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Using Optical Tweezers to Quantify the Interaction Force of Dengue Virus with Host Cellular Receptors

Bo-Ying Tsai[1, 2], Jyun-Yu Chen [1, 2], Arthur Chiou[1,2,], Yueh-Hsin Ping [1, 2, 3, 4]

[1] Institute of Biophotonics, National Yang-Ming University, Taipei, Taiwan
[2] Biophotonics Interdisciplinary Research Center, National Yang-Ming University, Taipei, Taiwan
[3] Infection and Immunity Research Center, National Yang-Ming University, Taipei, Taiwan
[4] Department and Institute of Pharmacology, National Yang-Ming University, Taipei, Taiwan

Optical tweezers (OT) is a powerful tool to manipulate a single particle in living cells. It is able to determine the interaction force of biological molecule(s) in an excellent resolvable range from 1 to 100 pN. Moreover, OT has been used to investigate the interaction between ligand and receptor [1] and to reveal the dynamics and properties of living cell elasticity, viscoelasticity and adhesion. Dengue virus (DENV) is one of the most widespread viral pathogens around the world. There is currently no anti-DENV drugs or vaccine to against DENV infection because little is known about the complex and highly dynamic process of dengue infection. Among DENV infectious process, receptor-binding is the first critical step contributes for successful infection. Elucidation of the receptor-binding details is helpful for developing anti-viral agents. Since force plays an important role in interaction dynamic and structure of biomolecule and the binding force between virus and receptor has not been extensively studied, we would like to measure the binding forces between ideally single virus particle and host cellular receptors by combining OT and a single-virus particle tracking approache that we had developed recently [2]. We have used OT to trap a single bead bound with DiI-labeled DENV particles (Figure 1). To determine the interaction force between DENV particle and host cellular receptor(s), a single cell ectopically expressed DC-SIGN was moved to touch the single virus-bound bead (Figure 2). The single virus binding forces is 3.4± 0.6 pN in the absence of the expression of DC-SIGN in THP-1 cells. In contrast, in the presence of DC-SIGN expression, the force is increased to 43.7± 8.1 pN. Herein, we not only have successfully elucidated the interaction force of DENV particle with a cellular receptor, but also demonstrate that OT is a real-time force measurement approach to determine the interaction forces between biological molecules in living cells.

[1] Stangner, T. et al, ACS nano 7 (2013), 11388-11396.
[2] Chu, L.W. et al, J Biomed Opt 19 (2014), 011018.

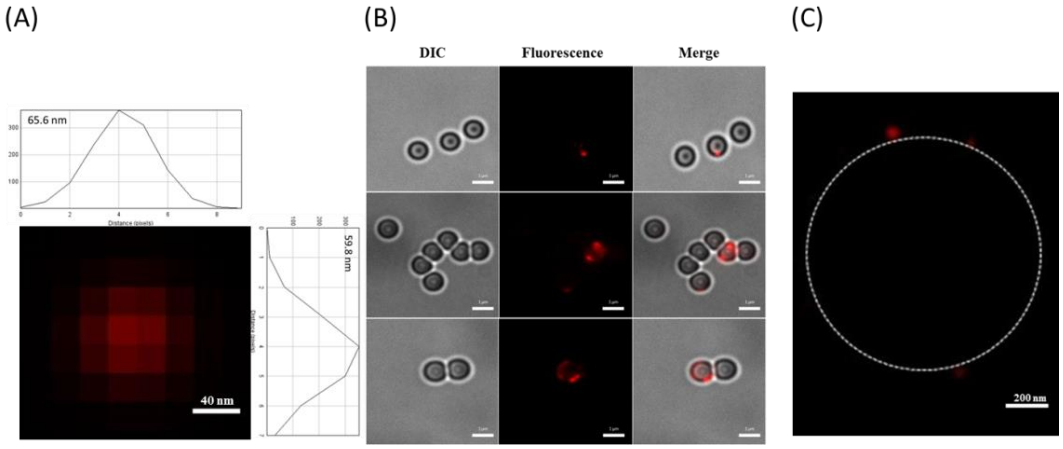

Figure 1. Design single quantity DiI-labeled DENV particles bound on polystyrene (PS) beads. (A) The size of single DiI-labeled DENV particle was measured using super-resolution microscopy. The scale bar: 40 nm. (B) The DIC and fluorescence images of single quantity DiI-labeled DENV particle bound on PS beads with epi-fluorescence microscopy. The scale bar: 1 μm. (C) The DIC and fluorescence images of single quantity DiI-labeled DENV particle bound on PS beads under super-resolution microscopy. The scale bar: 200 nm.

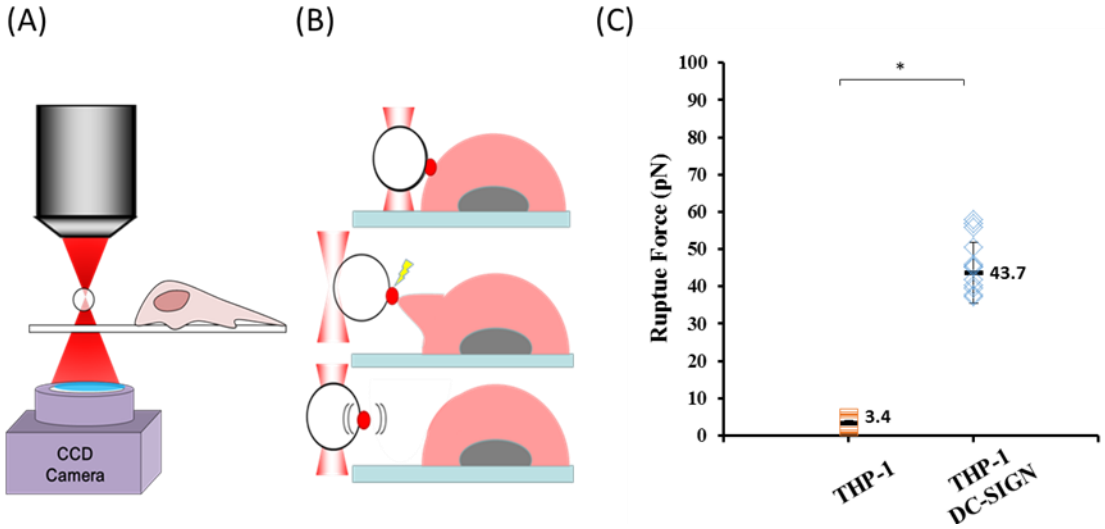

Figure 2. The measurement of force between virus bound on a bead and receptor on cell membrane surface by OT. (A) Schematic diagram of OT system. (B) Schematic diagram of the protocol to determine the binding force. (C) The binding force of DENV particle with DC-SIGN receptor
*: $p<0.05$

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