**MyD88-MEDIATED SIGNALING IS INVOLVED IN THE DEVELOPMENT OF T CELL RESPONSES TO AN ATTENUATED WEST NILE VIRUS NS4B-P38G MUTANT STRAIN INFECTION**

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West Nile Virus (WNV) belongs to the family of *Flaviviridae*, the genus *Flavivirus*, a group of positive-sense, single strand RNA viruses. Human infection results in various symptoms. No vaccines are available for human use. Development of a safe and effective vaccine against WNV remains as a high priority. The nonstructural (NS) proteins of WNV are associated with participation in evasion of host innate immune defenses. In a previous study, by utilizing site-directed mutagenesis, an attenuated WNV NY99 strain with a substitution of P38G in NS4B protein was identified. The NS4B-P38G mutant strain has both temperature-sensitive and small-plaque phenotypes, and significantly reduced neuroinvasiveness in outbred mice as compared to NY99 strain. We have found that NS4B-P38G strain infection caused no lethality and induced a higher innate cytokine production and antigen specific T cell responses in C57BL/6 (B6) mice. The myeloid differentiation primary response gene 88 (Myd88)-mediated innate immune responses are protective against wild-type WNV infection in mice. We also found that Myd88 deficient (*Myd88*−/−) mice primarily infected with NS4B-P38G strain were more susceptible to a secondary infection with a lethal dose of wild-type WNV compared with wild-type mice. In bone marrow derived DC, innate cytokine productions are reduced in Myd88−/− samples with NS4B-P38G strain infection. Further, T cells in Myd88−/− mice were shown to have a reduced effector functions compared to wild-type mice. Overall, these results suggest that MyD88-mediated signaling plays an important in regulation of adaptive immunity to the WNV NS4B-P38G strain infection.