論 文 の 内 容 の 要 旨

論文題目 Essential Roles of Np95 and Ecat8 in Regulation of Mammalian Epigenetics
（哺乳類のエピジェネティクス制御におけるNp95とEcat8の機能解析）

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Epigenetics is the mechanism to modulate gene expression in a reversible, heritable and dynamic manner without changing the DNA sequence. A central question in epigenetics is how the epigenetic marks are established and maintained in the genome. The aim of the present study was to characterize novel RNA-interacting molecules to examine their impacts on the epigenome. This study focused on the following two molecules, the SRA-RING protein Np95 (nuclear protein 95, also known as Uhrf1 and ICBP90) and the tudor/maternal tudor domain containing protein Ecat8 (ES cells specific transcript 8), because of their possible roles in epigenetics in mice. In this study, firstly, the author investigated the involvement of the SRA-RING protein Np95 in mammalian DNA methylation. Here, the author reports that Np95 interacts with Dnmt1 (DNA methyltransferase 1) and recruits Dnmt1 to the replicating heterochormatin. Furthermore, by using *Np95* deficient stem cells and embryos, the author finds that Np95 is essential for global and local maintenance of DNA methylation, genomic imprinting and repression of retrotransposons. Secondly, in the present study; the author examined the role of the tudor-domain containing protein Ecat8 in regulation of RNAs and epigenetics in germ cells. The author shows that Ecat8 is essential for male fertility and expression of germ cell specific piRNAs (Piwi interacting RNAs) in the testis. Investigating the role for Ecat8 in germ cell epigenetics, the author found that a significant loss of DNA methylation in the IAP and LINE retroelements is observed in the *Ecat8* knockout mice spermatogonia. Thus, the author shows a role for Ecat8 in epigenetics and regulation of piRNAs in mammalian germ cells that has not been reported before. In summary, this report suggests that RNA-associated proteins may have important functions in epigenetics and play crucial roles as master regulators of the epigenome.