

In vivo gene function analysis using lentiviral vector

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【Outline of survey】

Lentiviral (LV) vectors are efficiently integrated into the host genome and stably express the transgene for life-time so that they have been successfully used in biological and biomedical studies. We have previously demonstrated that lentiviral vector transduction of fertilized eggs is a facile and efficient method to generate transgenic animals (LV-Tg method). In this project, we are going to develop an “*in vivo* gene function analysis system” using LV-Tg method. For this purpose, tissue specific gene modification with cre/loxP system, targeted gene knockdown with RNAi system, and inducible gene expression with tet on/off system will be examined in combination with lentiviral vector mediated gene trap mutagenesis. Throughout the project, we investigate the gene trapped mice and elucidate the mechanism of reproduction at molecular basis. All the mice obtained will be distributed through public bioresource center.

【Expected results】

Combination with LV-Tg method with other techniques will provide a novel gene function analysis system that promotes biological science in the post-genome project. Since the knockout mice will be distributed through bioresource center, the individual researcher need not to generate mutant mice by themselves. Elucidation of the mechanism of reproduction and its clinical applications might help the couples suffered from infertility.

【References by the principal investigator】

- Inoue N., Ikawa M., Isotani A., and Okabe M. “The immunoglobulin superfamily protein Izumo is required for sperm to fuse with eggs” *Nature* 434, 234-238 (2005)
- Okada Y., Ueshin Y., Isotani A., Saito-Fujita T., Nakashima H., Kimura K., Mizoguchi A., Oh-Hora M., Mori Y., Ogata M., Oshima R.G., Okabe M., and Ikawa M. “Complementation of placental defects and embryonic lethality by trophoblast-specific lentiviral gene transfer” *Nature Biotechnology*. 25, 233-237 (2007)

【Term of project】 FY2008—2012

【Budget allocation】

74,500,000 yen (direct cost)

【Homepage address】

<http://kumikae01.gen-info.osaka-u.ac.jp/members/ikawa/index.htm>