

Molecular mechanism for neuronal diversity and organization in the brain

YAGI Takeshi

(Osaka University, Graduate School for Frontier Biosciences, Professor)

【Outline of survey】

Brain is a complex system composed of enormous number of diverse neurons. CNR/Protocadherin (Pcdh) family is diverse cadherin-related receptors in the brain. The CNR/Pcdh family is constituted with gene cluster like immunoglobulin and T cell receptor genes in genome. Their molecular members make multiple protein complex and are differentially expressed in individual neurons. In this project, firstly to examine molecular mechanism for generating neuronal diversity, we focus to selective gene-regulation of the CNR/Pcdh family in individual neurons. Each molecular member of the CNR/Pcdh family has conserved promoter region. It is thought that their differential expression in individual neurons is drove by somewhat choice mechanism for the multiple promoters. We will approach the molecular mechanism for the promoter choice in their gene cluster. Secondary to address molecular mechanism for generating complex and well organized neural networks in the brain, we examine molecular function of the diverse CNR/Pcdh family molecules by producing gene converted mice in their gene clusters. We will analyze their gene expression patterns, abnormal neural network formation and defects of brain function in their gene converted mice.

【Expected results】

By this project, we will gain several novel molecular mechanisms for generating diverse neurons and for generating and organizing complex neural network formation in the brain. These novel discovered molecular mechanisms will open the new fields for understanding development of the brain and regulation of the brain function.

【References by the principal investigator】

- Esumi S, Kaneko R, Kawamura Y & Yagi T. Split single cell RT-PCR analysis of Purkinje cells. **Nature Protocols** 1, 2143-2151, (2006).
- Kaneko R, Kato H, Kawamura Y, Esumi S, Hirayama T, Hirabayashi T & Yagi T. Allelic gene regulation of protocadherin- α and - γ clusters involving both monoallelic and biallelic expression in single Purkinje cells. **J Biol Chem** 281, 30551-30560, (2006).
- Hirayama T & Yagi T. The role and expression of the protocadherin-alpha clusters in the CNS. **Curr Opin Neurobiol.** 16, 336-342, (2006).
- Esumi S, Kakazu N, Taguchi Y, Hirayama T, Sasaki A, Hirabayashi T, Koide T, Kitsukawa T, Hamada S & Yagi T. Monoallelic yet combinatorial expression of variable exons of the CNR/Protocadherin-a gene cluster in single neurons. **Nature Genet** 37, 171-176, (2005).

【 Term of project 】 FY2007 – 2011

【Budget allocation】 19,100,000 yen
(2007 direct cost)

【Homepage address】

<http://www.fbs.osaka-u.ac.jp/labs/yagi/index.html>