Structural basis for the protection of a ZIKV specific neutralizing antibody

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ZIKV-specific neutralizing antibodies hold a great promise for antibody-based interventions and the development of vaccine against ZIKV infection. Here we report the structural basis for neutralization and protection of a potent and protective ZIKV-specific human antibody ZK2B10 initially isolated from a ZIKV convalescent individual. Crystal structure of the ZK2B10 Fab fragment (FabZK2B10) in complex with DIII of ZIKV envelope (E) protein was determined at a resolution of 2.32 Å. The epitope is confined to the edge of the lateral ridge on DIII and is constituted largely by ZIKV unique residues in BC and DE loops of DIII. Cryo-EM structure of FabZK2B10 in complex with the mature ZIKV showed that all the epitopes were covered by FabZK2B10 including those at the five-fold vertex of the virion. However, such binding pattern does not appear to influence the conformational changes of the E protein in the acidic environment nor the viral RNA copies before and immediately after viral attachment to the target cells, suggesting that ZK2B10 functions at the subsequent steps during viral entry. Indeed, modeling the binding of ZK2B10 to the post-fusion E trimer spike showed severe clashes between the bound antibody and the viral membrane. These findings have revealed a unique hot spot on the ZIKV E protein for inducing ZIKV-specific antibodies and should facilitate the development of ZIKV-specific vaccine.