Molecular Analysis of Light-signaling and Circadian Rhythm in the Brain

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【Outline of survey】

Animals have visual systems supported by highly differentiated photoreceptive organs, and most of them are endowed with circadian clock systems generating daily rhythms. The phase of the circadian clock is commonly entrainable to light-dark cycles, and therefore comparative studies on the molecular mechanisms underlying the both systems should lead to comprehensive understanding of how these light-sensitive systems have developed by interacting with each other. In this research project, we will focus on the dual aspects of the animal photosensitive systems, *i.e.*, the vision generating spatial information in a very short time scale, and the circadian clock providing temporal information in a long time scale. We will elucidate the functional principle linking molecular dynamism with individual output in terms of light-signaling. In parallel, non-photic entrainment of the clock will be studied in order to pursue comparative aspects of the photic and non-photic entrainment mechanisms, which should lead to profound understanding of the entrainment of the biological clock. For this purpose, we will produce various gene-targeted mice and transgenic zebrafish, and provide a new way in the research field of neurosciences.

【Expected results】

In this research project, functional properties of photosensitive neurons such as retinal visual cells and pineal photoreceptive cells are to be investigated not only through individual analysis at the molecular level but also by a comparative study between the two neurons. The studies based on this strategy should enable us to understand the genetic network that specifies each neuron subtype. The results of this project should provide a strong impact on the research area of photobiology and, in a broad sense, the area of neurosciences.

【References by the principal investigator】

- Okano *et al.* (1994) Pinopsin is a chicken pineal photoreceptive molecule. ***Nature,*** *372*, 94-97.
- Asaoka *et al.* (2002) Pineal expression-promoting element (PIPE), a *cis*-acting element, directs pineal-specific gene expression in zebrafish. ***Proc. Natl. Acad. Sci. USA.,*** *99*, 15456-15461.
- Doi *et al.* (2004) Negative control of circadian clock regulator E4BP4 by casein kinase Iε-mediated phosphorylation. ***Curr. Biol.,*** *14*, 975-980.
- Kassai *et al.* (2005) Farnesylation of retinal transducin underlies its translocation during light adaptation. ***Neuron,*** *47*, 529-539.

【Term of project】 FY2007-2011	【Budget allocation】 20,600,000 yen (2007 direct cost)

【Homepage address】 http://www.biochem.s.u-tokyo.ac.jp/fukada-lab/