DENDRITIC CELLS

Assessing cross-presentation *in vivo*

The capacity of dendritic cells (DCs) to cross-present exogenous antigens on MHC class I molecules is well established, although the importance of cross-presentation for different types of immune response *in vivo* is not clear. In a recent report published in *Science*, Murphy and colleagues show that deficiency in the transcription factor BATF3 (basic leucine zipper transcription factor, ATF-like 3) leads to impaired immune responses *in vivo* owing to the absence of a DC subset that is particularly important for cross-presentation.

The authors used global gene expression analysis to search for genes that might be involved in the development of different DC subsets and found that BATF3 was highly expressed by conventional DCs (cDCs). Deletion of *Batf3* in mice caused a selective loss of the CD8α$^+$ subset of cDCs in the spleen without affecting the development of other haematopoietic cell types. CD8α$^+$ cDCs are characterized by their efficient ability to cross-present antigen and their responsiveness to Toll-like receptor 3 (TLR3) ligands. Indeed, when the function of cDCs from *Batf3*$^{-/-}$ and wild-type mice was compared, those from the mutant mice showed marked impairments in TLR3-mediated cytokine production and antigen cross-presentation *in vitro*.

Having established that the transcription factor BATF3 is required for CD8α$^+$ cDC development in mice, the authors next investigated how a deficiency in this DC subset influenced immune responses in which cross-presentation is important *in vivo*. First, using a model of West Nile virus (WNV) infection, the authors found that *Batf3*$^{-/-}$ mice had a markedly impaired CD8$^+$ T-cell response, but had normal B-cell and CD4$^+$ T-cell responses to WNV. Second, the authors investigated the importance of CD8α$^+$ cDCs in tumour immunity. Wild-type mice could reject syngeneic fibrosarcomas, whereas these tumours grew rapidly in *Batf3*$^{-/-}$ mice. The failure to reject the tumours was associated with reduced infiltration of CD8$^+$ but not CD4$^+$ T cells into the tumours and an impaired development of tumour-specific CD8$^+$ T cells.

To rule out the possibility that the impaired antiviral and antitumour responses in *Batf3*$^{-/-}$ mice were due to intrinsic T-cell defects, the authors carried out several assays of T-cell differentiation and function. Defects in *Batf3*$^{-/-}$ T cells could not be detected, which supported the authors' conclusion that impaired antiviral and antitumour responses in *Batf3*$^{-/-}$ mice were due to the lack of CD8α$^+$ cDCs. However, a closer examination of antitumour responses in *Batf3*$^{-/-}$ mice indicated that immune-cell populations other than CD8α$^+$ cDCs were sufficient to promote an antitumour response in mice that carried a low tumour burden. Therefore, although cross-presentation that is mediated by CD8α$^+$ cDCs is important for optimal priming of CD8$^+$ T-cell responses, other subsets of antigen-presenting cells can also carry out this function *in vivo*.

This work shows that BATF3 is required for the development of CD8α$^+$ cDCs, a subset with cross-presenting ability that is required for optimal immune responses to viral infections and tumours in mice.

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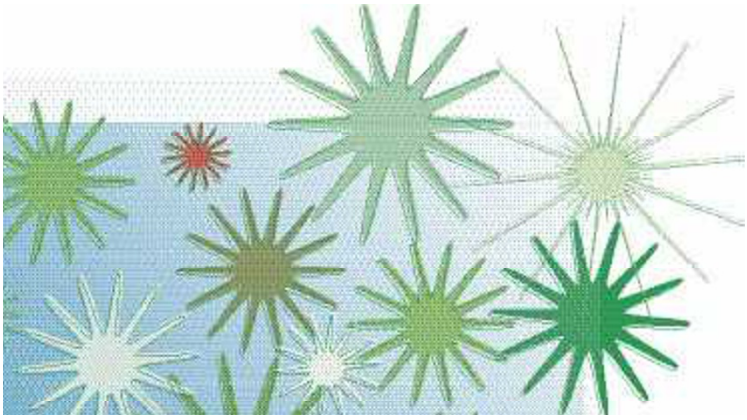

ORIGINAL RESEARCH PAPER Hildner, K. *et al.* *Batf3* deficiency reveals a critical role for CD8α$^+$ dendritic cells in cytotoxic T cell immunity. *Science* **322**, 1097–1100 (2008)