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Conventional dendritic cells (cDCs) consist of two major subsets, XCR1+ (CD8α+) cDC1 and CD11b+ cDC2, which play unique non-redundant roles in adaptive immune responses. The development of cDC1 is dependent on the transcription factors (TFs) IRF8, Batf3 and Id2, while cDC2 develop independently of these TFs but are partly dependent on IRF4 for their survival and function. The importance of these TFs in mature cDC remains unclear. In the current study we used cDC1 specific XCR1-cre mice crossed to reporter mice to assess the role of IRF8 and IRF4 in the survival, function and lineage specification of mature cDC1.
As expected, XCR1+ cDC1 were absent in XCR1-cre.IRF8fl/fl reporter mice. Strikingly however, YFP+ cDC were present in normal numbers and these YFP+ cells acquired a cDC2-like CD11b+ Sirpα+ IRF4+ phenotype. These 'ex cDC1' transcriptionally resembled cDC2 and occupied niches within lymph nodes usually restricted to cDC2. Functionally, these cells failed to cross-present antigen but had an enhance ability to prime CD4+ T cells in vitro. Finally, deletion of irf4 in these irf8-deficient 'ex cDC1' cells, resulted in reduced numbers of YFP+ cells, indicating that IRF4, similar to its function in cDC2, was required for their survival.
Collectively these results suggest that IRF8 is required for maintaining the lineage identity, but not survival, of cDC1, and in its absence cDC1 convert to cDC2-like cells.

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