

TRANCE, TRAF6 and dendritic cells

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TRAF6 is a cytoplasmic adapter molecule which transmits signals from CD40, TRANCE receptor and Toll/IL-1 receptor. Although signaling thorough these receptors has been shown to be involved in regulating DC functions, little is known about the role of TRAF6 in DCs. We made TRAF6-deficient (TRAF6^{-/-}) mice by homologous recombination in ES cells using the Cre/lox-P system, and chimeric mice by adoptive-transfer of TRAF6^{-/-} fetal liver (FL) hematopoietic cells, for analysis of DC development and function. The number of DC was significantly reduced in spleen and thymus in TRAF6^{-/-} mice as well as TRAF6^{-/-} FL-transplanted chimeras. Cytokine production (IL-6, IL-12), as well as upregulation of surface markers (MHC class II, B7), in response to microbial components (LPS, CpG-DNA, poly (I:C) dsRNA, PGN) and CD40L were significantly impaired in TRAF6^{-/-} DC. No induction of T cell stimulatory capacity of TRAF6^{-/-} DC by LPS was observed. These results suggest that TRAF6 is critical for regulation of normal DC development *in vivo*, as well as DC activation in response to the microbial components, that link innate and adaptive immunity.

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