Title of Project：Development of basic technologies for new *in vivo* imaging to promote life science research

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Research Area：Comprehensive fields
Keyword：research bioresource

【Purpose and Background of the Research】

In this application, using a variety of florescence-labeled proteins and genetic engineering strategies that have not been practically used, we will attempt to develop new *in vivo* imaging methods. Electrophysiological and histological analyses most often have been done for studies in neuroscience. However, using a new fluorescence labeling technology, we will develop a system to monitor history of neuronal activity, which has not been feasible to date by using gene-manipulated mice.

【Research Methods】

1. Development of a mouse with cells that can be labeled *in vivo* by fluorescence excitation (photo-conversion).

We will develop a mouse whose cells will be labeled with fluorescence protein Kaede and its derivatives *in vivo* by fluorescence irradiation, exhibiting photo-conversion from green to red by fluorescence irradiation.

2. Development of a mouse in which a non-labeled low molecular weight substance can be monitored by fluorescence (Degraton probe)

To date, monitoring of a non-labeled low molecular weight substance by fluorescence imaging technologies has not been done. We developed a Degraton probe to monitor the presence of a low molecular weight substance by fluorescence. We are planning to construct a mouse that expresses the Degraton probe that enables monitoring of *in vivo* dynamics of a low molecular weight substance.

3. Development of a mouse in which history of neuronal activity can be monitored (History tracer)

As a new method to support electrophysiological methods in neuroscience, we will develop a mouse in which history of neuronal activity can be monitored by accumulation of a long-life fluorescent protein.

4. Development of a mouse in which that status of neuronal activity can be monitored during a specific period.

Applying the technologies mentioned for the themes “Degraton probe” and “History tracer” and using the technology by which a fluorescent protein is stabilized only when a low molecular weight substance is present *in vivo*, we will develop a mouse in which history of neuronal activity can be monitored during the period of administration of a low molecular weight substance that is time-specifically labeled.

【Expected Research Achievements and Scientific Significance】

Establishment of these methods will enable a less invasive time-course observation in not only mice but also in other experimental animals. This will reduce pain and the number of sacrifices of such animals while scientific analyses are performed.

【Publications Relevant to the Project】

・Suzuki N, Ohneda O, Minegishi N, Nishikawa S, Ohta T, **Takahashi S,** Engel JD, Yamamoto M. Combinational Gata2 and Sca1 expression defines hematopoietic stem cells in the bone marrow niche. ***Proc Natl Acad Sci U S A.*** 103, 2202-2207, 2006.
・Tomura M, Yoshida N, Tanaka J, Karasawa S, **Miwa Y,** Miyawaki A, Kanagawa O. Monitoring cellular movement in vivo with photoconvertible fluorescence protein "Kaede" transgenic mice. ***Proc Natl Acad Sci USA.*** 105, 10870-10875, 2008.

【Term of Project】 FY2009-2013

【Budget Allocation】 144,200 Thousand Yen

【 Homepage Address and Other Contact Information】

http://www.md.tsukuba.ac.jp/basic-med/anatomy/embryology/index.html