Immune response differences might determine severity of West Nile Virus disease

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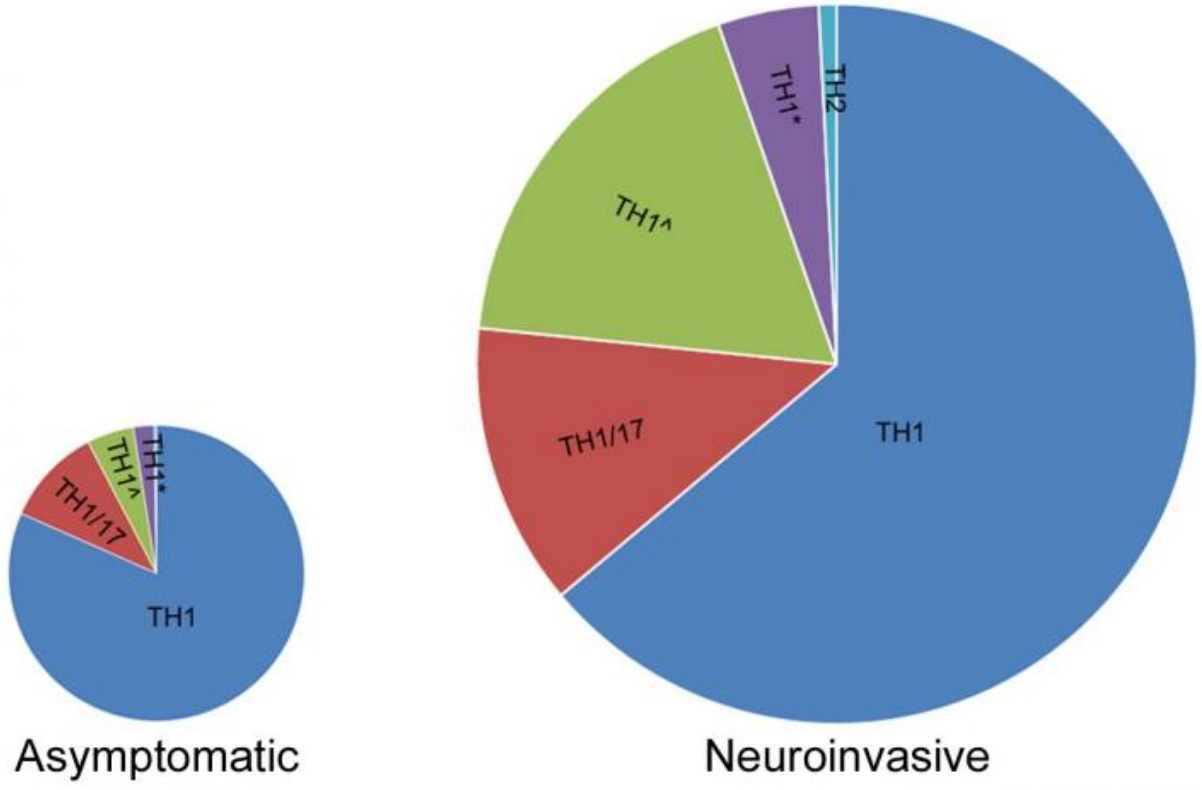

The magnitude and characteristics of WNV specific responses are different in subjects with asymptomatic infections (left) or neuroinvasive disease (right). Credit: James et al.

While most West Nile Virus (WNV) infections in humans are asymptomatic and go unnoticed, the virus causes serious and sometimes

fatal neurologic illness in some people. A study published on January 21st in *PLOS Pathogens* suggests that an exaggerated and abnormal immune response contributes to the development of neurologic symptoms following West Nile virus infection.

William Kwok and Eddie James, both from the Benaroya Research Institute at Virginia Mason in Seattle, USA, and colleagues are interested in what determines the different outcomes of WNV infection, and whether differences in the immune response play a role. In this study, they compare the immune responses in samples from 24 blood donors who had earlier asymptomatic infections (confirmed by laboratory tests) with those in blood samples from 16 individuals diagnosed with WNV infections that had caused neuro-invasive disease with neurologic symptoms including confusion, tremors, seizures, paralysis, and vision loss.

Because CD4+ (helper) T cell responses have been shown to be sufficient for protection from WNV challenge (independent of B cells and CD8+ T cells) and crucial for viral clearance from the CNS, the researchers focused on the WNV-specific CD4+ T cell repertoires present in the blood samples.

They observed that older individuals had higher numbers of WNV-specific T cells. In addition, WNV-specific cell lines isolated from older individuals had a higher proportion of T cells that produced IFN-γ, and also a higher proportion that co-produced IFN-γ and IL-4 (both molecules that promote a strong immune response).

Comparing the magnitude and characteristics of WNV-specific CD4+ T cell response in individuals of similar ages with either neuroinvasive disease or asymptomatic infection, the researchers found that, independent of age, individuals with neuroinvasive disease had higher numbers of WNV-specific CD4+ T cells. In addition, those T cells that

responded to the virus more frequently co-produced IFN-γ and IL-4. Moreover, the gene expression responses in CD4+ T cells stimulated with WNV differed between individuals with previous asymptomatic infection and those who had neuro-invasive WNV disease.

The researchers conclude that "individuals with neuroinvasive West Nile Virus infections have exaggerated and atypical responses to the virus". And while they acknowledge several limitations of the study, including the lack of data on the immune response close to the time of infection (the blood samples were drawn months and sometimes years after the diagnosis of WNV infection), they suggest that "immune mediated damage may indeed contribute to neurologic symptoms and pathogenic outcomes in the setting of WNV infection".

More information: James EA, Gates TJ, LaFond RE, Yamamoto S, Ni C, Mai D, et al. (2016) Neuroinvasive West Nile Infection Elicits Elevated and Atypically Polarized T Cell Responses That Promote a Pathogenic Outcome. *PLoS Pathog* 12(1): e1005375. DOI: 10.1371/journal.ppat.1005375

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