Quantitative Analysis of Multivalent Protein Binding to Cell Membranes

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ABSTRACT

The dynamic process of binding protein onto a biological membrane, driven by a series of binding domains, brings a protein to an active site for regulation of protein function. This reversible binding appears in a wide range of cellular events *and* often involves multiple ligand-binding domain interactions. The cooperative effort among multiple bound domains usually leads to higher binding avidity and specificity. Quantitative analysis of protein retention on cellular membranes is essential in determining the rate of these biochemical reactions. We have developed a nanocube sensor coupled with complex reaction analysis to quantitatively explore the multivalent protein binding. The nanocube sensor is surrounded by lipid bilayers that possess the same physical and chemical properties as cell membranes. This biomimetic surface then enables the label-free detection of protein bindings by observing the absorption spectra shift of localized surface plasmon resonance (LSPR) peak. This biosensor works with standard laboratory plate reader for high-throughput binding kinetic analysis. The simple protocol ("mix-and-then-detect") allows any end users performing the analysis in their own laboratories. We have successfully explored many essential protein binding events, including pleckstrin-homology (PH)-lipid and toxin-ganglioside interactions. Moreover, we have introduced complex reaction analysis to model the binding cooperativity among multiple binding domains. This technique will assist scientists in understanding basic principles of membrane protein binding and comprehensively designing new drugs to manipulate binding processes for therapeutic purposes.

BIOGRAPHY

Photo (1.5" x 2")

Dr. Hung-Jen Wu received his B.S. (1998) and M.S. (2000) in Chemical Engineering from the National Cheng-Kung University, Taiwan. He received his Ph.D. in Chemical Engineering from

Texas A&M University in 2006, working on developing advanced microscopy techniques to explore weak molecular interactions. From 2007 to 2011, he worked as a Postdoctoral Fellow at the University of California, Berkeley. During the postdoctoral training, he focused on studying the properties of biological membrane. Between 2011 and 2013, Dr. Hung-Jen Wu was appointed as a Research Associate in the Nanomedicine Department at the Houston Methodist Research Institute, and was involved in developing diagnostic tools for infectious diseases. Currently, he is an Assistant Professor of Chemical Engineering at Texas A&M University. Dr. Wu's research primarily focuses on the development of nanostructured materials for diagnosis of diseases, including cancer and infectious diseases.