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School of Life Sciences
Seminar Series

Thursday
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This seminar will be held face-to-face.

VENUE: S3 Life Sciences Bldg. Jukhyun Bio Hall(#121)

Revealing the deubiquitination mechanisms on the proteasome for actively regulating proteolysis

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언어: 한국어

학력

2004 Ph.D., Department of Pharmacology, UT Southwestern Medical Center
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2016 - current Assistant & Associate Professor, Department of New Biology, DGIST
2007 - 2016 Postdoctoral Fellow, Department of Cell Biology, Harvard Medical School, USA
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Abstract

The 26S proteasome, a master player in protein degradation, is the most complex protease in eukaryotes. While capable of hosting thousands of discrete substrates due to the selective recognition of ubiquitin tags, this protease complex is also under tight control through diverse regulatory mechanisms. Among the multi-layered processes regulating the proteasome's activity, deubiquitination reactions are prominent because they not only recycle ubiquitins, but also impose a critical checkpoint on the proteasome during substrate processing. We previously discovered that USP14/Ubp6, a major deubiquitinase on the proteasome, acts as a critical inhibitory component on the proteolytic pathway and also developed small-molecule inhibitors selectively targeting USP14 as proteasome activity enhancers. Our mechanistic studies suggest that USP14/Ubp6-mediated reactions exert dynamic influence over proteasome output while acting spatially on the proteasome, temporally through substrate processing, and differentially for ubiquitin topology in both catalytic activity-dependent and -independent manner. USP14/Ubp6 and the proteasome are also mutually linked through an allosteric bidirectional switch. Therefore, deubiquitinases on the proteasome may actively fine-tune the degradation in the context of proteasome and for dynamic proteolysis outcomes. Given that the ubiquitin-proteasome system is among the most important drug targets, the biology of deubiquitinases should be further elucidated for its potential targeting in human diseases.