

## **Murine CD8 $\alpha$ + DCs and human CD141+ DCs produce large amounts of IFN- $\lambda$ in response to dsRNA or DNA viruses [Abstract]**

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**PS2-006****Murine CD8 $\alpha$ <sup>+</sup> DCs and human CD141<sup>+</sup> DCs produce large amounts of IFN- $\lambda$  in response to dsRNA or DNA viruses**

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Dendritic cells (DCs) can be segregated into various subsets based on phenotypic and functional differences. Whereas plasmacytoid DCs are known for their type I interferon (IFN) producing capacity, conventional (c) DCs are better known for their roles in T cell homeostasis and priming. Among cDCs the CD8 $\alpha$ <sup>+</sup> subset is especially efficient in producing IL-12p70 and the induction of immunity against various pathogens and cancer. Here, we reveal a new hallmark function of murine CD8 $\alpha$ <sup>+</sup> cDCs and their human CD141<sup>+</sup> (BDCA3<sup>+</sup>) counterparts, namely the production of large amounts of IFN-lambda (IFN- $\lambda$ , also termed IL-28/29) upon stimulation with the dsRNAs poly (I:C) or poly(A:U). IFN- $\lambda$ s are potent immunomodulatory and antiviral cytokines. We demonstrate that the production of IFN- $\lambda$  upon poly(I:C) injection in vivo depends on hematopoietic cells and the presence of toll-like receptor (TLR)3, interferon regulatory factor (IRF)3, IRF7, IFN-IR, Fms-related tyrosine kinase 3 ligand (FL) and IRF8 but not on myeloid differentiation factor 88 (MyD88), Rig like helicases or lymphocytes. Furthermore, we show that both CD8 $\alpha$ <sup>+</sup> cDCs and plasmacytoid DCs produce large amounts of IFN- $\lambda$  in response to HSV-1 or parapoxvirus. Thus, IFN- $\lambda$  production in response to dsRNA is a novel hallmark function of mouse CD8 $\alpha$ <sup>+</sup> cDCs and their human equivalents.

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