Articles of Significant Interest in This Issue

Different Types of Extracellular Vesicles Populate the Microenvironment of Herpes Simplex Virus 1 Infection

Extracellular vesicles (EVs) constitute a form of cell-to-cell communication that impacts recipient cells in a substantial manner. EVs are modified during herpes simplex virus 1 (HSV-1) infection and communicate virus specific signals. Dogrammatzis et al. (e02357-20) show that a density gradient can separate EVs from HSV-1 virions and allow dissection of different EV populations. EVs enriched in CD63 carry the stimulator of interferon genes (STING) and display an antiviral role. EVs enriched in components of the endosomal sorting complexes required for transport (ESCRT) carry viral components and display a proviral role. These data highlight the complexity of the signals infected cells communicate to uninfected cells.

Cholesterol Levels Modulate Multiple Steps of the Nipah Virus Membrane Fusion Cascade

Nipah virus (NiV) is a highly pathogenic enveloped virus that relies on its ability to fuse cellular membranes to propagate. Contreras et al. (e02323-20) report that both viral entry and NiV-induced cell-cell fusion are highly influenced by the levels of membrane cholesterol. Interestingly, the various steps of the membrane fusion process are affected differently. For example, while depletion of membrane cholesterol induced an increase in fusion protein triggering, it also induced a decrease in fusion pore formation, and vice versa. Therefore, membrane composition affects individual intermediate steps of the fusion cascade differently.

Single-Cell Transcriptomics Reveals a Heterogeneous Cellular Response to BK Virus Infection

Infections with BK virus (BKV; human polyomavirus 1) are usually asymptomatic. However, robust BKV replication can cause serious disease in immunosuppressed patients. Gene expression profiling performed on bulk cell populations suggest a coordinate alteration of cellular gene expression by BKV as infection progresses. An et al. (e02237-20) performed single-cell transcriptomics analysis, which revealed high levels of heterogeneity in both viral and cellular gene expression among individual infected cells. Comparison of gene expression patterns in cells expressing high or low levels of viral transcripts uncovers cellular genes and signaling pathways that correlate with successful or restricted infection. These studies provide insights into factors that influence the one-on-one battle between the virus and each infected cell.
Uncovering Mechanisms of Immune System Subversion by Ebola Virus

Previous studies have demonstrated that infection with Zaire Ebola virus (EBOV) bearing a mutation in type 1 interferon antagonist VP35 (VP35m) severely attenuates EBOV pathogenicity and protects macaques against challenge with EBOV. Pinski et al. (e01995-20) determine the molecular basis of this protection by defining the transcriptional and cellular response in the lymphoid tissues and blood of macaques following VP35m infection and subsequent EBOV challenge. They report distinct early and robust antiviral and adaptive immune signatures associated with protection against lethal wild-type infection. These findings suggest a critical role for VP35 in mediating EBOV pathogenicity.

Zika Virus Infects New Cells with Groups of Genomes

Virus plaques are classically considered to result from an individual genome entering a cell. Sexton et al. (e00787-20) infected Vero cells with molecularly “barcoded” Zika virus (ZIKV) to identify the number of genomes present in an average plaque. Plaques contained a wide range of unique barcodes, ranging from 1 to 212, indicating that multiple ZIKV genomes typically initiate infection. Infectious particle size similarly ranged extensively, with larger particles tending to contain increased genome equivalents. These findings suggest that ZIKV infections rarely begin with a single viral genome but instead result from the delivery of viral aggregates that may harbor several distinct viral genotypes.