UDC 577.114.083 DOI: 10.25808/08697698.2018.202.6S.021

L.-C. LO

Development of chemical probes exploiting quinone methide chemistry for biochemical applications

In the post-genomic era, development of small molecules as tools to help studying biological phenomenon has gained increasing attention. It is especially true in the development of activity-based probes (ABPs) due to their remarkable ability to label and enrich the designated enzymatic activities on protein extracts or living cells. For nearly two decades, my group has been devoted to the development of functional molecules and exploited these molecules in a wide variety of biochemical applications. Here I would like to present our results on the design, synthesis, and applications of ABPs for tyrosine phosphatases, glycosidases, and sulfatases [2, 6, 7]. A typical probe consists of four structural components; a recognition head, a latent trapping device, a linker, and a reporter group. The probes themselves are also the substrates of the corresponding hydrolases. Once the recognition head is cleaved by the target hydrolase, the probe will be selectively activated, leading to covalent modifications of the enzyme. Activity-based probes have versatile applications. For example, a sialidase probe could be utilized to capture influenza viruses [4], while a fucosidase probe could be used to visualize and locate lysosomal α-L-fucosidase activity in cells [1]. In addition, we took advantage of the featured chemoselective reaction between arylborinic acids and hydrogen peroxide to develop probes for H_2O_2 [3, 5]. This was the pioneering work in this field.

REFERENCES:

1. Hsu Y.-L. et al., Development of activity-based probes for imaging human α-L-fucosidases in cells, *J. Org. Chem.* 2015, *80*, 8458-8463.

2. Lo L.-C. et al., Design and synthesis of class-selective activity probes for protein tyrosine phosphatases. *J. Proteome Res*.2002, *1*, 35-40.

3. Lo L.-C. et al., Development of highly selective and sensitive probes for hydrogen peroxide. *Chem. Commun.* 2003, 2728-2729.

4. Lu C.-P. et al., Design of a mechanism-based probe for neuraminidase to capture influenza viruses. *Angew. Chem. Int. Ed.* 2005, *44*, 6888-6892.

5. Lu C.-P. et al., Nitrophenylboronic acids as highly chemoselective probes to detect hydrogen peroxide in foods and agricultural products. *J. Agric. Food Chem.* 2011, *59*, 11043-11046.

6. Tai C.-H. et al., Synthesis and evaluation of turn-on fluorescent probes for imaging steroid sulfatase activities in cells. *Chem. Commun.* 2014, *50*, 6116-6119.

7. Tsai C.-S. et al., Design and synthesis of activity probes for glycosidases. *Org. Lett.* 2002, *4*, 3607-3610.

* Lo Lee-Chiang – PhD, Prof., Associate Chair (Department of Chemistry, National Taiwan University, Taipei 106, Taiwan). *E-mail: serg@ibch.ru

The work was supported by the Ministry of Science and Technology grant MOST106-2113-M-002-005.