Keio University Global Research Institute

# KGRI Lecture Series

2019年

## 10月18日 金 17:00–18:00

場所：慶應義塾大学信濃町キャンパス　3号館北棟ラウンジ


**Prof. Katsuhiko Mikoshiba, MD, Ph.D （御子柴　克彦　先生）**

Professor, SIAIS (Shanghai Institute for Advanced Immunochemical Studies), ShanghaiTech University

Specially Appointed Professor, Faculty of Science, Toho University

Guest Professor (Global) of Keio University


## $IP_3$ receptor/$Ca^{2+}$ channel: from its discovery to a new paradigm in health and disease


$Ca^{2+}$ plays an essential role in cell function. It conveys signals to the most important cell process but the detailed mechanism of signaling process is not clearly understood. We have discovered a key regulator of $Ca^{2+}$ signaling, the $IP_3$ receptor ($IP_3R$) as a $P_{400}$ protein greatly decreased in the cerebellum of Purkinje cell-degeneration mutant mice, and have subsequently cloned its cDNA. We identified it is endoplasmic reticulum (ER) channel that convert GPCR-$IP_3$ signals to $Ca^{2+}$ signal at the ER to produce $Ca^{2+}$ oscillation. We found that $IP_3R$ is essential for fertilization, dorso-ventral axis formation, neurite extension, cardiogenesis, exocrine secretion and behavior. We found $IP_3R$ interacts ER chaperons to protect from apoptosis caused by ER stress response. A newly discovered pseudo-$IP_3$ which we named IRBIT that binds to $IP^3R$ and is involved in apoptosis regulation in association with anti-apoptotic proteins. We recently crystalized a large cytosolic domain (2217aa) of $IP_3R$ in the presence and absence of $IP_3$ and solved the gating mechanism by biochemical and X-ray crystallographic analysis. We have identified a “leaflet” structure essential for allosteric channel gating, surrounded by functional molecules that may regulate $IP_3R$ activity to balance normal/abnormal state. I will discuss about a new paradigm in health and disease.


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お問い合わせ

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