Flavivirus vectors

Flaviviruses (family Flaviviridae) are enveloped, positive-sense, single-stranded RNA viruses that are normally transmitted between vertebrate hosts by insect vectors. Vertical transmission from mother to offspring in utero or through breastmilk has also been noted for some viruses and sexual transmission is of concern for Zika virus specifically. The flavivirus genome consists of a single long open reading frame that encodes both structural and non-structural proteins. Upon entry into the cell cytoplasm the viral RNA can serve as mRNA and is translated to form a single long polyprotein that is cleaved by cellular and viral proteases to form individual proteins. As such, viral vectors based on the flaviviruses require heterologous genes to be inserted in frame with the viral coding region and flanked by protease cleavage sights.

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LaboratoryAcquired Infections

Laboratory acquired infections have been documented for some flaviviruses. Exposure to aerosols, contact with broken skin or contaminated animal bedding, and accidental auto-inoculationas well as the bite of experimentally infected mosquitoes have all been implicated in laboratory acquired infections.

Host Range

Flaviviruses can infect a wide array of vertebrate and invertebrate species depending on the specific virus. Vertebrate species include dogs, cattle, horses, pigs, deer, rodents, killer whale, alligators, frogs, bats and birds, in addition to humans and other non-human primates. Invertebrate species include both Aedes and Culex species of mosquito; and Ixodes species of tick depending on the virus.

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hand-held or automatic pipettors and other instruments with toxic or infectious materials.

- Biohazard markings will be on all contaminated waste and waste disposal containers in addition to any equipment used for work or for storage of biological hazards
- Chewing gum, eating, drinking, or applying cosmetics are not permitted within any laboratory.
- Using tobacco products is not permitted within any University building.
- Personal reading materials such as magazines, newspapers, schoolwork and other

Precautions When Using Animals

Animals infected with flaviviruses or flavivirus vectors will be housed according to the RG assignment of the specific virus or vector. Live attenuated vaccine strains of RG-3 viruses which have been exempted by the CDC and/or USDA are classified as RG-2 pathogens and may be manipulated using ABSL-2 facilities and work practices. Work with replication defective replicons based on RG-3 flavivirus and containing two-thirds or less of the parental viral sequence can be handled at ABSL-2, only after the absence of replication competent virus has been documented using validated methods.

Some flaviviruses are shed in the animal's excreta thus cages and bedding should be handled as a biohazard. Avoid creating aerosols when emptying animal waste materials and decontaminate the bedding and cages via chemical treatment or autoclaving.

For work in the ABSL-3:

- Retractable or safety hypodermic needles and syringes will be used when feasible for injections and aspirations of fluids from lab animals and diaphragm bottles.
- Extreme caution must be used whenever handling needles and syringes to avoid self-inoculation and the generation of aerosols d(l)14 (f)]TJ 0 Tct (be)6d(l)1uelm[illegible]y s (ia

Employee Exposure

Eye Exposure- remove PPE if necessary, proceed to the eyewash station in the laboratory, and rinse eyes with cold running water for 15 min.
Skin Exposure- remove PPE if necessary

Apply the decontaminant solution starting at the perimeter of the spill and working towards the center.
Allow 30 minutes' contact time with the decontaminant solution before cleanup, except in emergencies (i.e. injury).
Remove paper towels or Red Z to a biohazard bag along with any paper towels used to wipe the area dry. If the decontaminant solution was used on metal, wipe the area with 70% ethanol.
Discard protective clothing into the biohazard bag and autoclave.

- Additional procedures/decontamination (chemical decontamination of surfaces or VHP) will be determined during the risk assessment and communicated to the response team as necessary.
- Confirm that the spill has been reported, and that the clean-up and all necessary paperwork have been completed.

Small spills (less than 1 ml) within a BSC can be handled by covering the spill with a paper towel soaked in disinfectant and allowing an appropriate contact time before cleaning the

- Work can resume after the BSC has been properl