

## SPOTLIGHT

### Articles of Significant Interest Selected from This Issue by the Editors

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#### **Chromatin Remodeling Is an Early Event in HSV-1 Reactivation**

Herpes simplex virus type 1 (HSV-1) latency in sensory neurons is characterized by the expression of the latency-associated transcript (LAT) and the suppression of lytic gene expression. Amelio et al. (p. 2063–2068) show that histones associated with the LAT promoter and enhancer are rapidly deacetylated during explant-induced reactivation. This deacetylation precedes a decrease in LAT abundance and is followed by an acetylation of the promoter of the lytic transactivator ICP0. These findings suggest that the initial reactivation stimulus may direct epigenetic changes in chromatin at the LAT/ICP0 regulatory region and that LAT expression must be silenced for reactivation to occur.

#### **Reovirus Induces and Benefits from a Cellular Integrated Stress Response**

Most strains of reovirus induce translational shutoff, in part by activating stress pathways that lead to phosphorylation of the essential eukaryotic translation initiation factor eIF2a. Although this cellular response thwarts replication of most viruses, Smith et al. (p. 2019–2033) found that reovirus replicates most efficiently under conditions in which eIF2a can be phosphorylated and inhibited. This work has implications for understanding the competition between cellular and viral molecules for limited cellular components and suggests that reovirus has evolved to benefit from the integrated stress response induced as a consequence of infection.

#### **LEDGF/p75 Is Important for HIV Replication**

The transcriptional coactivator lens epithelium-derived growth factor (LEDGF/p75) interacts with human immunodeficiency virus type 1 (HIV-1) integrase. Vandekerckhove et al. (p. 1886–1896) show, using RNAi-based experiments, that HIV-1 replication is reduced after transient and stable knockdown of LEDGF/p75. Quantitative PCR pinpoints the replication block to the integration step. This work validates LEDGF/p75 as an important cellular cofactor for HIV integration and suggests a potential new target for antiviral drug development.

#### **Lung Dendritic Cell Function Suppressed by Adenovirus**

Mechanisms by which adenovirus (Ad) infection induces pulmonary disease are unknown. Ad is an adjuvant for bone marrow and monocyte-derived dendritic cells (DCs); however, the effect of Ad infection on primary lung DCs, the key stimulator of pulmonary immunity, had not been reported. Thiele et al. (p. 1826–1836) demonstrate that Ad suppresses the capacity of lung DCs to stimulate T cells. These findings suggest that Ad induces pulmonary immune suppression, which has implications for an understanding of postviral pneumonias and the use of Ad in gene delivery.

#### **Novel Imaging Technique Analyzing Influenza Virus Membrane Fusion**

As new influenza viruses have the potential to cause worldwide pandemics, there is a pressing need for methodologies to quickly determine viral infectivity by using human cells. Sakai et al. (p. 2013–2018) have developed a new microscopic technique that allows for fast and sensitive detection of influenza virus membrane fusion, a crucial event in influenza virus replication. This work establishes a methodology with the potential to rapidly survey virulent influenza viruses.

#### **HIV *env* Evolves toward Ancestral States upon Transmission to a New Host**

Analyses of human immunodeficiency virus (HIV) evolution have generally assumed that genetic divergence accumulated within hosts is maintained through transmission events. However, Herbeck et al. (p. 1637–1644) show that this continuous divergence is partially reset following transmission. They demonstrate that convergent evolutionary changes toward a more ancestral state occur in the envelope gene within the first year of infection. These findings provide impetus for the development of vaccine immunogens that favor inclusion of viral sequences sampled from early in infection and that embody ancestral or consensus features of viruses circulating in a given population.

### **Structure-Function Analysis of the Epitope for 4E10, a Broadly Neutralizing Human Immunodeficiency Virus Type 1 Antibody**

Human monoclonal antibody 4E10 binds to a highly conserved epitope in the membrane-proximal external region (MPER) of human immunodeficiency virus type 1 (HIV-1) gp41. The crystal structure of this complex is characterized by a helical epitope and suggests that stabilized MPER peptides might be candidates for a synthetic HIV-1 vaccine. Brunel et al. (p. 1680–1687) report a detailed mapping of the 4E10 epitope by the use of synthetic peptides. This structural and functional analysis guided the design of conformationally constrained peptides that are helical in solution. These peptide mimics have low nanomolar affinity for 4E10 and are promising leads for a synthetic HIV-1 vaccine.

### **Respiratory Viruses Promote Bacterial Adhesion to Epithelial Cells**

Respiratory viruses predispose humans to secondary bacterial infections, but mechanisms responsible for this phenomenon are not well understood. Avadhanula et al. (p. 1629–1636) demonstrate that antecedent infection of respiratory epithelial cells by common viral pathogens increases the number of nontypeable *Haemophilus influenzae* and *Streptococcus pneumoniae* adhering to cells. The mechanisms and degree to which individual viruses promote bacterial colonization, however, differ and are cell type-dependent. This work underscores the need to consider this variation when extrapolating results of in vitro assays to human disease.