



Title of Project : Regulation of Signal Transduction by Post-translational Modifications and Its Pathogenic Dysregulation

Term of Project : FY2010-2014

Jun-ichiro Inoue
(The University of Tokyo, Institute of Medical Science, Professor)

【Purpose of the Research Project】

It is becoming clearer that spatiotemporal dynamics of post-translational modifications including ubiquitination, sumoylation, and glycosylation as well as phosphorylation play critical roles in regulation of signal transduction and cellular functions and that dysregulation of these modifications leads to onset of diseases (Fig. 1). Thus, interdisciplinary collaboration is essential for understanding the spatiotemporal regulation of signal transduction and developing novel therapeutic methods. Purpose is to establish collaborations between people in molecular biology, medical science, structural biology and mathematical science so that breakthrough results are achieved.

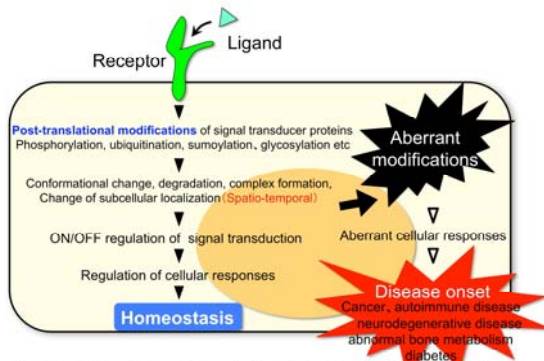


Fig. 1 Regulation of Signal Transduction by Post-translational Modifications and Its Pathogenic Dysregulation

【Content of the Research Project】

The following three groups have been formed; A01: Research based on molecular cellular biology and medical science, A02: Research based on structural biology, A03: Research based on mathematical science. Efficient interdisciplinary collaborations between scientists in A01 to A03 will be performed to elucidate the spatiotemporal regulation of signal transduction and its pathogenic dysregulation (Fig. 2). Goals are 1) Establishment of fundamental technologies to analyze signal transduction. 2) Elucidation of the molecular mechanisms by which signal transduction pathways are regulated. 3) Identification of pathogenic dysregulation of post-translational modifications in signal transduction. Therefore, in planned research members of A01, J. Inoue, S. Yamaoka (Tokyo Med. Dent. U.) and F.

Tokunaga (Osaka U.) focus on NF-κB signaling. M. Takekawa (Nagoya U.) focuses on MAPK signaling. M. Takahashi (Nagoya U.) focuses on Akt signaling. R. Ishitani (U. of Tokyo, A02) will resolve structure of proteins involved in regulation of above-mentioned three signals. M. Oyama (U. of Tokyo, A01) will analyze novel modifications of the proteins by the next-generation mass spectrometer. K. Ichikawa (Osaka U. A03) will propose mathematical models of the three signals. On the other hand, publicly invited research members may focus on various signal cascades and fundamental technologies to analyze signal transduction

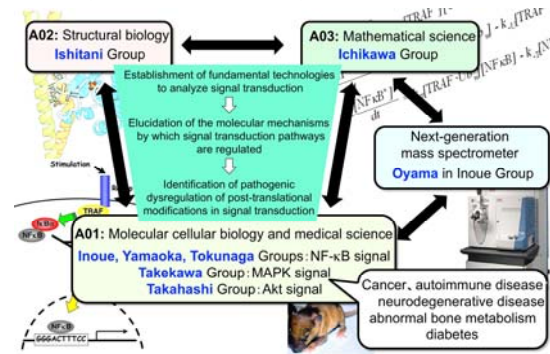


Fig. 2. Interdisciplinary collaborations in "Shushoku-signal Byou"

【Expected Research Achievements】

Our collaborative research will uncover novel mechanisms of spatiotemporal regulation of signal transduction and establish the novel research fields "Shushoku-Signal Byou". Our findings will contribute to development of efficacious diagnostic and therapeutic methods for important diseases such as cancer and immunological, neurological and metabolic disorders. Young investigators will be trained.

【Key Words】

Post-translational modification: Chemical modification of a protein after its translation.

Signal transduction: A process in which an extracellular stimulus is recognized by its specific receptor and cell converts the stimulus to a specific biological response.

【Homepage Address】

<http://shushoku-signal.com/>