Impact of Dengue Virus Infection on Global Metabolic Alterations in the Aedes aegypti Mosquito Vector

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Aedes aegypti mosquitoes are the primary vectors transmitting dengue virus (DENV), one of the most aggressive re-emerging pathogens worldwide causing more than 390 million infections per year. The spread of the virus is greatly dependent upon successful replication within both the human host and mosquito vector. Much effort has been placed in understanding the dynamics of virus transmission and replication in both organisms, but little is known about the global impact of DENV on metabolic pathways. Previous studies have demonstrated perturbations in human and Aedes albopictus cellular metabolic environments during DENV infection. Some of these perturbations include increasing the production of membrane lipids that had the capability to induce membrane curvature and permeability, as well as visibly altering both human and mosquito intracellular membrane architecture to support DENV replication. In this study, we have explored metabolic changes in Aedes aegypti midgut and salivary glands upon DENV (serotype 2) infection. We have found several significant fluctuations in the lipid and metabolite repertoire from infected tissues compared to uninfected controls, including differential expression of molecules that function as membrane building blocks, bioactive messengers, energy storage and intermediates in lipid biosynthesis and lipolysis pathways. These results and their relevance to dengue virus infection of its mosquito vector will be discussed.

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Alphavirus Infection of the CNS: Entry, Dissemination, and Neurodegeneration

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Alphaviruses most often associated with neuroinvasive disease are limited to the Americas and include strains of EEEV, VEEV, and WEEV. The process of alphavirus entry into the CNS of infected vertebrates following challenge is not well-understood. It is thought that virus entry into the CNS depends on the inoculation route. It is well-established that olfactory sensory neurons provide access to the CNS following challenge with airborne virus. However, less knowledge is available regarding virus entry into the CNS following peripheral, non-olfactory infection, which appears to rely on some form of hematogenous spread. We sought to determine the precise route of CNS entry following footpad inoculation by using a combination of in vivo/ex vivo bioluminescence imaging and traditional histological examination methods. We found a consistent pattern in the spatiotemporal distribution of virus among the imaged brains, none of which involved the olfactory bulb. Extending these studies by performing histological analysis on the imaged tissues, led to the finding that CNS entry by WEEV likely occurs in areas of the CNS where the blood-brain barrier is naturally absent. These areas include the hypothalamus, the subfornical organ, the pineal gland, and the area postrema. Importantly, these results reveal a previously unrecognized method of alphavirus entry into the CNS.

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Sterilization and Disposal of Agricultural Quarantine Waste

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Approximately 150 million people and almost $40 billion worth of agricultural commodities go through U.S. international ports annually. Ports seize animal and plant products potentially contaminated with high risk diseases that then must be decontaminated before entering the waste stream. Currently, there are only 3 methods of decontamination accepted by the Animal Plant and Health Inspection Service at U.S. ports and borders including incineration, high temperature cooking, and discharge of ground waste as sewage. In this study we assess the efficacy of a relatively new decontamination technology, alkaline digestion, to mitigate infectious agents. Transmissible Spongiform Encephalopathies (TSEs), a member of the protein misfolding diseases (ex: Alzheimer’s and Parkinson’s Diseases), were chosen as the infectious agent for this study because they rank as the hardest to kill microbe/pathogen, affect both human and animal species worldwide and are shed by infected hosts into the environment establishing highly infectious biota. Chronic wasting disease (CWD), an emerging TSE of cervid species (deer, elk, moose) in North America, has recently been spotlighted as a potential concern for European countries, and recapitulates human and animal TSE pathogenesis and shedding. For these reasons CWD is ideal for mitigation studies. We processed CWD positive and negative materials by alkaline digestion under standard temperature and pressure at time intervals of 2, 4, and 6 h. Samples were retrieved after digestion, were neutralized and inoculated intracerebrally into transgenic mice expressing the cervid protein to determine remaining prion infectivity. In addition, the samples (pre and post alkaline digestion) were tested for amplification competent prions in samples processed by alkaline digestion at 2, 4, and 6 h cycles as compared to nondigested samples. This work will provide a basis for future studies designed to unravel the mechanisms associated with the ability of prions to bind surfaces enhancing prion mitigation strategies for TSEs and by extension, other protein misfolding diseases.

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Alphavirus E1 Glycoprotein-Liposome-Nucleic Acid Complexes Protect Mice from Lethal Challenge with Multiple Alphaviruses


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