PS2-006

Murine CD8α+ DCs and human CD141+ DCs produce large amounts of IFN-λ in response to dsRNA or DNA viruses

Lauterbach H, Barbara Bathke [a], Stefanie Gilles [b], Claudia Traidl-Hoffmann [b], Christian A. Luber [c], György Fejer [d], Marina A. Freudenberg [d], Gayle M. Davey [e], David Vremec [f], Axel Kallies [f], Li Wu [f], Ken Shortman [f], Paul Chaplin [a], Mark Suter [a,g], Meredith O'Keeffe [a,h], Hubertus Hochrein [a], [a] *Department of Research Immunology, Bavarian Nordic, Martinsried, Germany,* [b] *ZAUM, Center for Allergy & Environment, Technical University Munich/Helmholtz Center, Munich, Germany,* [c] *Proteomics and Signal Transduction, Max-Planck-Institute of Biochemistry, Martinsried, Germany,* [d] *Max-Planck-Institute of Immunobiology, Freiburg, Germany,* [e] *Department of Microbiology and Immunology, The University of Melbourne, Parkville, Australia,* [f] *The Walter and Eliza Hall Institute of Medical Research, Parkville, Australia,* [g] *University of Zurich, Zurich Switzerland,* [h] *Centre for Immunology, Burnet Institute, Melbourne, Australia*

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 CD8α+ 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 CD8α+ cDCs and their human CD141+ (BDCA3+) counterparts, namely the production of large amounts of IFN-lambda (IFN-λ, also termed IL-28/29) upon stimulation with the dsRNAs poly (I:C) or poly(A:U). IFN-λs are potent immunomodulatory and antiviral cytokines. We demonstrate that the production of IFN-λ 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-lR, 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 CD8α+ cDCs and plasmacytoid DCs produce large amounts of IFN-λ in response to HSV-1 or parapoxvirus. Thus, IFN-λ production in response to dsRNA is a novel hallmark function of mouse CD8α+ cDCs and their human equivalents.

doi:10.1016/j.cyto.2011.07.166