Inhibition of flavivirus infection by human ZFP36L1 protein mediated by both XRN1 and RNA exosome

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Zinc-finger protein 36, CCCH type-like 1 (ZFP36L1), containing tandem CCCH-type zinc-finger motifs with an RNA-binding property, plays an important role in cellular RNA metabolism mainly via RNA decay pathways. Recently, we demonstrated that human ZFP36L1 has potent antiviral activity against influenza A virus infection. However, its role in the host defense response against flaviviruses has not been addressed. Here, we demonstrate that ZFP36L1 functions as a host innate defender against flaviviruses, including Japanese encephalitis virus (JEV) and dengue virus (DENV). Overexpression of ZFP36L1 reduced JEV and DENV infection, and ZFP36L1 knockdown enhanced viral replication. ZFP36L1 destabilized the JEV genome by targeting and degrading viral RNA mediated by both 5 -3 XRN1 and 3 -5 RNA-exosome RNA decay pathways. Mutation in both zinc-finger motifs of ZFP36L1 disrupted RNA-binding and antiviral activity. Furthermore, the viral RNA sequences specifically recognized by ZFP36L1 were mapped to the 3'-untranslated region of the JEV genome with the AU-rich element (AUUUA) motif. We extend the function of ZFP36L1 to host antiviral defense by directly binding and destabilizing the viral genome via recruiting cellular mRNA decay machineries.

Biography

Dr.REN-JYE LIN has completed his PhD at the age of 35 years from National Defense Medical Center (MDMC), Taiwan and postdoctoral studies from Institute of Biomedical Sciences (IBMS), Academia Sinica, Taipei, Taiwan He is the director of National Mosquito-Borne Diseases Control Research Center, National Health Research Institute, Taipei, Taiwan. He has published more than 20 papers in reputed journals.

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