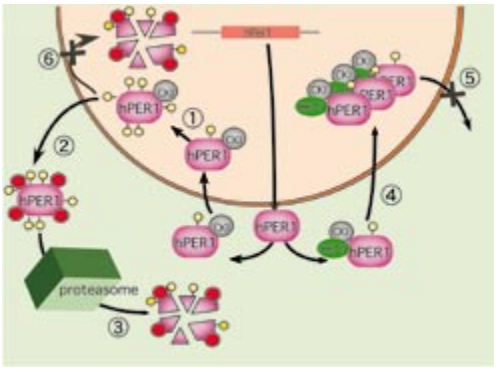
Circadian rhythm is regulated by phosphorylation of clock protein PER:Its phosphorylation and Degradation System

Koyomi MIYAZAKI
Institute for Biological Resources and Functions
e-mail: k-miyazaki@aist.go.jp
AIST Today Vol. 4, No.9 (2004)17

Serum stimulation caused daily oscillations of human PER1 protein (hPER1) and the apparent molecular mass of hPER1 changed. Inhibitor studies indicated that the casein kinase I family. phosphorylated hPER1 and increased the apparent molecular mass of hPER1. The inhibition of hPER1 Phosphorylation by CKI-7, a casein kinase I inhibitor, disturbed hPER1 degradation, delayed the nuclear entry of hPER1 and allowed it to persist for longer in the nucleus. Furthermore, proteasome inhibitors specifically blocked hPER1 degradation, while leptomycin B, an inhibitor of nuclear export, did not alter the degradation state of hPER1 protein. These findings indicate that circadian hPER1 degradation through a proteasomal pathway can be regulated through phosphorylation by casein kinase I, but not by subcellular localization.



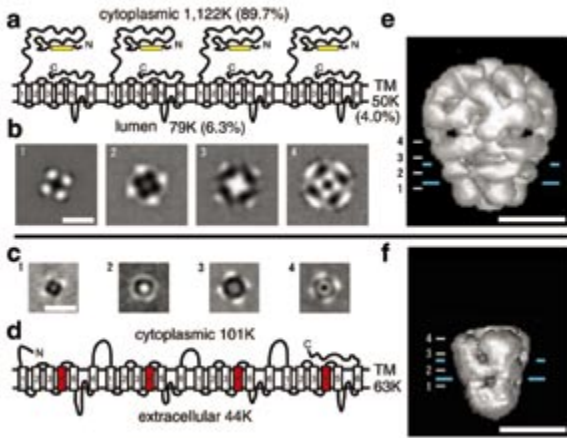
Phosphorylation of PER1 controls its degradation. CKI phosphorylates PER1 (1) and then degraded through ubiquitin-proteasome pathway (2,3). CKI-7 inhibits hPER1 phosphorylation and its degradation (4).

3D Structure of Inositol 1,4,5-Trisphosphate Receptor Channel

Chikara SATO
Neuroscience Research Institute and Biological Information Research Center
e-mail: ti-sato@aist.go.jp
AIST Today Vol. 4, No.9 (2004) 18

The inositol 1,4,5-trisphosphate receptor channel in the endoplasmic reticulum is involved in neuronal transmission via Ca2+ signaling and for many other functions that relate to morphological and physiological processes in living organisms. We analysed the three-dimensional structure of the ligand-free form of the receptor based on single particle technique using an automatic particle picking system. We propose a model which explains the complex mechanism for the regulation of Ca^{2+} release by co-agonists, Ca^{2+}, inositol 1,4,5-trisphosphate based on the structure of multiple internal cavities and a porous balloon-shaped cytoplasmic domain.

1) C. Sato, K. Hamada, T. Ogura, A. Miyazawa, K. Iwasaki, Y. Hiroaki, K. Tani, A. Terauchi, Y. Fujiyoshi, K. Mikoshiba : J. Mol. Biol., Vol. 336, 155-164 (2004).



Predicted membrane topology, Sections and surface-rendered representations with loops and terminal extensions for the IP_3R1 (upper) and the voltage-dependent Na+ channel (lower)