学位論文内容の要旨

Abstract of the dissertation

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学位論文題名

Genetic analysis of phenotypes caused by deficiency in the development of neural crest-derived cells in the rat

（ラットにおける神経堤細胞由来細胞の発達の欠陥によりもたらされる表現型の遺伝学的解析）

NCCs is one of the most critical cell lineages in the embryogenesis of vertebrates. The discoveries of complex gene-regulatory networks that revolved in the development of various NC-derived cells are never stopped. In this study, genetic analysis of NC-derived two lineages, development of ENS and melanocytes, were conducted using rat models.

In Chapter 1, generation of a new rat strain showing severe phenotype of aganglionosis caused by null mutation of the *Ednrb* gene was tried. To this end, the GK rat was selected, because the GK rat possessed haplotype in the specific region on chromosome 2 similar to that of the AGH rat, which showed the most severe phenotype of aganglionosis caused by null mutation of the *Ednrb* gene by possessing a particular haplotype in the specific region on Chr 2. However, it was found that introduction of null mutation of the *Ednrb* gene caused embryonic lethality in the GK rat. This result proposes the possibility that the *Ednrb* gene interacts with gene(s) located in the critical region on Chr 2 and such interaction plays a critical role in embryogenesis as well as ENS

development. The results in this study provide a valuable rat model for further investigation of gene-regulatory networks of the ENS development and embryogenesis.

In Chapter 2, modifier(s) that affect melanocyte development were investigated by QTL analysis. The LEA and F344 rats were used in this analysis. Although both strains possess the same allele of the *Kit* gene and therefore, showed hooded phenotype, pigmented proportion was different between the two rat strains. The QTL analysis identified a locus near the *D17Rat2* on Chr 17 as responsible for modifying the hooded phenotype. This result suggests that the LEA haplotype of the genomic region including this QTL rescues the dysregulation of melanocytes due to the mutation of *Kit* gene and provides new clues for the studies of melanocyte.

In summary, the results from these two investigations in this study will contribute to better understanding of the roles of NC-derived cells and gene-regulatory networks for the development of NC-derived cells during embryogenesis.