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The Chinese University of Hong Kong
Department of Chemistry
Research Seminar Series

Speaker: Dr. Clive Yik Sham Chung
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Title: Frontier Technologies in Chemical Biology: Activity-Based Imaging (ABI) and Activity-Based Protein Profiling (ABPP)

Date: December 16, 2019 (Monday)

Time: 10:00 a.m.

Venue: L3, Science Centre

<< Abstract >>

Application of functional chemical tools to study and manipulate biological systems and to advance drug research and development is the central goal of chemical biology. Activity-based protein profiling (ABPP), which utilizes reactivity-based compounds coupled with mass spectrometry (MS) and chemoproteomic platforms, has demonstrated great impact in chemical biology and cell biology by unraveling new functions and activities of proteins. It is also a powerful tool in drug discovery and development, as it can directly deconvolute the mechanism of actions of drug compounds and uncover unique and novel druggable modalities that would not be predicted *a priori*. On the other hand, activity-based imaging (ABI) employs reactivity-based probes, working with spectroscopies and microscopies, to detect target analytes in biological samples. With excellent spatial and temporal resolution, ABI enables real-time monitoring of cellular events mediated by target analytes and hence identifications of roles of the analytes in biology.

Today, I would like to illustrate new design and chemistry in ABPP and ABI for advancement in biological studies. (1) By coupling ABPP with a library of cysteine- or lysine-reactive small molecules, new compounds and mechanism have been identified for modulations of autophagy and mTORC1, which are both important for maintaining cellular homeostasis and dysregulations are known to associate with serious diseases, including aging, cancer and neurodegenerative disorders. (2) With the ratiometric fluorescence feature which allows self-calibration of non-homogenous probe loading across different specimens, **FCP-1** uncovers a labile Cu(I) deficiency in oncogenic $KRAS^{G12D}$ and $BRAF^{V600E}$ mutations, suggesting a connection between Cu and cancer. (3) Permanent-staining from **Peroxymycin-1** enables selective imaging of H_2O_2 in fixed samples, which is not feasible by most reported fluorescence probes. This allows the detection of elevated H_2O_2 levels in liver tissues of mouse model of nonalcoholic fatty liver disease (NAFLD), thus initiating further studies in the roles of H_2O_2 on NAFLD development and propagation.

References:

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2. C. Y. S. Chung, J. M. Posimo, S. Lee, T. Tsang, J. M. Davis, D. C. Brady and C. J. Chang, *Proc. Natl. Acad. Sci. U. S. A.*, in press, doi: 10.1073/pnas.1904610116.
3. C. Y. S. Chung, G. A. Timblin, K. Saijo and C. J. Chang, *J. Am. Chem. Soc.*, 2018, **140**, 6109.

ALL ARE WELCOME

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