

SPOTLIGHT

Articles of Significant Interest Selected from This Issue by the Editors

High-Resolution Molecular and Antigenic Structure Suggests Differences in the Spikes of Virulent Human Rotavirus Strains

To date, only rotavirus strains that attach to cells when their spikes bind sialosides have been analyzed structurally. Rotaviruses that cause human disease do not bind sialosides. Monnier et al. (p. 1513–1523) determined the crystal structure of spike heads from a virulent human rotavirus strain and mapped neutralization escape mutations selected by human monoclonal antibodies. The structure shows a disrupted sialoside-binding site and suggests an alternative ligand-binding region. Antigenic mapping and comparison to an electron cryomicroscopy image reconstruction of virions indicate that the surfaces and spike morphologies recognized by neutralizing antibodies differ between sialoside-dependent and sialoside-independent rotaviruses.

A Molecular Switch for Paramyxovirus Receptor-Binding Activity

The receptor-binding protein (hemagglutinin-neuraminidase, HN) of the paramyxovirus Newcastle disease virus (NDV) has two binding sites, only one of which has receptor-cleaving activity. Porotto et al. (p. 1204–1213) show that engagement of the first receptor-binding site by molecules that mimic the receptor leads to activation of the second binding site. The results provide a possible explanation for how the two disparate activities of a paramyxovirus HN molecule are regulated during infection; the second site may be activated upon attachment to the target cell, but shut off after budding. This work suggests new antiviral strategies that take advantage of the interdependence of the two binding sites.

Receptors for BK Virus

The BK polyomavirus is an emerging concern in the field of transplantation medicine. Advances in immunosuppression have led to BK virus reactivation in increasing numbers of bone marrow and kidney transplant recipients. Low et al. (p. 1361–1366) demonstrate that the gangliosides GD1b and GT1b are receptors for the virus and that disruption of endoplasmic reticulum trafficking inhibits infection. The identification of gangliosides as receptors for BK virus, as well as the characterization of an additional step in viral trafficking, may lead to new treatments for this ubiquitous virus.

Entry of Kaposi's Sarcoma-Associated Herpesvirus Requires Focal Adhesion Kinase (FAK)

Kaposi's sarcoma-associated herpesvirus (KSHV) is the first herpesvirus shown to interact with integrins. Within minutes of its binding to target cells, KSHV activates several integrin-dependent signaling molecules, including FAK, Src, PI-3K, RhoGTPases, PKC- ζ , MEK, and ERK1/2. Krishnan et al. (p. 1167–1180) demonstrate that FAK plays a critical role in KSHV DNA internalization. These data further support the hypothesis that via its interactions with cell-surface receptors, KSHV manipulates cellular signal-transduction pathways for its entry, movement in the cytoplasm, and establishment of infection.

Efficient Adenovirus Production Requires Viral miRNAs

Adenovirus virus-associated I (VAI) RNAs are 160-nucleotide RNA hairpins that block PKR activation in infected cells. Aparicio et al. (p. 1376–1384) provide evidence that VAI RNAs also are processed to form small RNAs that interact with the cellular silencing machinery and allow efficient virus production. These adenovirus miRNAs are suggested to control the expression of cellular or viral genes involved in adenovirus viability. Thus, animal viruses could use the cellular silencing machinery to control gene expression in infected cells.

Insights into Coronavirus Assembly

Coronaviruses assemble on intracellular membranes through a series of membrane protein interactions. Thorp et al. (p. 1280–1289) demonstrate that efficient spike glycoprotein assembly requires posttranslationally added palmitic acids. This

work reveals a novel role for palmitates in generating assembly-competent glycoproteins and underscores the importance of lipid adducts in enveloped virus infectivity.

Antibodies against a Nonstructural Protein Protect against West Nile Virus

Even though not contained in the virion, immunization with flavivirus nonstructural protein 1 (NS1) elicits a protective antibody response through poorly defined mechanisms. Chung et al. (p. 1340–1351) provide new mechanistic evidence about how anti-NS1 antibodies control flavivirus infection. Moreover, they suggest a therapeutic utility of anti-NS1 antibodies as passive transfer even 4 days after inoculation with a lethal West Nile virus strain. By performing studies using complement and Fc γ receptor-deficient mice, the authors demonstrate that anti-NS1 antibodies mapping to distinct protein regions protect against infection through independent mechanisms.

Comparative Quantitative Mass Spectrometry of Wild-Type and Mutant Herpesvirus Virions

A common strategy to elucidate functions of viral proteins is the analysis of specific gene deletion mutants. In an exemplary study on the alphaherpesvirus pseudorabies virus, Michael et al. (p. 1332–1339) present a generally applicable approach to assess qualitative and quantitative changes in protein patterns of mutant virus particles. Using metabolic stable isotope labeling and mass spectrometry, specific alterations in the composition of mutant virions beyond the loss of the targeted gene product were observed that shed new light on the network of protein-protein interactions within the herpesvirus virion.