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Both PB1 473V mutation in RNA polymerase activity and NP sumoylation plays an important role in the pathogenesis of influenza virus infection

Influenza A virus is a substantial threat to human health. After 1997, the emergence of highly pathogenic H5N1 avian viruses in humans caused great concern about the possibility of a new pandemic. It is reported that PB2 627K plays an important role in the cross-species transmission of avian viruses. In the new emergence of H7N9 avian viruses, we found the PB2 E627K promoted the replication and pathogenicity in mice. However, some avian viruses carrying PB2 627E still can replicate well in mammalian cells and animals. That means there are some key points can compensate the loss function of PB2 627E. By the mini-replicon system, we identified that PB1 473V and 598P can compensate the polymerase activity of avian viruses carrying 627E in mammalian cells and can restore the pathogenicity of viruses in mice. During the life cycle, viruses take advantage of host post-translational modifications for their own benefit. It was recently reported that influenza A virus proteins interact extensively with the host sumoylation system. Thereby, several viral proteins, including NS1 we had reported, are sumoylated to facilitate viral replication. However, the sumoylation in other proteins of influenza A virus is not fully understood. In our study, we found that influenza A virus Nucleo-Protein (NP) is a target of sumoylation in both NP-transfected cells and virus-infected cells at the two most N-terminal residues, lysine 4 and lysine 7, and that the sumoylation at lysine 7 of NP is highly conserved across different influenza A sub-types and strains. The NP-sumoylation-defective virus, WSN-NPK4, 7R virus, exhibited an early cytoplasmic localization of NP. The growth of the WSN-NPK4, 7R virus was highly attenuated compared to that of WSN-WT virus. We evaluated whether members of the PIAS family, the best-characterized E3 ligases, could function as an E3 ligase for NP. Among all PIAS homologs, over-expression of PIASxα had the strongest effect on NP sumoylation, suggesting that PIASxα is the predominant E3 ligase for NP. Thus, sumoylation of influenza A virus NP is essential for intracellular trafficking of NP and for virus growth, illustrating sumoylation as a crucial strategy extensively exploited by influenza A virus for survival in the host.

Biography

Bing Sun joined Institute of Biochemistry and Cell Biology, Chinese Academy of Sciences, China and was a Chief of Lab of Molecular Immunology. He has been appointed as Co-Director and Head, Lab of Molecular Virology in Institute Pasteur of Shanghai, Chinese Academy of Sciences, China. He has been working on dendritic cell maturation and Th1/Th2 cell differentiation over twenty years. He has been working on viral ion channel protein; he has discovered 3a protein of SARS and P7 protein of HCV are an ion channel protein, which are important for viral life cycle and potential a drug target. He has been working on RNA polymerase in influenza A virus.

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