Serodiagnosis of acute and past Zika virus infections without cross-reactivity to other flaviviruses by NS1-based ELISA

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Background: Currently, Zika virus (ZIKV) infections are spreading rapidly in Latin America. Although being a rather mild disease in immunologically competent persons, ZIKV is suspected to cause Guillain-Barré syndrome (GBS) or, during pregnancy, microcephaly in the fetus. Reliable serological tests may clarify the role of ZIKV infection in these diseases, but currently available diagnostics are of limited value due to the high immunological cross-reactivity between the different flavivirus species.

Material/methods: Recombinant ZIKV non-structural protein 1 (NS1) was expressed in HEK293 cells, purified and used as solid phase target antigen in an enzyme-linked immunosorbent assay (ELISA) for the determination of circulating anti-ZIKV IgM and IgG antibodies. Sensitivity and specificity were evaluated with 29 sera from ZIKV-infected patients and 799 healthy individuals, respectively. Samples from 128 patients with Dengue, West Nile, Japanese encephalitis and Chikungunya virus infections, and from Yellow fever-vaccinated individuals were examined as well.

Results: 28/29 ZIKV-infected patients reacted positive for anti-ZIKV NS1 IgM/IgG (96.6% combined sensitivity). Specificity based on the healthy individuals was 99.7%. Out of 128 sera from patients infected with Dengue, West Nile, Japanese encephalitis and Chikungunya virus and from Yellow fever-vaccinated individuals, only 1 (0.8%) showed a positive reaction for either IgM or IgG.

Conclusions: Recombinant ZIKV NS1 represents a very specific molecular basis for the serological diagnosis of acute or past ZIKV infections. Providing a high sensitivity and specificity and a remarkably low cross-reactivity with other flaviviruses, the new ELISA can serve as a specific diagnostic tool to elucidate the coherence of ZIKV infections, GBS and microcephaly.