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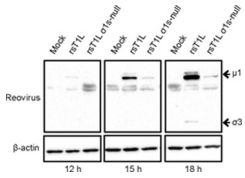
SPOTLIGHT

Articles of Significant Interest Selected from This Issue by the Editors

New Insights into Reovirus Replication

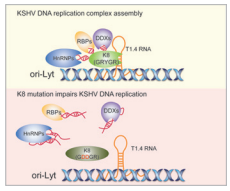
Nonstructural protein σ1s is required for reovirus bloodstream dissemination. However, σ1s function in the context of reovirus replication and the mechanisms by which σ1s promotes hematogenous spread are not well understood. Phillips et al. (e02259-17) discovered that σ1s promotes optimal reovirus protein expression, which is required for efficient viral replication. This work indicates a new function for viral protein σ1s during reovirus replication and a mechanism by which σ1s facilitates hematogenous reovirus dissemination.



Nonstructural protein σ1s is required for optimal reovirus protein expression.

Coordinate Regulation of Herpesvirus DNA Replication by a Virus-Encoded Protein and Noncoding RNA

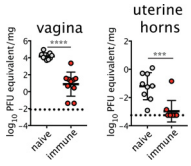
Analyses of mammalian transcriptomes reveal that sequences previously considered noncoding produce stable RNAs, potentially adapted for regulatory roles. K8, a bZip family protein encoded by Kaposi's sarcoma-associated herpesvirus (KSHV), has multiple regulatory roles in gene expression and DNA replication but lacks DNA binding capacity. Liu et al. (e02177-17) defined mechanisms underlying the regulation of KSHV DNA replication by K8. In coordination with noncoding RNA, K8 recruits cofactors, binds to DNA, assembles replication complexes, and initiates DNA replication. These data suggest a model of functional RNA-protein complexes that may shed light across species and transcriptomes.



Regulation of KSHV DNA replication by K8 in coordination with noncoding RNAs.

Prior Exposure to Zika Virus Protects against Vaginal Infection

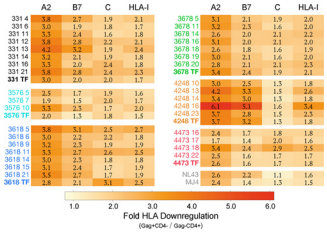
Although most flaviviruses are spread by mosquitos, the flavivirus Zika virus (ZIKV) is also sexually transmitted. Using a mouse model of infection, Scott et al. (e00038-18) found that previous subcutaneous infection with ZIKV elicits antibody and T cell responses that redundantly protect against vaginal infection. Transfer of immunoglobulin or T cells from ZIKV-immune animals is sufficient to protect naive animals from vaginal infection with ZIKV. These data begin to establish immune correlates of protection against intravaginal ZIKV infection, which should inform vaccination strategies for women.



Transfer of ZIKV-immune IgG protects against vaginal ZIKV infection.

Immune Evasion of Transmitted and Chronic HIV-1 through HLA Class I Downregulation

Human leukocyte antigen class I molecules (HLA-I) present viral peptides for immune recognition that are targeted for downregulation by HIV in infected CD4$^+$ T cells. Ende et al. (e01633-17) describe the variation in HLA-A, HLA-B, and HLA-C downregulation by transmitted and quasispecies variants from heterosexual transmission pairs. While a common signature was not observed for transmitted variants, the studies highlight the importance of HLA-C downregulation in natural killer cell recognition of HIV-1-infected cells. These phenotypic attributes of different viral variants within and between individuals illuminate the complexities of HIV-1 pathogenesis.

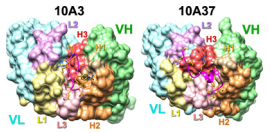


HLA downregulation in HIV-1-infected CD4$^+$ T cells *in vitro*.

https://doi.org/10.1128/JVI.00185-18

Structural Analyses of New Neutralizing Antibodies against the HIV-1 V3 Loop

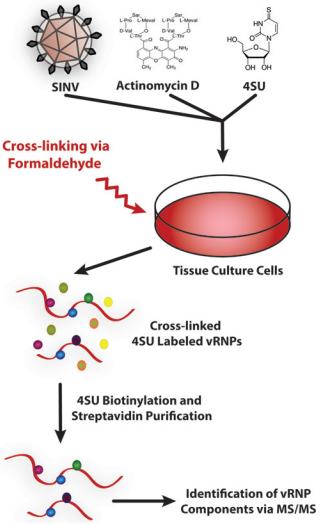
Structural information about neutralizing antibody (nAb)-antigen interactions provides insights for designing immunogens. Pan et al. (e01894-17) describe crystal structures of two nAbs bound to the V3 loop of HIV-1 gp120. The two nAbs, 10A3 and 10A37, were isolated from a vaccinated rabbit. The results reveal that epitope complexity evolves with affinity maturation, the C-terminal region of the V3 crown adopts a helical structure, and this helical region harbors epitopes of high potency and breadth. These data indicate that the V3 loop remains a viable vaccine target and that rabbits are a useful animal model to evaluate human vaccine candidates.



Cocrystal structures of 10A3 and 10A37 bound to epitopes.

New Strategy To Identify and Characterize Viral RNA-Host Protein Interactions

As a positive-sense RNA virus, Sindbis virus (SINV) must interact with host RNA-binding proteins to regulate viral replication and gene expression. The breadth and importance of alphavirus RNA-host protein interactions have remained elusive. LaPointe et al. (e02171-17) developed a viral RNA discovery method, cross-link-assisted mRNP purification (CLAMP), to identify and characterize viral RNA-host protein interactions with UV cross-linking and immunoprecipitation sequencing (CLIP-seq) technologies. The methodology assesses interactions in an unperturbed system, enabling mechanistic characterization of host RNA-binding proteins during viral infection.



Identification of SINV vRNA-protein interactants by CLAMP assay.