OMICS Group Conferences
Accelerating Scientific Discovery

International Conference and Exhibition on
Biosensors & Bioelectronics

May 14-16, 2012 Embassy Suites Las Vegas, USA

Antiviral mode of action of AH peptide determined by combined surface science techniques

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AH peptide protein is a breakthrough, broad-spectrum antiviral drug candidate. It ruptures the lipid envelope of virus particles in a size-dependent manner. The size range of virus particles susceptible to treatment with AH peptide encompasses a wide range of deadly viral pathogens including HCV and HIV. Uniquely compared to other antiviral medicines in development or in the clinic, the virocidal activity of the AH peptide was originally discovered by surface science techniques probing model biological interfaces—namely lipid vesicles serving as surrogates for lipid-enveloped virus particles. Quartz crystal microbalance with dissipation (QCM-D) monitoring identified that addition of the AH peptide ruptures a layer of intact lipid vesicles to promote structural transformation to a planar lipid bilayer. Based on this in situ structural transformation, we have used simultaneous QCM-D monitoring and four-detector optical reflectometry to determine the antiviral mode of action of the AH peptide. The combination of optical and acoustic sensor techniques for simultaneous measurement on the same substrate offered several advantages, including: (1) monitoring of the complex biological interactions with both acoustic and optical mass measurements, (2) calculation of the amount of dynamically coupled water, (3) identification of mechanistic steps based on hydration signature, and (4) multi-parameter analysis of the structural transformation arising from biological interactions. Collectively, these results lay the groundwork for the engineering of AH peptide therapeutics with optimized properties as well as for the broader application of surface science techniques to antiviral drug discovery and development.

Biography

Nam-Joon Cho is Nanyang Associate Professor at Nanyang Technological University and Visiting Associate Professor at Stanford University. His research focuses on engineering approaches to solve important biomedical problems and to translate this knowledge into real-world improvements for healthcare and biodefense. Dr. Cho's scientific work has been highlighted by international media organizations such as Reuters, CNBC, and Businessweek, and is leading to major breakthroughs for the treatment of deadly pathogens. Through the first demonstration of engineering approaches for antiviral drug discovery, he identified novel classes of drugs to treat hepatitis C virus which affects over 170 million people worldwide. Based on the success of this early work, Dr. Cho's team is now pursuing similar strategies to examine the causes and consequences of human diseases, including infectious diseases, inflammatory disorders, and cancer, in order to provide improved diagnostic and therapeutic interventions. He is a graduate of Stanford University and the University of California, Berkeley.

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