

# Dmrt family genes regulate embryonic cortical neurogenesis in Pax6-dependent and -independent manners

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## 要約

The transcription factor Pax6 controls cell proliferation and neuronal differentiation in the developing mammalian neocortex by regulating the expression of its target genes.

Using microarray analysis, we observed the downregulation of *Dmrta1* (*double-sex and mab-3* related transcription factor-like family A1) in the telencephalon of *Pax6*

homozygous mutant rats (*rSey<sup>2</sup>/rSey<sup>2</sup>*), except for in the medial cortical region, which was negative for Pax6. *Dmrta1* expression was restricted to the neural stem/progenitor cells in the dorsal telencephalon and was expressed in early-born neurons in the

Pax6-negative medial cortical region. These observations raise the possibility that

*Dmrta1* is regulated by Pax6-dependent and -independent pathways in specific cortical regions. Within the Pax6-dependent *Dmrta1* pathway, the overexpression of *Dmrta1*

induced the expression of the proneural gene *Neurogenin2* (*Neurog2*) and, conversely, repressed *Ascl1* (*Mash1*), a proneural gene expressed in the ventral telencephalon. It

was also observed that another Dmrt family molecule, *Dmrt3*, induced *Neurog2*

expression in the dorsal telencephalon. Therefore, *Dmrt3*, whose expression pattern

overlapped with that of *Dmrta1*, may compensate for the loss of *Dmrta1* function

downstream of Pax6 in cortical regions. In the *Dmrt1* KO mouse cortex, production of Cajal-Retzius (CR) cells was severely reduced, while that of other neurons seemed to be quite normal. These novel findings suggest that Dmrt family members are involved in the regulation of proneural genes downstream of Pax6 and are crucial for the production of CR cells independent of Pax6.