

Establishment and application of lentivector-based production of gene-rescue mouse for exploring gene functions

Hirokazu Hirai

(Gunma University, Graduate School of Medicine, Professor)

【Outline of survey】

Using developmental engineering many conditional gene-modified mice have been generated for studying genes of unknown function. This approach is useful, but time-consuming and requires a lot of effort for crossing different lines of mice, genotyping and maintenance of animals. If a gene of interest can be transferred to and efficiently expressed in a specific subset of neurons in developing and mature animals, it saves much time, effort and money. A goal of this project is to establish a lentivector-based method that allows efficient gene expression in a specific subset of cerebellar neurons of gene-deficient mice in vivo: we call this gene-rescue-mouse. To attain this, we try to clarify the mechanisms by which lentiviral tropism for a specific cell type is determined. Using the newly established technique, we challenge to elucidate the molecular basis underlying synaptic development and synaptic plasticity in the cerebellum.

【Expected results】

The “gene-rescue-mouse” that will be developed by this project allows us to study functions of genes very efficiently. Although production of conventional gene-modified mice may be required for finally confirming results obtained by viral-vector-based method, this technique is thought to be promising and widely used as an alternative to conventional gene-modified mice for studying gene functions in vivo.

【References】

- **Hirai H.** Progress in transduction of cerebellar Purkinje cells in vivo using viral vectors. *Cerebellum* 6: 1-6, 2007 (Review)
- Jin D*, Liu H*, **Hirai H*** et al. CD38 is critical for social behaviour by regulating oxytocin secretion. *Nature* 446: 41-5, 2007 (*Equally contributed)
- **Hirai H** et al. Cbln1 is essential for synaptic integrity and information processing in the cerebellum. *Nat. Neurosci.* 8: 1534-1541, 2005

【Term of project】 FY2007 - 2011

【Budget allocation】 17,700,000 yen

(2007 direct cost)

【Homepage address】 <http://www.med.gunma-u.ac.jp/graduate/med/index-en.html>