A New BAC Clone for the Study of Kaposi’s Sarcoma-Associated Herpesvirus

Kaposi’s sarcoma-associated herpesvirus (KSHV) is an oncogenic virus causing Kaposi’s sarcoma, primary effusion lymphoma, and multicentric Castleman’s disease. In related studies, Brulois et al. and Toth et al. constructed a new BAC clone of KSHV, BAC16, which was used to generate KSHV mutants to allow functional analysis of viral gene products in the context of the KSHV genome. Brulois et al. (p. 9708–9720) provide evidence that K5 is independently required for downregulation of MHC-I during lytic reactivation. Toth et al. (p. 9696–9707) used an RTA-deficient BAC16 to show that regulation of transcriptional elongation plays a critical role in RTA-independent viral gene expression during latency. Together, these studies demonstrate the utility of BAC16 for providing new insights into the immune evasion and gene regulation mechanisms of KSHV.

Hypervariability in Hepatitis E Virus Explained

The hepatitis E virus polyproline region is hypervariable. Purdy (p. 10186–10193) shows that this hypervariability is caused by intrinsic disorder in that region. Relaxed tertiary structure constraints result in high-substitution promiscuity in the first and second codon positions. Additionally, high transition and transversion bias results in an accumulation of cysteine residues at the second codon, leading to an increase in proline content and a decrease in aromatic amino acid residues. These alterations favor the formation of intrinsically disordered structures.

Poliovirus Increases COPII Vesicle Budding

Poliovirus infection significantly alters host intracellular membranes, but the mechanisms underlying these changes are not completely understood. It is clear that poliovirus co-opts membranes of the intermediate compartment and Golgi apparatus to establish replication organelles. Trahey et al. (p. 9675–9682) now demonstrate that poliovirus infection also increases functional COPII vesicle budding from the endoplasmic reticulum, leading to an increase in the precursor pool required for the viral replication organelles. This alteration is accompanied by an increase in sec16A, a key regulator of COPII vesicle formation, suggesting a mechanistic basis.

Conformational Switch Mutations Temporally Dissect Virus Assembly

Scaffolding proteins mediate conformational switches during virus assembly. While comparisons between virions and procapsids have defined late coat protein switches, rapid morphogenesis and small particle size hinder the analysis of early processes. Gordon et al. (p. 9911–9918) demonstrate that mutations in the øX174 scaffolding protein confer two distinct molecular defects: coat protein binding and conformational switching, a novel phenotype. Conformational switch mutations kinetically trap one of three pre-procapsid assembly intermediates. However, common second-site suppressors rescue these mutants. These findings suggest that the scaffolding protein induces a single conformational switch. Within this paradigm, incomplete switches create conformations that kinetically trap assembly intermediates.

Molecular Basis of the Transmission of the 2009 H1N1 Pandemic Influenza Virus

A novel reassortant swine influenza virus acquired sustained human-to-human transmissibility and caused the 2009 influenza pandemic. However, the molecular aspects of influenza virus transmission remain poorly understood. Zhang et al. (p. 9666–9674) identified the key amino acid in the viral hemagglutinin (HA) protein that is required for the 2009 H1N1 pandemic virus to bind to human-type receptors and confer respiratory droplet transmissibility in mammals. They also identified a residue in PB2 that plays a key role in virus acquisition of the HA mutation. This work provides important information for monitoring and evaluating the pandemic potential of influenza viruses in nature.