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## **BATF family AP-1 transcription factors control development of diverse immune cell lineages**

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T helper cells producing IL-17 (T<sub>H</sub>17) are induced by the combined actions of IL-6 and TGF- $\beta$  and coordinate acute inflammatory responses. The orphan nuclear receptors ROR $\gamma$ t and IRF-4 regulate Th17 differentiation, but the transcriptional hierarchy is unknown. We find the bZIP family member BATF is a main regulator of Th17 development. *Batf* is expressed in all Th subsets, yet *Batf*<sup>-/-</sup> T cells exhibit a selective block in Th17 development with normal Th1 and Th2 development. Subsequently, *Batf*<sup>-/-</sup> mice are completely resistant to EAE, a Th17 mediated autoimmune disease. Moreover, we show that BATF regulates sustained ROR $\gamma$ T expression by regulating ROR $\gamma$ T transcription. We thus present a novel regulator of Th17 differentiation and the first transcription factor responsible for regulating expression of ROR $\gamma$ T in Th17 cells.

Cross-presentation has been studied in the context of infectious diseases and responses to tumors. It remains unresolved whether the process of cross-presentation is a property generally active in all professional APCs, or whether it is limited to specific APC subsets. Likewise, it is unclear to what degree direct presentation versus indirect presentation contribute to the priming of T cell responses. For most infections, antigen presentation by professional APCs, such as dendritic cells, is required for effective CTL responses. Lymphoid-organ resident DCs are a heterogeneous group of cells composed of two major subsets, plasmacytoid DCs (pDCs) and conventional CD11c<sup>+</sup> (cDCs). cDCs comprise various subpopulations (e.g., CD8a<sup>+</sup>DEC205<sup>+</sup>, CD4<sup>+</sup>, CD8a<sup>-</sup>CD4<sup>-</sup>) which may exert distinct functions during immune responses. Indirect evidence has suggested that CD8a<sup>+</sup> cDCs play a predominant role in cross-presentation, but this evidence has been based on their *ex vivo* antigen-presentation capacity after infection or using systems in which antigen loading is carried out *in vitro*. The *in vivo* requirement for CD8a<sup>+</sup> cDCs during immune responses to pathogens has not been firmly established.

The analysis of the role of CD8a<sup>+</sup> DCs *in vivo* has been made difficult by lack of systems that selectively eliminate them. We have found that that deletion of the transcription factor *Batf3* selective ablates development of CD8a<sup>+</sup> DCs *in vivo*. This system allowed us to examine the *in vivo* role of CD8a<sup>+</sup> DCs in viral and tumor immunity. *Batf3*<sup>-/-</sup> mice were defective in cross-presentation and lacked virus-specific CD8<sup>+</sup> T cell responses. Importantly, rejection of highly immunogenic syngeneic tumors was completely absent in *Batf3*<sup>-/-</sup> mice, indicating a requirement for CD8a<sup>+</sup> DCs in tumor rejection. Notably, DNA-based vaccination was defective in *Batf3*<sup>-/-</sup> mice, implicating a possible role in cross-presentation in this route of immune vaccination. This system offers a valuable new way to study the role of CD8a<sup>+</sup> DCs and cross-presentation in various pathogen and vaccine models.

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2. Hildner K, Edelson BT, Purtha WE, Diamond M, Matsuhita H, Kohyama M, Calderon B, Schraml B, Unanue ER, Diamond MS, Schreiber RD, Murphy TL, Murphy KM. *Batf3* deficiency reveals a critical role for CD8alpha+ dendritic cells in cytotoxic T cell immunity. *Science*. 2008 Nov;322:1097-100. [PMID:19008445](#)

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