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## COLLOQUIUM

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- **SPEAKER**

Prof. Yongli Zhang (Dept. of Cell Biology, Yale University, USA)

- **TITLE**

Single-molecule force spectroscopy of protein folding and dynamics

- **ABSTRACT**

Forces hold everything together and determine the structures and dynamics of macromolecules. We have broad interests and skills in measuring the intra- and inter-molecular forces and the forces generated by molecular machines as a crucial step to understand their biological functions. We combine high-resolution optical tweezers and single-molecule fluorescence spectroscopy to manipulate and visualize single molecules in real time, revealing dynamic structures of proteins inaccessible by other experimental methods. Using this new approach, we have elucidated the molecular mechanisms of SNARE assembly and its regulation by Munc18-1 and other proteins. SNARE proteins and Munc18-1 constitute the core machinery for fusion involved in neurotransmission and insulin secretion. Dysfunction of the machinery has been linked to neurological disorders and diabetes. However, the pathway of SNARE assembly and the mechanistic role of Munc18-1 in membrane fusion have remained enigmatic despite intensive research spanning four decades. We found that Munc18-1 acts as a non-classical protein chaperone to catalyze step-wise assembly of three SNAREs (syntaxin, VAMP2, and SNAP-25) into a four-helix bundle. The catalysis requires formation of an intermediate complex as recently hypothesized, in which Munc18-1 juxtaposes the N-terminal SNARE motifs of syntaxin and VAMP2 but keeps their C-termini separated. Next, SNAP-25 quickly binds the templated SNAREs to form a partially-zipped SNARE complex. Finally, full zippering displaces Munc18-1. Munc18-1 phosphorylation and disease mutations modulate the stability of the template complex in a way that correlates with their effects in membrane fusion, indicating that the chaperoned SNARE assembly is essential for exocytosis. Finally, I will describe a new assay recently developed in our lab to study protein-membrane interactions based on optical tweezers.

- **DATE AND VENUE**

May 21, 2018 (Monday, 4:00 - 5:00 pm)  
Seminar Room 116, KU R&D Center

- **LANGUAGE**

English

- **INVITED BY** - Prof. Hong, Seok-Cheol