P-2.59

Probing Molecular Interactions Between Virus and Host Cell Under Physiologically Relevant Conditions

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Reovirus is a widespread pathogen and a model for studying viral entry and host interactions. It is highly infectious and environmentally stable. The Junctional Adhesion Molecule-A (JAM-A) serves as the primary reovirus receptor, while sialic acid and other glycans act as co-receptors facilitating initial attachment. However, the precise role of sialic acid in infection remains unclear. Atomic force microscopy (AFM) enables the quantitative analysis of virus-host interactions at the molecular level. This study aims to characterize the early stages of reovirus entry by comparing wild-type and sialic acid-deficient strains under physiological conditions. Using AFM in single-molecule force spectroscopy mode, we determined the kinetic parameters of reovirus binding. This approach provided a quantitative understanding of the initial virus-host interactions. We also combined confocal imaging with AFM to analyze dynamic virus-host interactions in live Caco-2 cells, an intestinal model expressing JAM-A and glycans, we examined how receptor availability and cellular differentiation influence viral attachment. Our results show that both reovirus strains exhibit similar binding affinities. Furthermore, viral binding to Caco-2 cells increased with cellular differentiation, suggesting that receptor expression levels and distribution change over time.