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Roles of the ubiquitin proteasome system in endocrinology and metabolism

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Ubiquitin is a small protein composed of 76 amino acids, which is conjugated covalently to various substrate proteins in manners dependent on three kinds of enzymes, ubiquitin-activating enzymes (E1), ubiquitin-conjugating enzymes (E2) and ubiquitin ligases (E3). Substrate proteins conjugated with a poly-ubiquitin chain, which is typically linked between Lys48 and the C-terminal Gly76, are targeted to 26S proteasome for degradation. The ubiquitin proteasome system plays important roles in essentially all biological events via regulating stability and functions of numerous cellular proteins. For instance, most cell cycle-regulatory proteins are known to undergo ubiquitination and subsequent proteasome-dependent degradation, and the impacts of deregulated ubiquitination on cell proliferation and cancer development have been extensively studied. While the roles of the ubiquitin proteasome system in endocrinology and metabolism has been relatively understudied, recent investigations have suggested that defective ubiquitin-dependent degradation of signaling molecules, e.g., IRS1 and IRS2, in insulin target tissues or pancreatic beta cells could lead to insulin resistance or insufficient insulin secretion. Also, there is evidence that ubiquitination of transcription factors in adipose tissues controls metabolic homeostasis. Current insights into the involvement of the ubiquitin proteasome system in endocrinology and metabolism will be discussed, together with implications of our recent studies on the roles of ubiquitination and cell cycle regulation in metabolic disorders.

Biography

Hiroaki Kiyokawa obtained his M.D. in 1986 and a Ph.D. in 1990 from Osaka University, Japan, and completed postdoctoral studies in 1994 at Memorial Sloan-Kettering Cancer Center in New York. He is currently Professor of Molecular Pharmacology and a Co-Leader of the Cancer Cell Biology Program in the NIH-designated Robert H. Lurie Comprehensive Cancer Center. He has published more than 98 papers in high profile journals and has served to multiple NIH study sections and the editorial boards of BMC Cell Division and Breast Cancer Research & Therapeutics.

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