Previous studies have reported that domestic cats can be naturally infected with bovine herpesvirus 4 (BHV4), and experimental inoculations have been linked to feline urolithiasis. It has been difficult to recapitulate initial diagnostic and experimental observations, thus here we have initiated a study to evaluate BHV4 presence in a large cohort of cats at risk for exposure to circulating feline viruses using a sensitive and specific assay. Domestic cat blood DNA samples (n = 101) collected from California, Colorado, and Florida were screened for BHV4 using sensitive real time PCR. In contrast to BHV4 containing tissue culture extracts, all domestic cat blood samples were negative for BHV4. Samples were shown to contain intact DNA and to be infected with other horizontally-transmitted feline infections. We conclude that BHV4 is unlikely to be a common pathogen of domestic cats.

http://dx.doi.org/10.1016/j.nhtm.2015.07.008

Longitudinal analysis of blood-borne prion infection

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Transmissible spongiform encephalopathies (TSEs), or prion diseases, affecting human and animal species can be transmitted from TSE-infected individuals to naïve susceptible hosts during the long asymptomatic (years to decades) and symptomatic disease stages. The presence of infectious hematogenous prions in asymptomatic TSE-infected hosts demonstrates the highly infectious nature of blood-borne prions in hosts lacking overt clinical symptoms. It is currently unknown when and how infectious prions first enter the blood following initial exposure. We have previously shown that the whole-blood real-time quaking-induced conversion assay (wbRT-QuIC) possesses 100% specificity and > 92% sensitivity, making it an ideal tool to address this question. Here, we use wbRT-QuIC to analyze whole blood collected from oral, extranasal or aerosol TSE-exposed hosts for blood-borne prions. Our results demonstrate that conversion competent prions in the inoculum are capable of crossing mucosal surfaces and entering the circulatory system within 30 min—no matter the route of exposure. Detection of the inoculum minutes post exposure is followed by a steady decline in the detection of blood-borne prions up to 3 days which is followed by a progressive increase in the detection of nascent conversion competent prions between 1 and 17 months post exposure. These data provide the first evidence for the facile transport of mucosally acquired prions into the circulatory system, providing evidence for multiple routes of inter- and intra- host prion trafficking and shedding.

http://dx.doi.org/10.1016/j.nhtm.2015.07.009

Dengue virus requires the unsaturated fatty acid biosynthesis pathway for its infection in the mammalian host

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Dengue virus (DENV) infection is a significant global health concern with over 40% of the world's population at risk and currently no therapeutics or vaccines available. Understanding host viral interactions is key to developing novel therapeutic options. Dengue virus is a positive sense RNA virus that induces the formation of invaginations in the endoplasmic reticulum to replicate its genome. Increased phospholipid biosynthesis is key to the formation of these replication compartments as well as viral maturation and release. It is now evident that viral proteins mediate this change in the cellular phospholipid repertoire, but the precise mechanisms are unknown. We have shown that siRNA mediated knockdown as well as pharmacological inhibition of key enzymes in the unsaturated phospholipid biosynthesis pathway reduces DENV replication. Unsaturated fatty acids, when incorporated into membrane phospholipids are a key mechanism for providing fluidity and curvature of membranes enhancing the assembly and function of membrane bound enzymes. Several of the enzymes are conserved from bacteria to mammals and are high profile therapeutic targets for obesity, hepatic steatosis and metabolic disease. This indicates a novel pathway for drug discovery and exploration of viral host interactions. We will discuss mechanistic details of how this pathway influences DENV replication.

http://dx.doi.org/10.1016/j.nhtm.2015.07.010

Chikungunya virus in non-mammalian species: a possible new reservoir

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Chikungunya virus (CHIKV) is an arbovirus distributed widely in tropical regions of the world that causes a febrile and often painful disease in adults and children. Recent outbreaks of CHIKV infection in the Caribbean have raised concerns about establishment of this virus in North America. A significant question about the transmission cycle of CHIKV is whether non-human reservoir hosts are important in maintenance or transmission of the virus. We conducted experimental infections with CHIKV and discovered that several reptiles and amphibians developed viremia of sufficient magnitude to possibly serve as reservoir hosts. One or two strains of CHIKV were inoculated into a variety of ball pythons, Burmese pythons, Northern garter snakes, American alligators, green iguanas, painted turtles, leopard frogs, Bufo species toads and cane toads. Viremia was not detected in alligators or cane toads but all other species developed viremia at variable magnitude. Peak viremia in the other species varied from 2.8 (Burmese pythons) to 4.7 (leopard frogs) log10 pfu/ml. We also conducted experiment to evaluate the effect of ambient temperature changes to monitor the "over wintering" capabilities of CHIKV in snakes. Northern garter snakes were inoculated a South African strain of CHIKV at temperatures of 16 C versus 26 C and tested for viremia. The snakes kept at 26 C developed a short term viremia, whereas in snakes kept at 16 C, the virus was maintained for a longer period and viremia titers as high as 7.2 log10 pfu/ml were achieved when animals were subsequently slowly warmed to 26 C.

http://dx.doi.org/10.1016/j.nhtm.2015.07.011

Experimental Modoc virus infection of deer mice (*Peromyscus maniculatus*)

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Modoc virus (MODV) is a flavivirus that was first isolated from deer mice (*Peromyscus maniculatus*) in Modoc County, California during a 1958 surveillance study for novel viruses. Although many flaviviruses are arthropod-borne, MODV has no known intermediate. Subsequent to its initial isolation, MODV was detected in deer mice found in other regions of the United States, including northeastern Colorado. These findings suggested that deer mice may be a reservoir host of MODV. We intramuscularly inoculated 18 deer mice with 10^5 $TCID_{50}$ of MODV strain