

UMP-CMP kinase 2 Inhibits ZIKV Replication through Activation of Type I IFN Signaling Pathway

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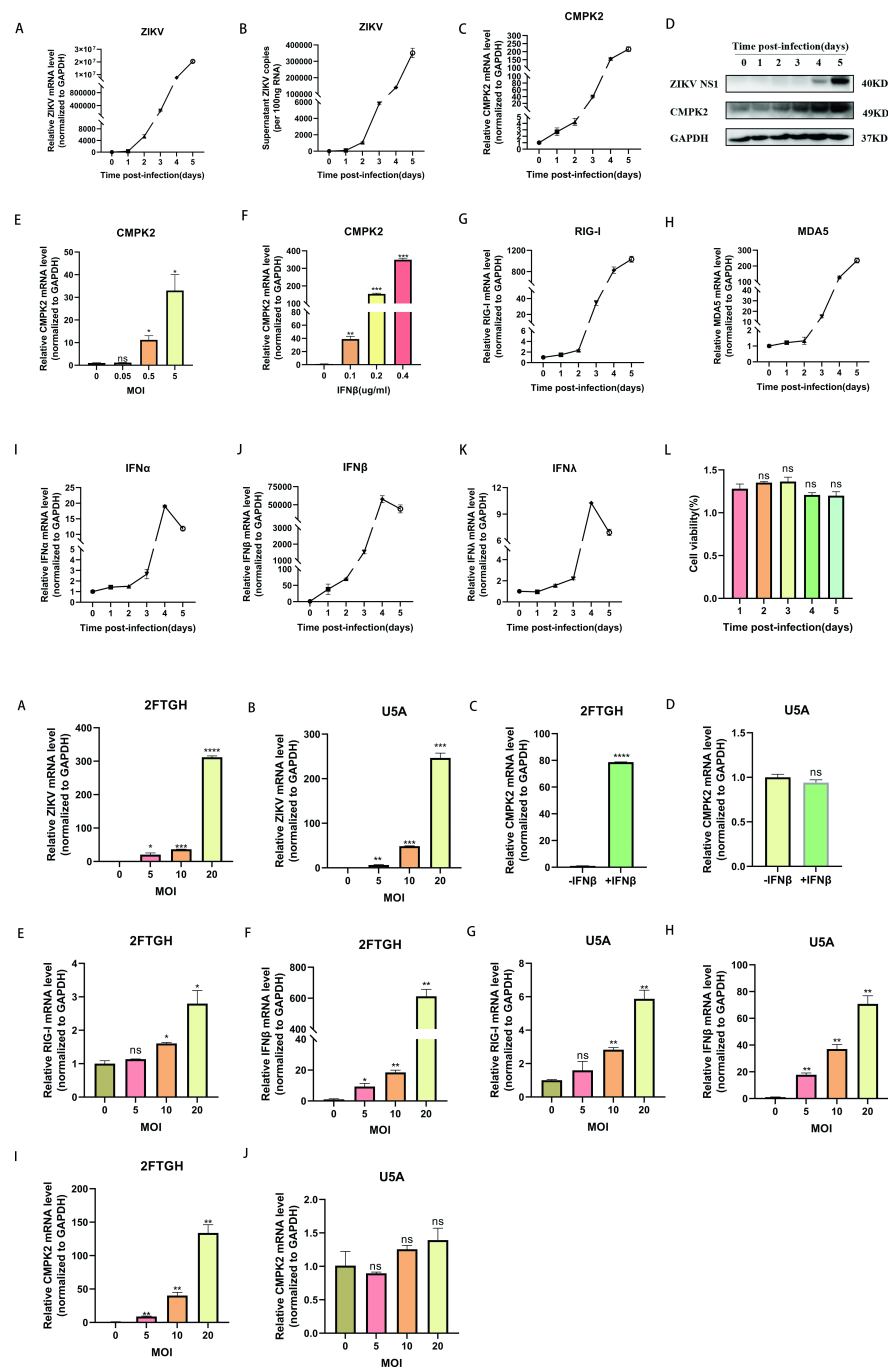
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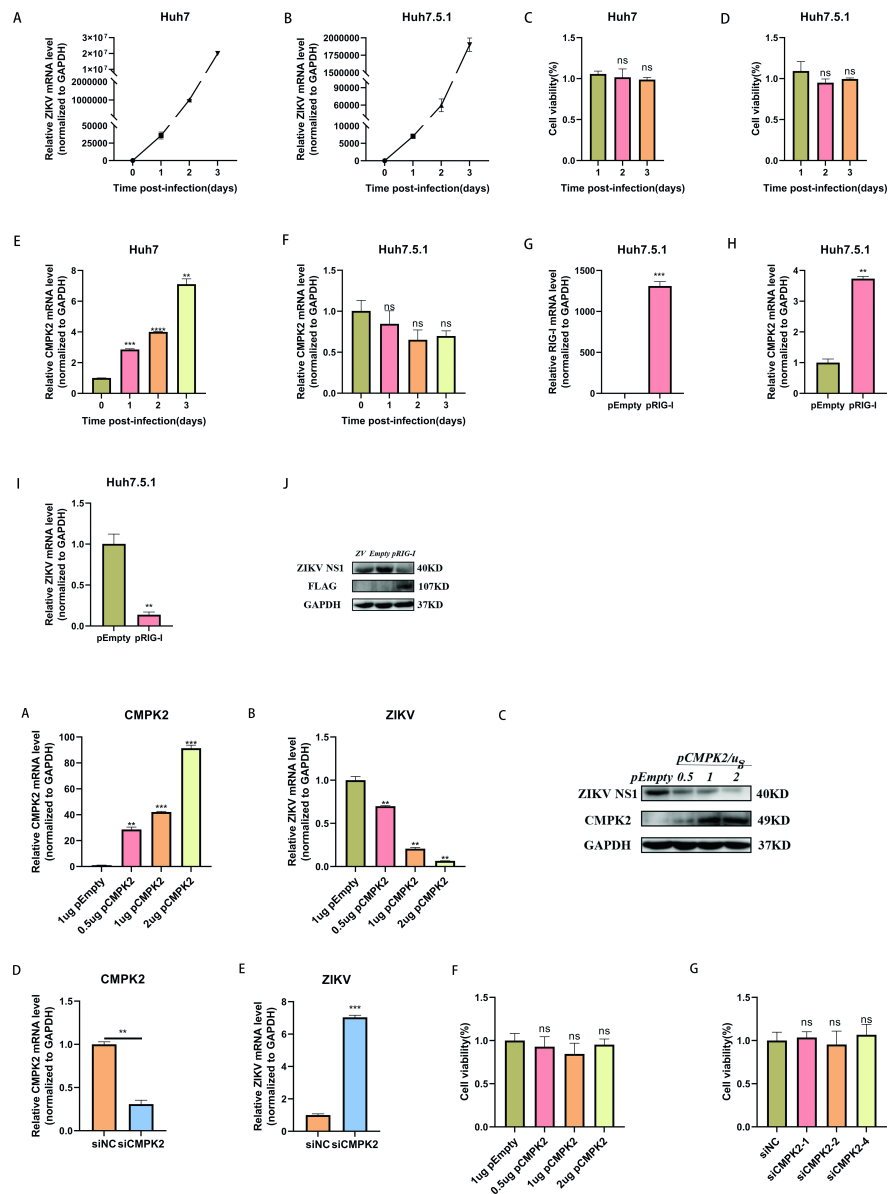
Abstract

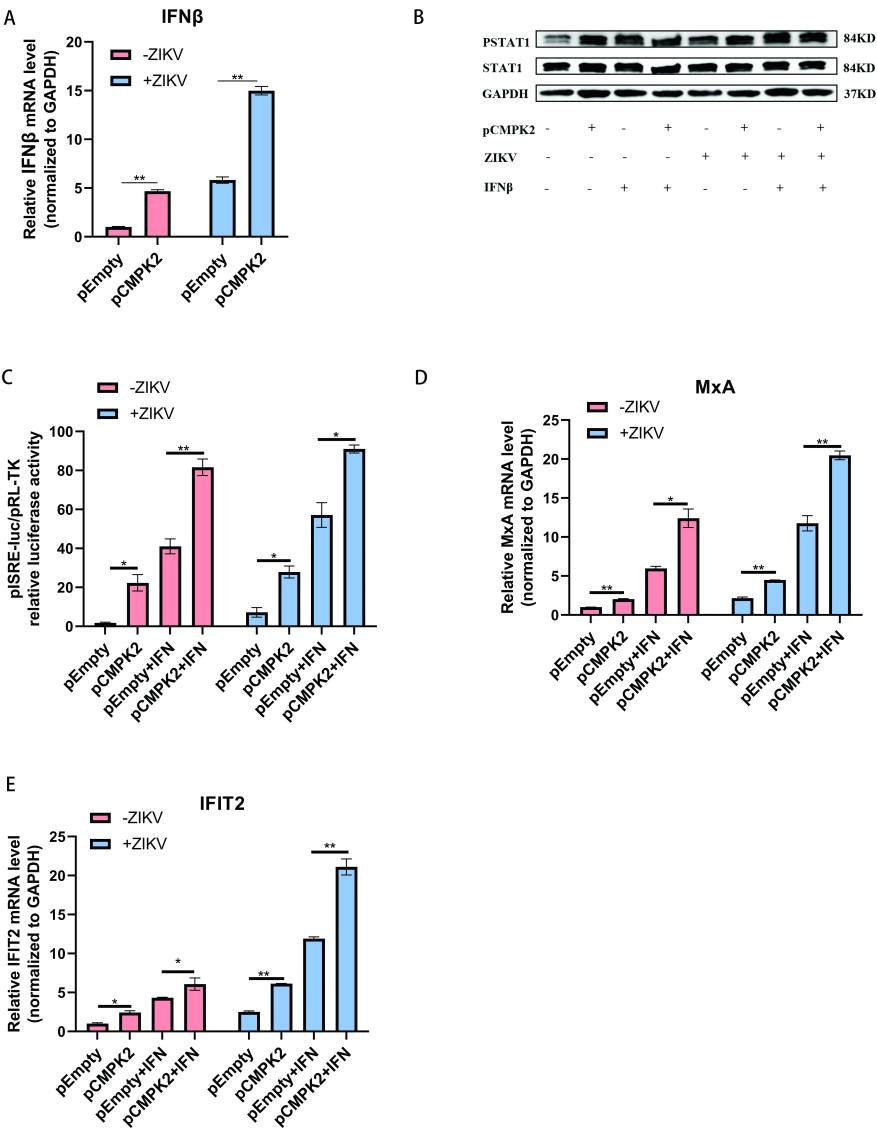
Abstract: Background: Cytidine/uridine monophosphate kinase 2 (UMP-CMP kinase 2, CMPK2) has been reported as an antiviral interferon-stimulated gene (ISG). We previously observed that the expression of CMPK2 was significantly upregulated after Zika Virus (ZIKV) infection in A549 cells. However, the role of CMPK2 in ZIKV replication remains to be determined. **Methods:** CMPK2 or retinoic acid inducible gene I (RIG-I) was overexpressed by plasmid transfection or knocked down by siRNA, respectively in A549 cells before the cells were infected with ZIKV. ZIKV RNA and NS1 protein were detected by RT-qPCR and Western Blot, respectively. The activation status of Jak-STAT signaling pathway was determined by the evaluation of the phosphorylation level of STAT1 (p-STAT1, by Western Blot), interferon stimulated response element (ISRE) activity (by dual luciferase assay) and interferon stimulated gene (ISG) expression (by RT-qPCR). **Results:** We found that ZIKV infection induced CMPK2 expression dependent on RIG-I. Overexpression of CMPK2 inhibited while CMPK2 knockdown promoted ZIKV replication. Mechanically, we found that CMPK2 inhibited ZIKV replication probably through the activation of Jak/STAT signaling pathway as shown by the increased level of p-STAT1, enhanced activity of ISRE, and the up-regulated expression of some downstream ISGs. **Conclusion:** ZIKV infection induced CMPK2 expression, which activated the Jak/STAT signaling pathway to inhibit ZIKV replication. **Keywords:** CMPK2; ZIKV; Jak/STAT signaling pathway

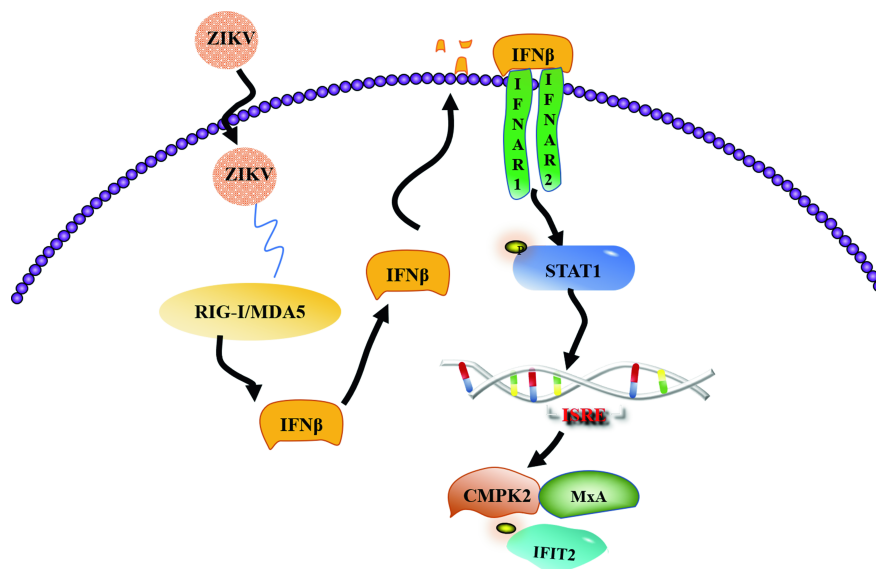
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