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Transcriptomic Analyses Reveal Differential Gene Expression of Immune and Cell Death Pathways in the Brains of Mice Infected with West Nile Virus and Chikungunya Virus

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West Nile virus (WNV) and chikungunya virus (CHIKV) are arboviruses that are constantly (re-)emerging and expanding their territory. Both viruses often cause a mild form of disease, but severe forms of the disease can consist of neurological symptoms, most often observed in the elderly and young children, respectively, for which the mechanisms are poorly understood. To further elucidate the mechanisms responsible for end-stage WNV and CHIKV neuroinvasive disease, we used transcriptomics to compare the induction of effector pathways in the brain during the early and late stage of disease in young mice. In addition to the more commonly described cell death pathways such as apoptosis and autophagy, we also found evidence for the differential expression of pyroptosis and necroptosis cell death markers during both WNV and CHIKV neuroinvasive disease. In contrast, no evidence of cell dysfunction was observed, indicating that cell death may be the most important mechanism of disease. Interestingly, there was overlap when comparing immune markers involved in neuroinvasive disease to those seen in neurodegenerative diseases. Nonetheless, further validation studies are needed to determine the activation and involvement of these effector pathways at the end stage of disease. Furthermore, evidence for a strong inflammatory response was found in mice infected with WNV and CHIKV. The transcriptomics profile measured in mice with WNV and CHIKV neuroinvasive disease in our study showed strong overlap with the mRNA profile described in the literature for other viral neuroinvasive diseases. More studies are warranted to decipher the role of cell inflammation and cell death in viral neuroinvasive disease and whether common mechanisms are active in both neurodegenerative and brain infectious diseases.

Keywords: transcriptomics, Genomics, West Nile virus, chikungunya virus, neuroinvasive disease, cell death mechanisms, immune response