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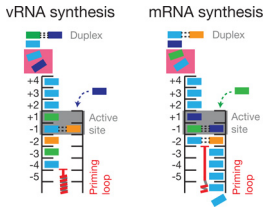
SPOTLIGHT

Articles of Significant Interest Selected from This Issue by the Editors

Correct and Efficient RNA Synthesis by the Influenza A Virus RNA Polymerase

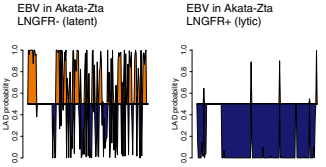
Influenza A virus replicates and transcribes its viral genome using an RNA polymerase. To ensure optimal viral replication, the enzyme uses prime-realign mechanisms to copy the genome correctly and initiate genome transcription efficiently. Oymans et al. (e01775-17) use structure-guided mutagenesis to show that polymerase mutants with a truncated priming loop fail to execute these prime-realign mechanisms, resulting in incomplete copies of the viral genome, less processive transcription *in vitro*, and no viral replication in cells. Since prime-realignment mechanisms are common among negative-strand RNA viruses, the priming-loop-dependent mechanism described here may elucidate transcription by other viruses.



Model of influenza A virus replication and transcription initiation.

Host-Pathogen Genomic Interactions Reorganize during Epstein-Barr Virus Reactivation

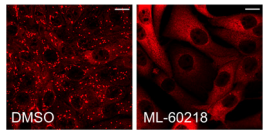
Much remains unknown about how DNA viruses interface with the compartmentalized, three-dimensional structure of a folded human genome. Moquin et al. (e01413-17) measure and characterize spatial interactions between the Epstein-Barr virus (EBV) episome and host chromosomes. During latency, the viral genome distributes near heterochromatin. Upon reactivation, the viral genome switches associations toward euchromatin. In both latent and lytic states, the EBV episome is surrounded by human chromatin of similar function. This work links positioning in the nuclear environment to changes in viral transcription.



The EBV episome interacts with human heterochromatin during latency (left) and euchromatin upon reactivation (right).

Identification of a Small Molecule as an Antirotavirus Agent

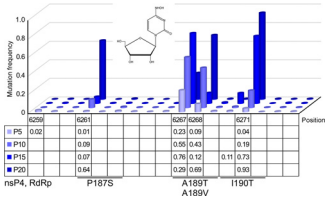
The search for effective antivirals against rotavirus (RV) is important in reducing morbidity and mortality of RV infections and gastroenteritis, especially in developing countries. Eichwald et al. (e01943-17) describe the anti-RV activities of the small molecule ML-60218. This compound disrupts assembled viral replication organelles, interferes with the formation of higher-order structures of the capsid protein VP6, and compromises particle stability. These findings are first steps toward the design of a new class of potent and selective anti-RV compounds.



Effects of ML-60218 on RV viroplasms.

Development of Alphaviral Resistance to β-D-N^4-hydroxycytidine

Alphaviruses, including Venezuelan equine encephalitis virus (VEEV), cause widespread epidemics among humans and domestic animals. Urakova et al. (e01965-17) report that β-D-N^4-hydroxycytidine (NHC) induces a high mutation rate in replicating VEEV and inhibits infectivity of the released viral progeny by a few orders of magnitude. Resistance to this drug develops inefficiently and requires a combination of mutations, all closely located in the same segment of the viral RNA-dependent RNA polymerase. These results suggest that NHC is a potent, broad-spectrum anti-alphavirus agent.



Accumulation of mutations in VEEV nsP4 that reduce sensitivity to NHC.

https://doi.org/10.1128/JVI.02026-17

Attenuated, Trivalent VesiculoVax Vaccine Protects Macaques from Lethal Filovirus Challenge

Filovirus outbreaks represent a major public health concern, which could be addressed with an effective prophylactic, pan-filovirus vaccine. Matassov et al. (e01190-17) describe a trivalent filovirus vaccine using a highly attenuated recombinant vesicular stomatitis virus (rVSV) vector. The vaccine induces high antibody titers and balanced cell-mediated immune responses specific to each filovirus glycoprotein. A single dose of the trivalent rVSV filovirus vaccine protected nonhuman primates from death and serious disease following challenge with highly pathogenic, low-passaged Ebola viruses and Marburg viruses.

Genetic organization of attenuated rVSV filovirus vaccine vector.