ABSTRACT

Chikungunya has emerged as the most prevalent arboviral disease affecting millions of people across the globe. The causative agent Chikungunya virus (CHIKV) is a positive strand RNA virus belonging to family Togaviridae of genus Alphavirus. CHIKV epidemic has drawn significant attention since its reemergence in 2005. The introduction of new molecular features in its genome has resulted in wider vector infectivity, enhanced human incidences and severity. Sequencing and analysis of changes acquired by circulating strains and an understanding of the mechanism in which the structural components of the virus interact to facilitate multiplication of the virus, is of scientific interest. In this study, viral genes of an emergent strain of CHIKV from year 2006 Gujarat outbreak (IND-06-Guj) have been cloned and characterized by sequencing. Sequence alignment and phylogenetic analysis of the characterized viral genome with other reported CHIKV isolates from South Asia, identified it as a possible prototype virus for the region. Protocols were optimized for over-expression and solubilization of CHIKV structural proteins (sPs; Capsid-E3-E2-6K-E1) using different tags and small scale purification of these proteins has been reported. Further, intraviral interaction analysis among the sPs has been studied using yeast two-hybrid (Y2H) and GST pull-down assay. A total of four novel and six known interactions among sPs have been reported that may be responsible for particle assembly, budding and virion maturation. In addition, the screening of human brain cDNA library with envelope proteins E1 and E2 has been carried out using Y2H assay. Cellular targets obtained from Y2H assay have been compared with protein interaction data obtained from computational analysis of CHIKV envelope and human proteins, to arrive at a set of cellular interactors that were further validated using protein interaction ELISA and pull-down assay. On the basis of functional relevance of the interactors identified in this study possible mechanism with which the virus multiplies and manipulates the host machinery has been proposed. The data generated also provides potential targets for further investigation and for devising intervention strategies.