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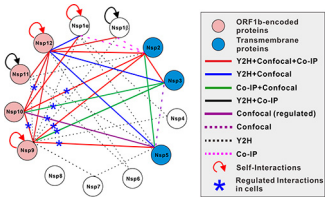
Articles of Significant Interest in This Issue

Recruitment of Porcine Reproductive and Respiratory Syndrome Virus RNA Polymerase and Helicase Involves Regulated Interactions

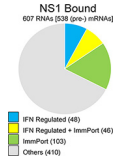
Synthesis of porcine reproductive and respiratory syndrome virus (PRRSV) RNAs within host cells depends on the efficient and correct assembly of replication and transcription complexes that form on modified intracellular membranes. Song et al. (e01112-18) mapped interactions of PRRSV nonstructural proteins and discovered regulated interactions of core enzymes nsp9 (RdRp) and nsp10 (helicase) with the membrane-associated replicase nonstructural proteins. These findings provide insight into PRRSV replication and transcription complex assembly and suggest an orderly mechanism for this process.



Summary of the interaction network among PRRSV nonstructural proteins.

Influenza NS1 Protein Interacts with Host Introns

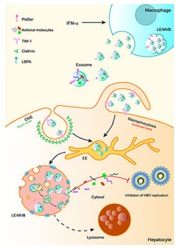
Influenza virus NS1 is a multifunctional protein that interacts with host factors to restrict host gene expression and thereby suppress antiviral immune responses. Zhang et al. (e01634-18) mapped an NS1 protein-RNA interactome and found that NS1 binds introns of host pre-mRNAs, including transcripts that encode immune factors such as RIG-I, which serves as an antiviral sensor of influenza virus. NS1 inhibits intron processing of RIG-I pre-mRNA and thus prevents its expression. This work provides a new mechanism by which NS1 antagonizes antiviral host responses.



NS1 associates with introns of pre-mRNAs.

Dissection of Exosome Entry Strategy for Alpha Interferon-Induced Antiviral Activity in Hepatocytes

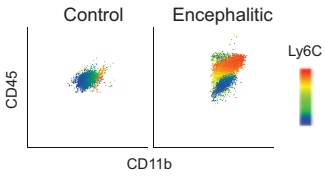
Exosomes released from alpha interferon (IFN-α)-treated nonparenchymal liver cells transmit antiviral molecules to hepatocytes infected with hepatitis B virus (HBV). Yao et al. (e01578-18) identify TIM-1, also a virus receptor, as a host factor for macrophage exosome entry into hepatocytes. After attachment, exosomes are internalized through rapid clathrin-mediated endocytosis and sustained macropinocytosis, which is followed by lysobisphosphatidic acid-dependent exosome-endosome fusion for efficient transfer of IFN-α-induced antiviral molecules. These findings suggest that virus entry mechanisms are used for exosome-mediated cell-to-cell transmission and provide a basis for engineering exosomes as antiviral vehicles.



Proposed model of exosome entry and delivery of IFN-α-induced HBV resistance.

Immune Coordination Prevents Rift Valley Fever Virus Encephalitis

Rift Valley fever virus (RVFV) causes encephalitis in a subset of infected individuals. Harmon et al. (e01270-18) found that RVFV encephalitis in mice is accompanied by T cell and monocyte infiltration into the brain, raising the question of immune-mediated pathology. Depletion of T cells or monocytes eliminates cellular brain infiltration but leads to an increased frequency of clinical RVFV encephalitis, while viral loads in the brain remain unaffected. These findings suggest that multiple aspects of cellular immunity function to prevent RVFV encephalitis by controlling virus replication in the periphery.



Inflammatory monocytes in the brains of mice with RVFV encephalitis.

https://doi.org/10.1128/JVI.01841-18