ABSTRACT

Chikungunya virus (CHIKV) is an increasingly significant arthropod-borne alphavirus which has recently caused epidemic outbreaks infecting millions of people worldwide and thus considered as a re-emerging pathogen for which no effective treatment or vaccine is available till date. In fact the formation of virus specific replicase complex by the four viral nsPs together with certain host factors is among the most important steps that determines the fate of viral transcription and replication. The elucidation of presence and/or absence of interactions among nsPs and their domain mapping in a systematic manner is thus of scientific interest. With this aim, the interactions among the nsPs were studied using systems such as yeast two-hybrid (Y2H), pulldown and protein interaction ELISA. The analysis identified six novel interactions among full length nsPs and twelve interactions after domain mapping. These interactions form a network of organized associations that were used to computationally generate a 3D model of CHIKV late replicase complex. Since the knowledge of virus-host protein interface is of great significance for understanding the virus biology and pathogenesis, a structural similarity based computational approach was subsequently employed to study the protein interactions between CHIKV and both its human host and mosquito vector. The interactions identified suggested the involvement of CHIKV in intracellular cell signaling, programmed cell death and transcriptional/translational regulation. Given nsP2 is the most significant viral component involved in both viral replication and combating antiviral response generated in host cell, it was selected as a candidate for screening the human brain cDNA library using Y2H assay. The host proteins identified as nsP2 interactors were further validated and mapped for domain of nsP2 involved in these interactions. The associations identified in this study provide a conservative set for future experimental studies. Moreover, the data obtained should be useful for understanding the interplay between CHIKV and its hosts and may provide potential candidates for drug targets.