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BMS

Judging Dept.

Barbara Stewart

Student

BMS

3

Kristen Bernard

Dept or Program Years in program

Mentor

Leukocyte populations present in the mouse central nervous system during persistent West Nile virus infection

Author (s)

Barbara Stewart, Kim A. Appler, Ashley N. Brown and Kristen A. Bernard

West Nile virus (WNV) causes varying degrees of disease in humans ranging from mild fever to severe encephalitis. Since its introduction in 1999, there have been over 24,000 cases of West Nile fever and encephalitis. In individuals recovering from encephalitis, IgM antibody against WNV persists for up to 11 months, suggesting that virus and/or viral antigen persists in these patients. Mouse studies in our laboratory have shown that WNV RNA persists in central nervous system (CNS) tissues for up to six months post-inoculation (p.i.), and infectious virus can be isolated from CNS tissues for up to four months p.i. We hypothesized that the host immune response is ineffective in clearing WNV from the CNS, allowing the virus to persist. In our initial studies, we characterized the leukocyte populations present in the mouse brain and spinal cord at various time points encompassing the acute disease and persistence phases of WNV infection. By 7 days p.i., activated CD4 and CD8 T cells (CD69+ and CD25+) were present in the CNS. The activated CD8 T cells increased in the CNS and remained high for up to 63 days p.i. In contrast, activated CD4 T cells began to decrease in the CNS by day 28, and this decline continued until the end of the experiment. T regulatory cells (CD25+, FoxP3+) were observed at all time points and peaked on day 28. Throughout the time course of the experiment very few CD19+ B cells were observed in the CNS; however, high numbers of plasma cells (CD138+) were found on days 28 and 63. In summary, CD8 T cells and plasma cells were recruited and maintained in the CNS during WNV persistence for at least 63 days p.i., suggesting that these cells may be inadequate and/or ineffective for viral clearance. Future studies will be directed towards determining the cytokine milieu present in the CNS during a persistent infection.