AMERICAN SOCIETY FOR MICROBIOLOGY | Journal of Virology

SPOTLIGHT

Articles of Significant Interest Selected from This Issue by the Editors

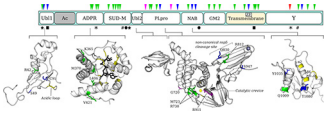
Archael Large Tailed Spindle Virus Discovered by Culture-Independent Methods

Virologists have traditionally depended on propagation of both host and virus in culture for virus discovery and characterization. Development of viral metagenomics breaks this dependence on culture-based methods but often results in only fragmented viral genome sequences. Hochstein et al. (p. 3458–3468) move beyond this limitation and report the isolation of an archaeal virus directly from a hot spring in Yellowstone National Park. The complete genome was assembled and host defined, all directly from environmental samples without culturing. The pipeline described in this report should be applicable for virus discovery in almost any environment, from hot springs to humans.

Hot spring in Yellowstone National Park where the virus was isolated.

ORF1a Is a Major Selection Target in Lineage C Betacoronaviruses

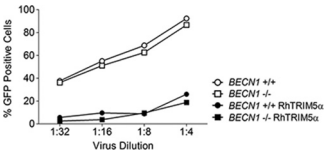
Middle East respiratory syndrome coronavirus (MERS-CoV) originated in bats and spread to humans via an intermediate host. Understanding the molecular events underlying the adaptation of betacoronaviruses to new hosts is essential to defining how species transmission barriers are overcome. Forni et al. (p. 3627–3639) investigated the evolution of ORF1a and ORF1b (both encoding nonstructural proteins) in lineage C betacoronaviruses and MERS-CoV isolates. Widespread positive selection was observed, especially in nsp3, with several selected sites located in functionally relevant protein domains and corresponding to functional mutations. These findings suggest that adaptive evolution in ORF1a contributes to host shifts or immune evasion and that nsp3 sequencing should be prioritized in coronavirus monitoring programs.



Representation of nsp3 domains (triangles, positively selected sites; symbols, coevolving sites).

TRIM5α Degradation via Autophagy Is Not Required for Retroviral Restriction

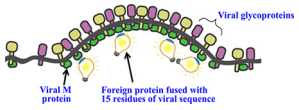
The restriction factor TRIM5α inhibits retroviral infection by recognizing incoming viral cores and promoting their disassembly. Autophagic degradation is thought to be required for TRIM5α restriction of retroviral infection. Imam et al. (p. 3400–3410) demonstrate that while the turnover of TRIM5α is autophagy dependent, retroviral restriction by TRIM5α is potent in cells depleted of macroautophagy factors by small interfering RNA and CRISPR/Cas9 gene editing. Thus, while autophagic degradation mechanisms likely function in the regulation of TRIM5α and other TRIM family proteins, autophagy is not required for retroviral restriction by TRIM5α.



Knockout of Beclin1 and other autophagic mediators does not affect restriction of HIV-1 by rhesus TRIM5α.

Virus-Like Particles Engineered To Package Foreign Proteins

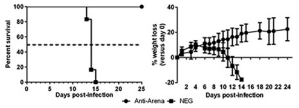
Paramyxovirus RNA genomes are packaged into budding virions as a result of protein interactions between viral matrix (M) proteins and the RNA-bound nucleocapsid (N) proteins. Ray et al. (p. 3650–3660) identify amino acid residues near the C-terminal end of N protein that mediate this interaction, transplant those residues to a foreign protein, and induce the foreign protein to incorporate efficiently into budding virus-like particles (VLPs). This work sets the stage for development of VLP-based protein delivery vehicles in which tagged foreign proteins are engineered to incorporate into fusion-competent VLPs that could deliver the contents into target cells.



Manipulating paramyxovirus genome packaging interactions to direct a foreign protein into budding particles.

Protective Antibodies Targeting South American Arenaviruses Produced Using DNA Vaccines

Several rodent-borne arenaviruses circulating in South America cause hemorrhagic fever in humans. Golden et al. (p. 3515–3529) show that envelope glycoprotein-based DNA vaccines in rabbits can elicit potent neutralizing antibodies that target several arenaviruses, including Guanarito virus (GTOV), Junín virus (JUNV), Machupo virus, and Sabia virus. Passive transfer of DNA vaccine-derived polyclonal antibodies after exposure protected guinea pigs against lethal infection by GTOV and by JUNV. These findings indicate that DNA vaccines can generate candidate neutralizing antibody-based products for use in combating disease caused by South American arenaviruses.



Antiarenavirus glycoprotein-specific antibodies protect guinea pigs from lethal disease caused by JUNV.

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