



Houk-Jung Organic Colloquium

Natural Recognition Motifs for the E3 Ligase Adapter Cereblon

Abstract: Understanding the biology of drug target proteins is essential to enhance drug discovery efforts and mechanistic studies. The clinical drugs thalidomide and its derivatives, known as immunomodulatory drugs (IMiDs), are recognized by a conserved binding domain on the E3 ligase adapter cereblon (CRBN), resulting in lifesaving anti-cancer treatments or horrific teratogenicity. However, despite the growing use of CRBN in the lab and clinic, the mechanisms CRBN uses to recognize protein substrates have escaped definition to date. E3 ligase complexes select proteins for degradation by recognizing degrons, specific amino acid sequences sufficient to promote ubiquitination and degradation when embedded in a protein substrate. We hypothesized that degrons for the thalidomide-binding domain of CRBN could be installed on its substrates via post-translational modifications. Here, I will discuss our chemical approaches to discovering a degron for the thalidomide-binding domain of CRBN and its implications for the physiological function and therapeutic engagement of CRBN.

Bio: Saki Ichikawa is currently a postdoctoral fellow in the laboratory of Professor Christina M. Woo at Harvard University, where she investigates natural substrate recognition mechanisms of the E3 ligase adapter cereblon (CRBN). She obtained a BS in Chemistry from the University of Tokyo (2014), where she conducted undergraduate research in the laboratory of Professor Eiichi Nakamura. In 2019, Saki received her Ph.D. in Chemistry from the Massachusetts Institute of Technology (MIT) under the guidance of Professor Stephen L. Buchwald. While at MIT, she focused on the development of copper-catalyzed asymmetric hydroamination reactions. By integrating chemical biology, organic chemistry, and chemical proteomics, Saki aims to address significant questions in the chemistry and biology of protein modifications.

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Mani L. Bhaumik Collaboratory - YH 4222
Dongwon Yoo Seminar & Conference Hall

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