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Model membrane biosensor for probing the interfacial binding mechanism of phospholipase A$_2$

Joshua A. Jackman[1] and Nam-Joon Cho[2]

[1]School of Materials Science and Engineering, Nanyang Technological University, Singapore
[2]Department of Medicine, Division of Gastroenterology and Hepatology, Stanford University, USA

Phospholipase A$_2$ (sPLA2) is an important class of interfacial enzyme involved in key biological processes such as signal transduction and lipid metabolism. Pharmacologic modulation of sPLA2 represents an attractive therapeutic strategy for several medical diseases including cancer, but efforts toward this goal have been stymied by the limited knowledge about the link between how sPLA2 members interact with target lipid membranes and their respective physiological functions. To gain insight into the biophysical mechanism underlying membrane association of sPLA2 enzymes, we developed a model membrane biosensor platform to probe the role of membrane electrostatics in this process. Real-time monitoring of the membrane association step with the quartz crystal microbalance with energy dissipation (QCM-D) technique enabled us to identify a novel bilayer-disrupting behavior that is dependent on membrane electrostatics. The data identified that 1) enzyme adsorption to model membranes is primarily mediated by non-electrostatic interactions; 2) nonhydrolytic bilayer-disruption can follow enzyme adsorption; and 3) this disruptive activity is directly related to electrostatic interactions. Based on these findings, we conclude that interfacial binding of sPLA2 enzymes is a dynamic process, and identify promising opportunities for therapeutic intervention as well as engineering approaches for sPLA2-triggered liposomal drug delivery.

Biography

Jackman attended the University of Florida where he earned a bachelor's degree with highest honors in chemistry, and was a member of Phi Beta Kappa. During his undergraduate studies, he was named a Beckman Scholar and pursued extensive research at Stanford University on the design and application of model membranes for biomedicine. Mr. Jackman then began his doctoral studies in biomedical engineering at Harvard University-Massachusetts Institute of Technology as an NSF Graduate Fellow, before transferring to Nanyang Technological University in Singapore in order to become involved in the emerging Asian biotechnology community, and to reunite with his former mentor from Stanford, Dr. Nam-Joon Cho.

josh0018@e.ntu.edu.sg, jackmanfutbol@gmail.com