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A high-throughput and multiplex microsphere immunoassay based on non-structural protein 1 discriminates three flavivirus infections

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Abstract

The four serotypes of dengue virus (DENV) are the leading cause of arbovirus infections in humans. The recent outbreaks of Zika virus (ZIKV) and associated complications in DENV-endemic regions highlight the critical need for sensitive and specific serodiagnostic tests. ZIKV and DENV belong to the genus Flavivirus of the family Flaviviridae. Traditional envelope protein-based serological tests for flavivirus infections have been hampered by extensive cross-reactivity among different flaviviruses. In this study, we developed a high-throughput and multiplex IgG microsphere immunoassay (MIA) using the NS1 proteins of DENV1-DENV4, ZIKV and West Nile virus (WNV) to test samples from reverse-transcription-polymerase-chain reaction-confirmed cases, including primary DENV1, DENV2, DENV3, WNV and ZIKV infections, secondary DENV infection, and ZIKV infection with previous DENV infection. Combination of four DENV NS1 IgG MIAs revealed a sensitivity of 94.3% and specificity of 97.2% to detect DENV infection. The ZIKV and WNV NS1 IgG MIAs had a sensitivity/specificity of 100%/87.9% and 86.1%/78.4%, respectively. A positive correlation was found between the readouts of enzyme-linked immunosorbent assay and MIA for different NS1 tested. Consistent with our previous reports (Tsai et al. Clin Infect Dis 2017, 65:1829-1836; Emerg Infect Dis 2018, 24: 1355-1359), secondary DENV infection panel cross-reacted to ZIKV NS1 in IgG MIA, and ZIKV infection with previous DENV infection panel recognized both DENV and ZIKV NS1. Based on the ratio of relative median fluorescence intensity of ZIKV NS1 to DENV1 NS1, the IgG MIA can distinguish ZIKV infection with previous DENV infection and secondary DENV infection with a sensitivity of 88.9–90.0% and specificity of 91.7–100.0%. The multiplex and high-throughput assay could be applied to serodiagnosis and serosurveillance of DENV, ZIKV and WNV infections in endemic regions.

Biography:

Dr. Wei-Kung Wang received his M.D. from National Taiwan University in 1986 and Sc.D. from Harvard School of Public Health in 1995. He is currently Professor at the Department of Tropical Medicine, Medical Microbiology and Pharmacology at the University of Hawaii at Manoa. His research focuses on dengue and other flaviviruses, virus-like particles, antibody response and vaccine development. He has published more than 65 papers in peer-review journals and has been serving on various panels of NIH grant review as well as guest editor of reputed journals as such PLoSNegl Trop Diseases.

Speaker Publications:

1. Wei Kung Wang, Hawaii. J Med Public Health. 2018 Dec;77(12):315-318.
2. Wei Kung Wang, Hawaii. Nat Immunol. 2015 Feb;16(2):170-177. doi: 10.1038/ni.3058. Epub 2014 Dec 15.
3. Wei Kung Wang, Hawaii PLoS Negl Trop Dis. 2019 Aug 23;13(8):e0007649. doi: 10.1371/journal.pntd.0007649. eCollection 2019 Aug.
4. Wei Kung Wang, Hawaii J Virol. 2018 Mar 14;92(7):e01992-17. doi: 10.1128/JVI.01992-17. Print 2018 Apr 1.

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