

## “ Structural and thermodynamic insights into the mechanisms of cation-coupled symport ”



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**Time** : 13:30 – 15:00  
**Venue** : Lecture room No. 2  
(Graduate School of Agricultural Science)

The major facilitator superfamily (MFS) of membrane transport proteins is the largest family of solute carriers. MFS permeases play important roles in physiology and drug *absorption*/distribution; they are often drug targets. The bacterial Na<sup>+</sup>-coupled melibiose permease of *Salmonella typhimurium* (MelB<sub>St</sub>) and H<sup>+</sup>-coupled lactose permease of *Escherichia coli* (LacY) are two well-characterized cation-coupled symporters. X-ray crystal structures of both proteins show a typical MFS fold; the N- and C-terminal six-helix bundles surround an aqueous cavity containing the binding sites for a sugar molecule and its coupling cation. Transport in both permeases utilizes an alternating-access mechanism involving sequential binding and releasing of sugar and cation. This lecture will focus on the basic principle governing transport process, and present the studies utilizing an integrated approach, including X-ray crystallography, isothermal titration calorimetry, and other biochemical & biophysical techniques, to gain structural and functional insights into the cation-coupled symport mechanisms.

Ethayathulla, A. S., Yousef, M. S., Amin, A., Leblanc, G., Kaback, H. R., and Guan, L. (2014) Structure-based mechanism for Na<sup>+</sup>/melibiose symport by MelB. *Nature Communications* 5: 3009 doi:10.1038/ncomms4009

Hariharan, P., Balasubramaniam, D., Peterkofsky, A., Kaback, H.R. and Guan, L. (2015) Thermodynamic mechanism for inhibition of lactose permease by the phosphotransferase protein IIA<sup>Glc</sup>. *Proc Natl Acad Sci U S A.* 112(8):2407-12. doi: 10.1073/pnas.1500891112

Guan, L., Nurva, S., and Ankeswarapu, S. P. (2011) Mechanism of melibiose/cation symport of the melibiose permease of *Salmonella typhimurium*. *J Biol Chem.* 286(8):6367-6374 doi: 10.1074/jbc.M110.206227