Essential Role of Canonical NF-κB Activity in the Development of Stromal Cell Subsets in Secondary Lymphoid Organs

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Organized tissue structure in the secondary lymphoid organs (SLOs) tightly depends on the development of fibroblastic stromal cells (FSCs) of mesenchymal origin; however, the mechanisms of this relationship are poorly understood. In this study, we specifically inactivated the canonical NF-κB pathway in FSCs in vivo by conditionally inducing IκBα mutant in a mouse system in which NF-κB activity is likely to be suppressed in fetal FSC progenitors. Given that NF-κB activation in fetal FSCs is essential for SLO development, the animals were expected to lack SLOs. However, all SLOs were preserved in mice. Instead, the T cell area was severely disturbed by the lack of CCL21-expressing FSCs, whereas the follicles and associated FSC networks were formed. Fate mapping revealed that IκBSR-expressing cells constituted only a small fraction of stromal compartment outside the follicles. Taken together, our findings indicate an essential role of the canonical NF-κB pathway activity in the development of three FSC subsets common to SLOs and suggest transient or stochastic CCL19 expression in FSC progenitors and a compensatory differentiation program of follicular FSCs.

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