Abstract ID : **78**

Interferon-beta stimulation by aberrant influenza virus RNAs is sequence dependent

Content

The influenza A virus (IAV) genome consists of eight segments of negative strand viral RNA (vRNA). These segments are replicated in the nucleus of the host cell by the viral RNA dependent RNA polymerase (RdRp) in the context of nucleoprotein (NP)-coated viral ribonucleoprotein (vRNP) complexes. In addition to making full-length copies of the vRNA segments, the RdRp generates a range of aberrant RNA products resulting from internal deletions, such as defective interfering RNAs and <125 nt-long mini viral RNAs (mvRNA). The cytoplasmic RNA sensor retinoic acid-inducible gene-I (RIG-I) can detect mvRNA molecules and trigger innate immune responses, such as interferon (IFN)-β expression. Such responses are important in the outcome of viral disease. To understand which type of mvRNAs contribute most to innate immune signalling, we here performed vRNP reconstitutions of different mvRNA-like templates with polymerases of different IAV strains. We measured mvRNA binding to RIG-I and the induction of IFN-β promoter activity, and found that the IAV mvRNA sequence strongly influences IFN-β promoter activity in a template sequence-dependent manner, independent of RIG-I binding. This effect is conserved for the RdRps of the 1918 Spanish Flu, an H5N1 avian IAV, or the lab-adapted WSN IAV. Our results suggest that different mvRNAs contribute differently to RIG-I activation and IAV induced immune responses. Subsequently, sequence differences between flu strains could be indicative of their immunogenicity, representing an interesting avenue for further investigation.

Choose primary session

Viral Replication

Choose secondary Session

Innate Immunity

Contribution Type : Paper presentation