Y Chromosome-linked B and NK cell deficiency in mice

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DOCTORAL PROGRAM

（博士論文）

Y Chromosome-linked B and NK cell deficiency in mice

(Y染色体連鎖遺伝を示す免疫不全症の解析)

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要約

There are no primary immunodeficiency diseases linked to the Y chromosome, because the Y chromosome does not contain any vital genes. I have established a novel mouse strain in which all males lack B and NK cells and have Peyer's-patch defects. By 10 weeks of age, 100% of the males had evident immunodeficiencies. Mating these immunodeficient males with wild-type females on two different genetic backgrounds for several generations demonstrated that the immunodeficiency is linked to the Y chromosome and is inherited in a Mendelian fashion. Although multicolor fluorescence in situ hybridization (FISH) analysis showed that the Y chromosome in the mutant male mice was 1/3 shorter than that in wild-type males, exome sequencing did not identify any significant gene mutations. The precise molecular mechanisms are still unknown. Bone marrow chimeric analyses demonstrated that an intrinsic abnormality in bone marrow hematopoietic cells causes the B- and NK-cell defects. Interestingly, fetal liver cells transplanted from the mutant male mice reconstituted B and NK cells in lymphocyte-deficient *Il2rg-/-* recipient mice, while adult bone marrow transplants did not. Transducing the EBF gene, a master transcription factor for B cell development, into mutant hematopoietic progenitor cells (HPCs) rescued B-cell but not NK-cell development both *in vitro* and *in vivo*. These Y-chromosome-linked immunodeficient mice, which have preferential B- and NK-cell defects, may be a useful model of lymphocyte development