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Novel mutations in E2 gene of 2009 CHIKV isolates from South India and the clinical correlation

Gopalsamy Sarangan¹, Seema A. Nayar², Sudharsan Sundarrajan³, Monika Mani¹. Sathish Sankar⁴ and Padma Srikanth^{1*}

¹Department of Microbiology, Sri Ramachandra University, Chennai, INDIA

Abstract

Chikungunya virus (CHIKV) is a single stranded positive sense enveloped RNA virus. Re-emergence of CHIKV caused a massive outbreak with severe clinical manifestation affecting multiple organs. The genetic diversity of CHIKV which caused recurring outbreaks in India was studied. Blood samples were collected from suspected human cases of CHIKV infection in Chennai, Tamil Nadu and three Northern districts of Kerala in Southern India during the CHIKV outbreak in 2008 and 2009. A partial E2 gene segment was amplified by RT-PCR. CHIKV RT-PCR positive samples were sequenced (partial E2) by Sanger's method. Among 119 samples 37 samples were positive for CHIKV. Phylogenetic analysis revealed that the isolated sequences belonged to Indian Ocean lineage (IOL) of ECSA genotype. The mutational analysis revealed the presence of substitutions such as \$299N, T312M, A344T, \$375T, V386G, W339R and \$375P in the current study sequences. In addition, a novel mutation V386G was observed in all the sequences. Two of the study isolates also enclosed unique substitutions W339R and S375P. A structural deviation of 0.019 Å was observed when the wild-type and mutant proteins were superimposed. The intra-molecular interaction analysis revealed various changes in the main chain hydrogen bonds, main chain - side chain hydrogen bonds, side chain-chain hydrogen bonds and hydrophobic interactions. The structural analysis of the wild type and mutant proteins revealed that the structural changes are accompanied by modification in the intra-protein interactions. The structural modifications and the selection pressure investigations disclose the viral genome is constantly evolving leading to enhanced pathogenicity and virulence.

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²Department of Microbiology, Trivendrum Medical College, Trivandrum, INDIA

³Department of Biotechnology, Vellore Institute of Technology, Vellore, INDIA

⁴Sri Sakthi Amma Institute of Biomedical Research, Sri Narayani Hospital and Research Centre, Sripuram, INDIA