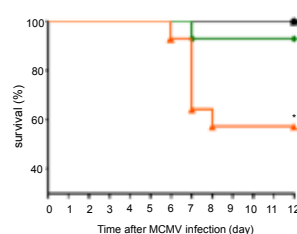
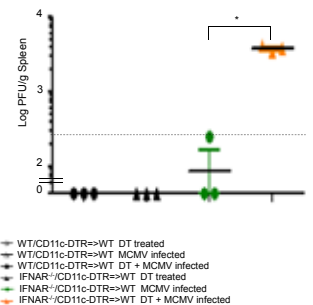


Fig 4: Cell-intrinsic responses of DC to IFN-I are critical to control MCMV infection.

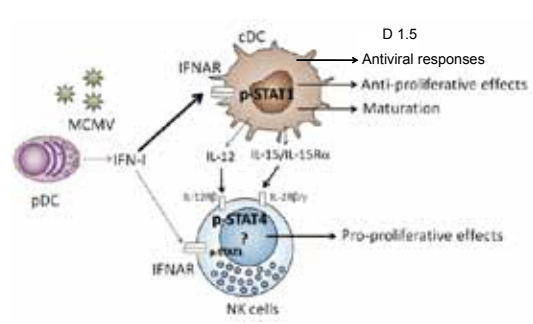
A) Survival curve



B) Virus titer in spleen



Conclusion / model



dalod@ciml.univ-mrs.fr

