

学 位 論 文 の 要 旨

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<p>主論文の題名</p> <p>Depletion of Neural Crest-Derived Cells Leads to Reduction in Plasma Noradrenaline and Alters B Lymphopoiesis</p> <p>主論文の要旨</p> <p>Hematopoietic stem cells (HSCs) and their lymphoid progenitors are supported by the bone marrow (BM) microenvironmental niches composed of various stromal cells and Schwann cells and sympathetic nerve fibers. Although neural crest (NC) cells contribute to the development of all the three, their function in BM is not well understood. In this study, NC-derived cells were ablated with diphtheria toxin (DT) in double-transgenic mice expressing NC-specific Cre and Cre-driven DT receptor (DTR) with YFP reporter. We found that YFP-expressing, NC-derived nonhematopoietic cells in BM expressed hematopoietic factors <i>Cxcl12</i> and <i>stem cell factor</i>. The ablation of NC-derived cells led to a significant decrease in B cell progenitors but not in HSCs or myeloid lineage cells in BM. Interestingly, plasma noradrenaline was markedly decreased in these mice. The intraperitoneal administration of 6-hydroxydopamine, a known neurotoxin for noradrenergic neurons, led to a similar phenotype, whereas the administration of a noradrenaline precursor in NC-ablated mice partially rescued this phenotype. In addition, the continuous administration of adrenergic receptor beta antagonists partially decreased the number of B cell progenitors while preserving B lymphopoiesis <i>in vitro</i>. Taken together, our results indicate that NC-derived cell depletion leads to abnormal B lymphopoiesis partially through decreased plasma noradrenaline, suggesting this as a novel mechanism regulated by molecules released by the sympathetic neurons.</p>			