Articles of Significant Interest in This Issue

**Elements in the HPV18 Genome That Regulate Viral DNA Replication, Genome Copy Number, and Partitioning**

Human papillomavirus (HPV) genomes replicate as extrachromosomal minichromosomes in persistently infected cells. Coursey at al. (e00686-21) defined elements in the HPV18 enhancer element that promote stable replication of viral DNA in dividing keratinocytes. They concluded that multiple elements within the enhancer contribute to stable replication and proposed that cellular pioneer factors create a favorable chromatin environment that supports and enhances the maintenance of the extrachromosomal minichromosomes.

**CRISPR/CasRx Mediates Robust RNA Virus Interference in Fish**

Many of the dangerous viral pathogens infecting vertebrates are RNA viruses. However, it is difficult to find a widely effective way to inhibit RNA viruses because of their dynamic nature due to short generation times, large population sizes, and high mutation frequencies. Wang et al. (e00461-21) established CRISPR/CasRx, an efficient, specific, cost-effective, and straightforward method for systematic and tractable interference against RNA virus, in vivo in fish. This work provides potential novel mechanisms for RNA-guided immunity against RNA viruses in vertebrates.

**Functional Significance of Marburg and Ebola Virus 3’ Untranslated Regions**

The filovirus family, which includes the deadly Ebola and Marburg viruses, produces mRNAs with long untranslated regions (UTRs). The function of these UTRs has been ambiguous. Khadka et al. (e00652-21) demonstrate that select Marburg and Ebola virus 3’ UTRs contain elements that decrease translation efficiency. They also demonstrate that the interferon-induced RNA-editing enzyme ADAR1 can modify the viral genomic RNA so as to disrupt the inhibitory elements and relieve the inhibition of translation. This suggests a positive feedback mechanism whereby the translation efficiency of some filovirus mRNAs is regulated, depending on the status of the innate immune response.
Achilles’ Heel of a Capsid: Mason-Pfizer Assembly Mutants

The C terminus of the capsid protein of many retroviruses contains a “clasp motif,” a short sequence important for virion assembly, stability, and maturation. Mason-Pfizer monkey virus (MPMV), a member of the betaretrovirus family, is unusual among retroviruses in its assembling of virions in the cytoplasm. Buckmaster et al. (e00615-21) report the effects of single amino-acid substitutions in the MPMV clasp motif on virion assembly in vitro and on virion release, RNA packaging, and infectivity in vivo.

Dynamics of the 5-Fold Channel of Adeno-associated Virus 9

Adeno-associated viruses (AAVs) are widely utilized as gene therapy vectors, but there is still much to understand about the interplay of the capsid structure and its function. Penzes et al. (e00843-21) present high-resolution capsid structures of AAV9 at the pH levels experienced during endosomal trafficking. The results indicate that acidification induces the externalization of the enzymatic phospholipase A2 (PLA2) domain through the 5-fold channel that is essential for lysosomal membrane disruption. Additionally, they show that glycan attachment alters these dynamics along with the ordering of a region of the capsid responsible for the blood-brain barrier-crossing ability of AAV9.