Articles of Significant Interest Selected from This Issue by the Editors

Insight into the Cell Biology of Bunyavirus Entry

Bunyavirus attachment and entry mechanisms are poorly understood. Using a human genome-wide small interfering RNA (siRNA) screen, Meier et al. (p. 8565–8578) identified more than 562 cellular factors that potentially function in bunyavirus cell entry and replication. Evaluation of these candidates identified v-SNARE VAMP3 as an important mediator of bunyavirus late penetration and infection. The experimental and bioinformatics procedures described in this study may facilitate the comprehensive analysis of past and future data obtained using siRNA screening.

Aae-miR-2940-Mediated Control of West Nile Virus Replication

MicroRNAs (miRNAs) function in virus-host interactions. Slonchak et al. (p. 8457–8467) demonstrate that mosquito-specific miRNA aae-miR-2940-5p, which normally upregulates expression of a cellular metalloprotease gene required for West Nile virus (WNV) replication, is selectively downregulated in response to WNV infection in mosquito cells. Diminished expression of aae-miR-2940-5p in response to WNV infection leads to reduced metalloprotease levels and consequent restriction of WNV replication. These findings identify a new miRNA-mediated antiviral response to WNV in mosquito cells.

Cellular Deubiquitinases Stimulate Human Papillomavirus Genome Replication

The E1 helicase of human papillomavirus (HPV) influences replication of the viral episome. Lehoux et al. (p. 8545–8555) demonstrate that the E1 protein from mucosal HPV types interacts with the cellular deubiquitinases, USP1, -12, and -46, in complex with their stimulatory subunit, UAF1. E1 recruits these enzymes to the HPV genome where their catalytic activity stimulates viral DNA replication. This work suggests that E1-associated deubiquitinases are required for efficient replication of the HPV episome and illuminates these enzymes as potential antiviral targets.

Vaccinia Virus Targets Bim To Prevent Apoptosis

The vaccinia virus F1L protein is essential for cell survival, but it lacks discernible sequence homology to known cell-death inhibitors. Campbell and Thibault et al. (p. 8667–8677) determined the crystal structures of F1L in complex with its ligands Bim and Bak. Structure-guided mutagenesis of the F1L binding pocket was used to define the function of Bim and Bak binding in cell death inhibition. These experiments demonstrate that F1L engagement of Bim and Bak is required for subversion of apoptosis. F1L sequestration of Bim is primarily responsible for preventing cell death during vaccinia virus infection.

Single-Domain Antibodies Targeting Neuraminidase Protect against H5N1 Influenza Virus

Zoonotic infections with pathogenic H5N1 influenza viruses are rare yet often fatal. Cardoso et al. (p. 8278–8296) isolated recombinant single-domain antibodies specific for the H5N1 neuraminidase. These antibodies were produced in *Escherichia coli* and transgenic *Arabidopsis thaliana* seeds, two economical gene expression platforms. The recombinant antibodies inhibit neuraminidase activity and H5N1 influenza virus replication *in vitro* and *in vivo*. This work underscores the potential of single-domain antibodies to prevent and treat influenza virus infection.

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