NF-κB2/p100 deficiency impairs immune responses to T-cell-independent type 2 antigens.

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Abstract

Formation of the splenic marginal zone (MZ) depends on the alternative NF-κB signaling pathway. Recently, we reported that unrestricted activation of this pathway in NF-κB2/p100-deficient (p100(-/-)) knock-in mice alters the phenotype of MZ stroma and B cells. Here, we show that lack of the p100 inhibitor resulted in an expansion of both MZ B and peritoneal B-1 cells. However, these cells failed to generate proliferating blasts in response to T-cell-independent type 2 (TI-2) Ags, correlating with dampened IgM and absent IgG3 responses. This phenotype was in part due to increased activity of the NF-κB subunit RelB. Moreover, p100(-/-) →B6 BM chimeras were more susceptible to infection by encapsulated Streptococcus pneumoniae bacteria, pathogens that induce TI-2 responses. In contrast to the TI-2 defect, p100 deficiency did not impair immune responses to the TI-1 Ag LPS and p100(-/-) MZ B cells showed normal Ag transportation into B-cell follicles. Furthermore, p100(-/-) MZ B and B-1 cells failed to respond to TI-2 Ags in the presence of WT accessory cells. Thus, NF-κB2/p100 deficiency caused a predominant B-cell-intrinsic TI-2 defect that could largely be attributed to impaired proliferation of plasmablasts.

Importantly, p100 was also necessary for efficient defense against clinically relevant TI-2 pathogens.

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