Antibody Walking on Membranes filmed with High-Speed AFM

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Abstract

Binding of antibodies to their cognate antigens is fundamental for adaptive immunity. Molecular engineering of antibodies for therapeutic and diagnostic purposes emerges to be one of the major technologies in combating many human diseases. Despite its importance, a detailed description of the nanomechanical process of antibody-antigen binding and dissociation on the molecular level is lacking. Here, we utilize single molecule force spectroscopy and high-speed atomic force microscopy to examine the dynamics of antibody recognition and uncover a new principle. Contradicting the current textbook view, antibodies do not remain stationary on surfaces of regularly spaced epitopes; they rather exhibit “bipedal” random walking. As monovalent Fabs do not move, steric strain is identified as the origin of short-lived bivalent binding. Randomly walking antibodies gather in transient clusters that might serve as docking sites for the complement system and/or phagocytes. Our findings will inspire the rational design of antibodies and multivalent receptors to exploit/inhibit steric strain-induced dynamic effects.