

Cryo-EM Structure of Inactivated Tick-borne Encephalitis Virus from Sofjin-Chumakov Vaccine Strain

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Tick-borne encephalitis (TBE) is considered as one of the most dangerous infections in Eurasia, caused by tick-borne encephalitis virus (TBEV). Several TBEV subtypes have been extinguished, with European affecting Europe while Siberian subtype and Far-Eastern subtype affecting Russia and China (Valarcher et al., 2015). The primary prevention method recommended by WHO is vaccination and several formalin-inactivated virion vaccines have been developed based on European subtype or Far-Eastern subtype (Moiseenko et al., 2022). It has been discovered that the phenomenon of antibody immunodominance is affected by the homogeneity of vaccine preparation (Vratskikh et al., 2013). Thus, considering the continuous increase of TBEV cases reported globally, a better understanding of the TBEV virion is required.

Cryo-EM has been applied in biological studies since its introduction, enabling vitrification of specimens in the native state. In this experiment, the structure of TBEV vaccine strain Sofjin-Chumakov is studied. Sofjin-Chumakov strain is a prototype strain of the Far-Eastern subtype of TBEV, which is used to produce commercial inactivated TBE vaccines. Virions were reproduced in the primary cell culture of chicken embryo fibroblasts in Eagle's MEM and then inactivated with formaldehyde solution. The inactivated virions were then negatively stained, applied to a copper Quantifoil grid, and observed under cryo-EM (Titan Krios, 300 Kv accelerated voltage, TFS). Obtained images were then processed with CryoSPARC (Punjani et al., 2017) for a high-resolution 3D-structure.

As a result, a 3D model of the full virion with a resolution of 3.70 Å is obtained, and the published model of TBEV strain HYPR (PDB 5O6A) was docked into the model. In the following study, an improved resolution is desired with the processing of the model in UCSF Chimera and Relion. With the Alphafold 2 prediction and the 3D model, an atomic model of TBEV will be built. In conclusion, the experience obtained from this study can be of use for research on other enveloped viruses of small sizes and the properties of nanobiological objects.

Research has been supported by the Interdisciplinary Scientific and Educational School of Moscow Lomonosov University «Molecular Technologies of the Living Systems and Synthetic Biology» and MSU-BIT Shenzhen University.

Источники и литература

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