CDB SEMINAR

Speaker: **Junji Takeda**

<Collaborative Research Center for Advanced Science and Technology, Osaka University>

Title: **"Analyses of Gene Functions with Sleeping Beauty Transposon System and Introduction of Bi-allelic Mutagenesis"**

Date:	Friday, April 16
Time:	17:00 P.M.～18:00 P.M.
Place:	6th floor Conference Room of Building C, CDB

Summary:

Transposons are the mobile elements that can change location in the genome and have been used for insertional mutagenesis in many organisms, such as *Drosophila melanogaster*, *Caenorhabditis elegans*, and plants. Utilization of transposon system has been hampered in mouse genome because of no active transposon in mammals. However, this situation has changed, since Minnesota's group discovered that a reconstructed *Tc1/mariner*-like transposon from salmonid fish, *Sleeping Beauty (SB)* transposon, was active in mammalian cultured cells. We have recently found that *SB* transposon can mobilize very efficiently in mouse germline and transmit mutations to the next generation. We have also demonstrated that generation of mutant mice were greatly accelerated by incorporation of gene trap scheme into the *SB* transposon system. This method opens the way to introduce mutations without ES cell culture nor embryo manipulation. Therefore, both speed and cost-efficiency for creating mutant mice are greatly improved. The *SB* transposon was shown to transpose locally: 80 % of transposition occurs on the same chromosome and 50 % happens within 3 Mb from the donor site. For this reason, we plan to introduce donor transposon sequences into various locations of the genome.

Difficulty of phenotype-based screening in mice is the diploid nature of the genome. Introduction of bi-allelic mutations was described with loss of the Bloom's syndrome gene (*BLM*) that induces an increased rate of loss of heterozygosity (LOH). We used the tetracycline-regulated *Blm* allele (Blm^{tet}) to demonstrate genome-wide introduction of bi-allelic mutations in mouse ES cells.

Taken together, combination of *SB* transposon and Blm^{tet} allele would facilitate analyses of gene functions in mice.

Host Kazuki Nakao Animal Resources and Genetic Engineering ,CDB

E-mail kazuki@cdb.riken.jp Tel:078-306-0106(ext.4331)

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