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SPOTLIGHT

Articles of Significant Interest Selected from This Issue by the Editors

New Insights into Paramyxovirus Fusion from an HN Stalk Crystal Structure

Parainfluenza virus 5 (PIV5), a member of the paramyxovirus family, enters cells by membrane fusion, a process that involves the receptor-binding hemagglutinin-neuraminidase (HN) protein and the fusion (F) protein. HN, through its stalk region, activates F, allowing F to proceed through conformational changes leading to fusion. Bose et al. (p. 12855–12866) have obtained the crystal structure of the PIV5 HN stalk region, revealing an unusual 4-helix bundle. Addition of carbohydrate chains to stalk residues and testing of fusion activation highlight possible interfaces on the PIV5 HN stalk that are important for triggering fusion upon HN binding to its receptor.

The Cargo-Binding Domain of TNPO3 Is Required for Lentivirus Nuclear Import

Transportin 3 (TNPO3), an importin β family member, is required for the nuclear import of lentiviruses such as HIV-1 and SIV. TNPO3 was thought to interact directly with the viral integrase protein to chaperone the viral genome through the nuclear pore. Logue et al. (p. 12950–12961) provide evidence that TNPO3 mediates lentivirus nuclear import by interacting with a cargo protein through its carboxy-terminal cargo-binding domain. This work suggests that TNPO3 plays a more indirect role in lentivirus nuclear import by binding to a cellular protein.

Generation of High-Titer Prions in the Laboratory

Prions are composed mainly, if not entirely, of PrP^{Sc}, an infectious, misfolded isoform of PrP^{C}, the normal isoform of the prion protein. Shikiya and Bartz (p. 13439–13442) show that protein misfolding cyclic amplification (PMCA)-generated hyper-transmissible mink encephalopathy (HY TME) PrP^{Sc} is highly infectious and has a titer that is similar to that of brain tissue derived from animals infected with the HY TME agent late in the disease course. This finding demonstrates that PMCA efficiently replicates the prion agent in a cell-free environment.

Autophagy Required for Hepatitis B Virus Replication *In Vivo*

Autophagy can be used by host cells to control viral infection or by viruses to augment their own replication. Using transgenic mice that carry the entire hepatitis B virus (HBV) genome with and without liver-specific knockout of Atg5, a protein essential for autophagy, Tian et al. (p. 13453–13456) now provide direct evidence that autophagy is required for HBV DNA replication *in vivo*. This finding raises the possibility that therapeutic inhibition of autophagy may ameliorate the effects of HBV disease.

Genome Variation in Smallpox Vaccines

The classical smallpox vaccines comprise a mixture of many different viruses, but the extent of genetic variation is not well understood. Qin et al. (p. 13049–13060) determined the genome sequences of 11 different vaccinia viruses, all cloned from a vial of Dryvax vaccine. These viruses exhibit a great deal of genetic variation and a pattern of polymorphic sites that suggests repeated recombination during passage. This work illustrates how old culture methods can affect vaccine evolution and also provides new insights into the relationship between vaccinia virus and other extant orthopoxviruses.