PACT- and RIG-I-dependent Activation of Type I Interferon Production by a Defective-interfering RNA Derived from Measles Virus Vaccine

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Background/Objective

Live attenuated vaccines of measles virus activate innate antiviral response much more potently than the virulent strains. Defining their immunostimulatory components might derive new agents and approaches for design and development of vaccines and adjuvants. Here we demonstrate the type I interferon (IFN)-inducing activity of a defective-interfering (DI) RNA derived from Hu-191, a vaccine strain of measles virus that has been widely used in China for decades.

Method

We identified a copy-back type of DI-RNA in Hu191-infected cells by primer-specific RT-PCR. We determined the immunostimulatory role of this DI-RNA using PACT knockout and knockdown cells. We further dissected the mechanism of IFN induction in cells transfected with in-vitro transcibed DI-RNA or infected with Hu191 measles virus.

Result

We found that Hu-191 infection induced a higher amount of IFN when compared with the infection by a more virulent strain of Measles virus. We further identified a DI-RNA expressed in Hu-191-infected cells and found that this copy-back type of DI-RNA could potently induce IFN production. We further demonstrated that DI-RNA associated with PACT and RIG-I; and knockdown of PACT/RIG-I abolished the IFN induction. However, this induction is reverted upon deletion of the stem region and removal of the 5’ end triphosphate of the DI-RNA.

Conclusion

The presence of the DI-RNA in vaccine strain Hu191 might function as an adjuvant, possibly optimizing the adaptive immune response. Our work might also pave the way for the identification of novel PACT agonists and the development of novel adjuvants or antivirals.