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Effect of retinoic acid receptor β (RARβ) deficiency on DC in a conditional mouse line

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Vitamin A and its active derivatives (referred to as retinoids) play critical roles in a variety of biological processes and functions. Retinoids are ligands that bind and activate retinoic acid receptors (RAR) and retinoid X receptors (RXR) each consisting of three isotypes (α, β and γ) and these, in turn, function as transcription factors that regulate the expression of target genes[1,2]. Vitamin A plays an important role in maintaining dendritic cells (DC). Loss of retinoic acid (RA) signalling prevents myeloid DC development *in vitro*[3]. It has previously been described that spleens resected from Vitamin A-deficient mice show alterations in DC subsets[4]. Macrophage population in the spleen also decreases in transgenic mice expressing RARβ antisense sequences[5]. The production of conditional RARβ-deficient mice generated by floxing RARβ gene in mice expressing Cre recombinase ($RAR\beta^{L-/L-}$), represents a useful model to analyse the role of this receptor[6]. This work examined the role of RARβ on DC in spleen. DNA from ear and spleen of $RAR\beta^{L-/L-}$ conditional mutant mice was used to identify the recombined RARβ alleles and C57BL/6 mice were used as control (data not shown)[6]. Sections of paraffin-embedded spleens were used for immunohistochemistry and histopathological analyses. Leucocytes obtained from spleens were used for Western blotting and flow cytometry analyses. In addition, total RNA was isolated from spleen and used for cDNA synthesis and quantitative real-time PCR (*n* 3).

Our results showed that RARβ is expressed mainly in the splenic white pulp zone of wild-type mice (data not shown). Low levels of RARβ expression were detected in the spleen of $RAR\beta^{L-/L-}$ mice, as determined by immunohistochemistry (Fig. 1A) and Western-blot analysis (Fig. 1B). These results are consistent with a decrease in the population of splenic CD11c + MHC-II + white cells (Fig. 2) and decrease in TLR2 expression (Fig. 3). Histopathology analyses of conditional mice spleen showed a reduction of macrophage-like cells and loss in cell organisation and structure (data not shown). Our results suggest that RARβ is involved in spleen cell organisation and the homeostatic maintenance of DC (Figs 1–3).

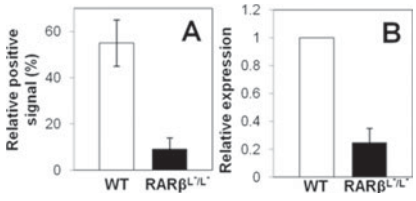

Fig. 1. RARβ protein levels in spleen of $RAR\beta^{L-/L-}$ conditional mice.

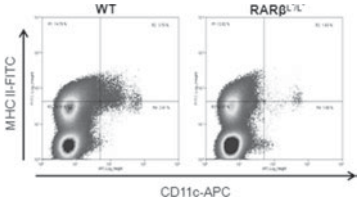

Fig. 2. Splenic Dendritic cells are reduced in $RAR\beta^{L-/L-}$ conditional mice.

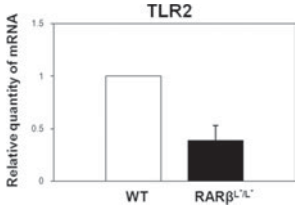

Fig. 3. TLR2 expression in spleen of $RAR\beta^{L-/L-}$ conditional mice.

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