

セミナーのお知らせ

5月27日(水) 14:00-15:00 B2棟 4階 大会議室

Chemical Biology with the Ubiquitin Signal

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In this talk, I will present our synthetic approaches for protein ubiquitination to shed light on the various unknown aspects of the ubiquitin signal in cellular pathways. The enzymatic attachment of ubiquitin to a specific protein target is a widely utilized posttranslational modification in eukaryotes, which is involved in various aspects of cellular functions and has been implicated in several diseases. The overwhelming majority of biochemical, biophysical and structural studies in the field rely on the in vitro enzymatic reconstitution of this complex modification for the protein of interest. However, the enzymatic approaches are often challenged by the isolation of the specific ligase, the heterogeneity of the modified protein and obtaining workable quantities of the ubiquitinated conjugates. Our group is developing novel non-enzymatic methods for the efficient and site-specific protein ubiquitination to overcome the limitations of the enzymatic machinery. These approaches allowed for the semisynthesis of homogeneous ubiquitinated protein such as alpha-synuclein and histone H2B to support the ongoing efforts aiming at studying the effect of ubiquitination in these systems. We are also expanding these approaches to study and target different deubiquitinases to shed light on their role in health and disease, and ultimately, for drug development.

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2. Total Chemical Synthesis of a 304 Amino Acid K48-Linked Tetraubiquitin Protein: K. S. Ajish Kumar, S. N. Bavikar, L. Spasser, T. Moyal, S. Ohayon, A. Brik, **Angew. Chem.** 2011, 123, 6261.
3. Targeting Deubiquitinases Enabled by Chemical Synthesis of Proteins: S. Ohayon, L. Spasser, A. Aharoni, A. Brik, **J. Am. Chem. Soc.** 2012, 134, 3281.
4. Synthetic polyubiquitinated α -Synuclein reveals novel insights into the roles of ubiquitin chain in regulating its pathophysiology: M. Haj-Yahya, B. Fauvet, Y. Herman-Bachinsky, M. Hejjaoui, S. N. Bavikar, S. V. Karthikeyan, A. Ciechanover, H. A. Lashuel, A. Brik, **Proc. Natl Acad. Sci. USA.** 2013, 110, 17726.
5. Non-Enzymatic Polyubiquitination of Expressed Proteins: H. P. Hemantha, S. N. Bavikar, Y. H. Bachinsky, N. Haj-Yahya, S. Bondalapati, A. Ciechanover, A. Brik, **J. Am. Chem. Soc.** 2014, 136, 2665.

Ashraf Brik 博士は、ユビキチン化蛋白質の全化学合成などで著名な蛋白質化学の研究者です。11th Hirata Award の授賞講演のため来日される機会に、東工大でもセミナーをしていただくことになりました。是非ご来聴下さい。

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