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Interactions between HIV-1 Neutralizing Antibodies and Model Lipid Membranes imaged with AFM STEFAN ZAUSCHER, GREGORY HARDY, MUNIR ALAM, Duke University, JOSEPH SHAPTER, Flinders University — Lipid membrane interactions with rare, broadly neutralizing antibodies (NAbs), 2F5 and 4E10, play a critical role in HIV-1 neutralization. Our research is motivated by recent immunization studies that have shown that induction of antibodies that avidly bind the gp41-MPER antigen is not sufficient for neutralization. Rather, it is required that antigen designs induce polyreactive antibodies that recognize MPER antigens as well as the viral lipid membrane. However, the mechanistic details of how membrane properties influence NAb-lipid and NAb-antigen interactions remain unknown. Furthermore, it is well established that the native viral membrane is heterogeneous, representing a mosaic of lipid rafts and protein clustering. However, the size, physical properties, and dynamics of these regions are poorly characterized and their potential roles in HIV-1 neutralization are also unknown. To understand how membrane properties contribute to 2F5/4E10 membrane interactions, we have engineered biomimetic supported lipid bilayers (SLBs) and use atomic force microscopy to visualize membrane domains, antigen clustering, and antibody-membrane interactions at sub-nanometer z-resolution. Our results show that localized binding of HIV-1 antigens and NAbs occur preferentially with the most fluid membrane domain. This supports the theory that NAbs may interact with regions of low lateral lipid forces that allow antibody insertion into the bilayer.

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