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Structural basis of Zika virus neutralization by highly potent antibody

Arvind Sharma[1], Félix Rey[1]
[1]*Structural Virology, Institut Pasteur, Paris, France*
E-mail: arvind.sharma@pasteur.fr

Zika virus (ZIKV) has become a prominent human health concern with recent outbreaks and links to microcephaly in newborns in Brazil and Guillain–Barré syndrome in adults in French Polynesia. The near-atomic structure of ZIKV mature particles shows that they have essentially same organization as the other flaviviruses of known structure, such as Dengue virus (DENV) and West Nile virus(1). ZIKV and DENV are arthropod-borne enveloped viruses belonging to the Flavivirus genus in the family Flaviviridae. A number of antibodies elicited against the DENV envelope (E) protein can react with ZIKV, where a subset of antibodies targeting a conformational epitope can efficiently neutralize both viruses(2). One of the most potent cross-reactive antibodies is C10, which can efficiently neutralize ZIKV both in-vitro and in-vivo. A high-resolution (2.1 Å) crystal structure of ZIKV soluble E (sE) protein with FabC10 gives atomic level insight into the neutralization mechanism. C10 binds to the conformational intra-dimer epitope previously annotated as E-dimer epitope 1 (EDE1), and locks the dimer preventing structural rearrangement of E proteins during the fusion event. The high resolution structure of ZIKV sE and the FabC10 immunocomplex, along with the previously available Cryo-EM structure of ZIKV particle with FabC10 and DENV2 crystal structure with ScFvC10(3) helps in better understanding of EDE1 and can guide us in designing a rational, epitope-focused universal vaccine capable of eliciting potent cross-neutralizing antibodies to protect simultaneously against both ZIKV and DENV infections.

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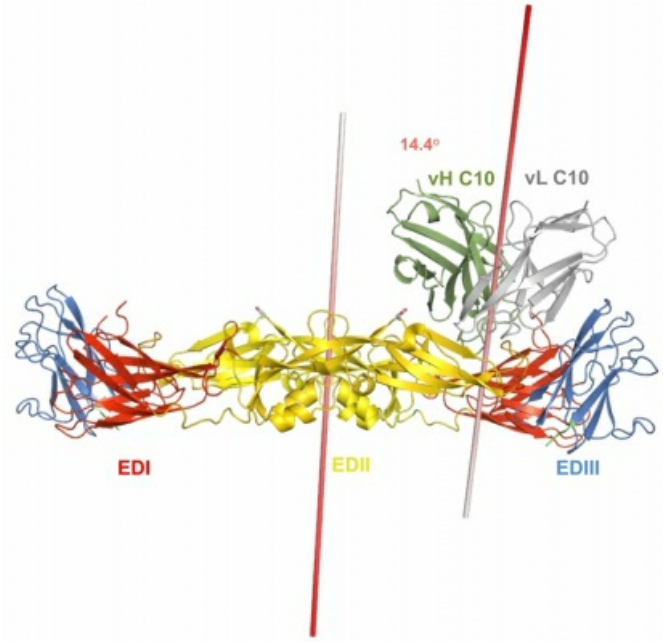

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