Special Issue

Allosteric Regulation in Ubiquitin Proteasome System

Message from the Guest Editors

As knowledge of the ubiquitin-proteasome system (UPS) has been accumulating, this multiprotein intracellular machinery has become recognized as one of the major guardians of proteostasis. However, further structural studies have started to reveal the dynamics and allosteric regulation involved in proteasome assembly. Since impairment or vulnerability of intracellular proteostasis is a hallmark of many diseases, harnessing allosteric interactions for regulation of the proteasome and other components of UPS would offer rich opportunities of translational significance. So far, the only proteasome-targeting drugs used in clinics are competitive inhibitors as anticancer agents. Since allosteric drugs may offer exceptionally diverse actions with low toxicity and superb specificity, it is of no surprise that multiple allosteric regulators of the proteasome and proteins involved in polyubiquitination are in preclinical development, with an eye on cancer and neurodegenerative diseases. This Special Issue aims to present the rich and diverse aspects of allosteric regulation, both intrinsic and drug-related, in the ubiquitin-proteasome system.

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