Protective Antibody Responses in Congenital Zika Virus Infection

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BACKGROUND

ZIKV infection during pregnancy is associated severe birth defects and mild neurodevelopmental deficits. However, it is unclear why some infants are severely affected, and others are asymptomatic. Some evidence indicates that the protection of infants from Zika virus is strongly associated with the maternal antibody response. Therefore, ZIKV immunotherapy is an attractive target to treat maternal ZIKV infection and limit vertical transmission to the fetus. We need to define antibody immune correlates of protection, specifically related to the breadth of the antibody response, in order to develop effective immunotherapy. Our goal is to define the magnitude and breadth of the maternal antibody response that correlates with fetal protection.

METHODS

We used a high-density peptide micro array to define the breadth, or number of reactive epitopes, of the antibody response. We measured the reactivity of ZIKV-immune serum (from 14 days post infection) to overlapping linear epitopes spanning the entire viral polyprotein. This pilot experiment explored the optimized experimental conditions by testing multiple serum and secondary antibody (anti-IgG, -IgM, -IgA) dilutions.

RESULTS

We defined the most optimal experimental condition as one that has the precision-recall curve achieving the highest area under the curve (AUC). We demonstrate that 1:50 is the optimal serum dilution for all of the secondary antibodies (Figure 2B, 2C and 2D), and the optimal secondary antibody dilution differs among antibody classes, with a dilution of 1:20,000 optimal for anti-IgA and anti-IgM (Figure 2C and 2D), and a dilution of 1:40,000 optimal for anti-IgG (Figure 2D).

• Establishment of a high-density peptide micro array analysis pipeline.
• Defined the optimal experimental conditions for multiple secondary antibodies (anti-IgG, -IgM, -IgA).
• The number of reactive ZIKV epitopes was highest at 14 days post-infection for IgM and IgA antibodies, and highest at 28 days post infection for IgG antibodies.

CONCLUSIONS

We developed a standard high-density peptide micro array analysis pipeline, including data normalization and reactive epitopes detection, to ensure the reproducibility of data analysis results. We defined the optimal experimental conditions that will be used in for future high-density peptide micro array experiments. We also detected the reactive epitopes using data generating under optimal experimental conditions and found that the breadth, or number of positive epitopes, varies by time since infection and antibody class, with the number of IgM and IgA epitopes peaking earlier than the IgG epitopes. Future peptide microarrays will build on these optimal experimental conditions to define the breadth of the maternal Zika virus-specific antibody response.

ADDITIONAL KEY INFORMATION

Reference:

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