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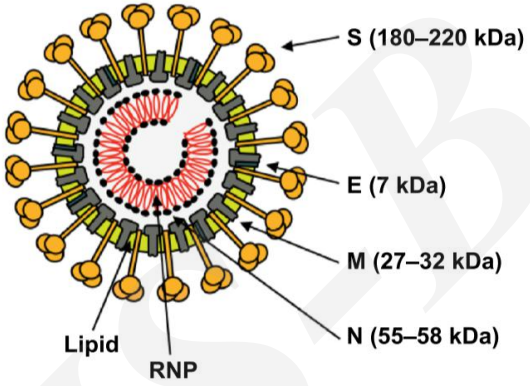
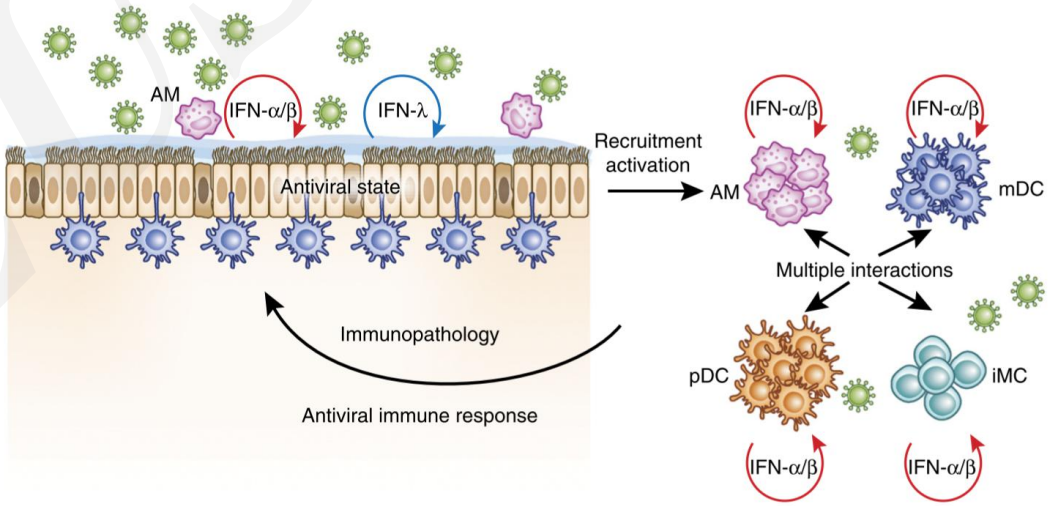
Nucleocapsid protein from porcine epidemic diarrhea virus isolates can antagonize interferon-λ production by blocking the nuclear factor-κB nuclear translocation

Key words: **Porcine epidemic diarrhea virus, Nucleocapsid protein, Interferon Lambda, NF-κB, Intestinal epithelial cells**

Research Summary

- Porcine epidemic diarrhea virus (PEDV) is a highly infectious pathogen that can cause severe diseases in pigs and result in enormous economic losses in the worldwide swine industry.
- The recently discovered IFN-λ has been reported to play a critical role in antiviral defense at the mucosal surface.
- Coronavirus evolved ingenious mechanisms to respond against the antiviral response of IFN.

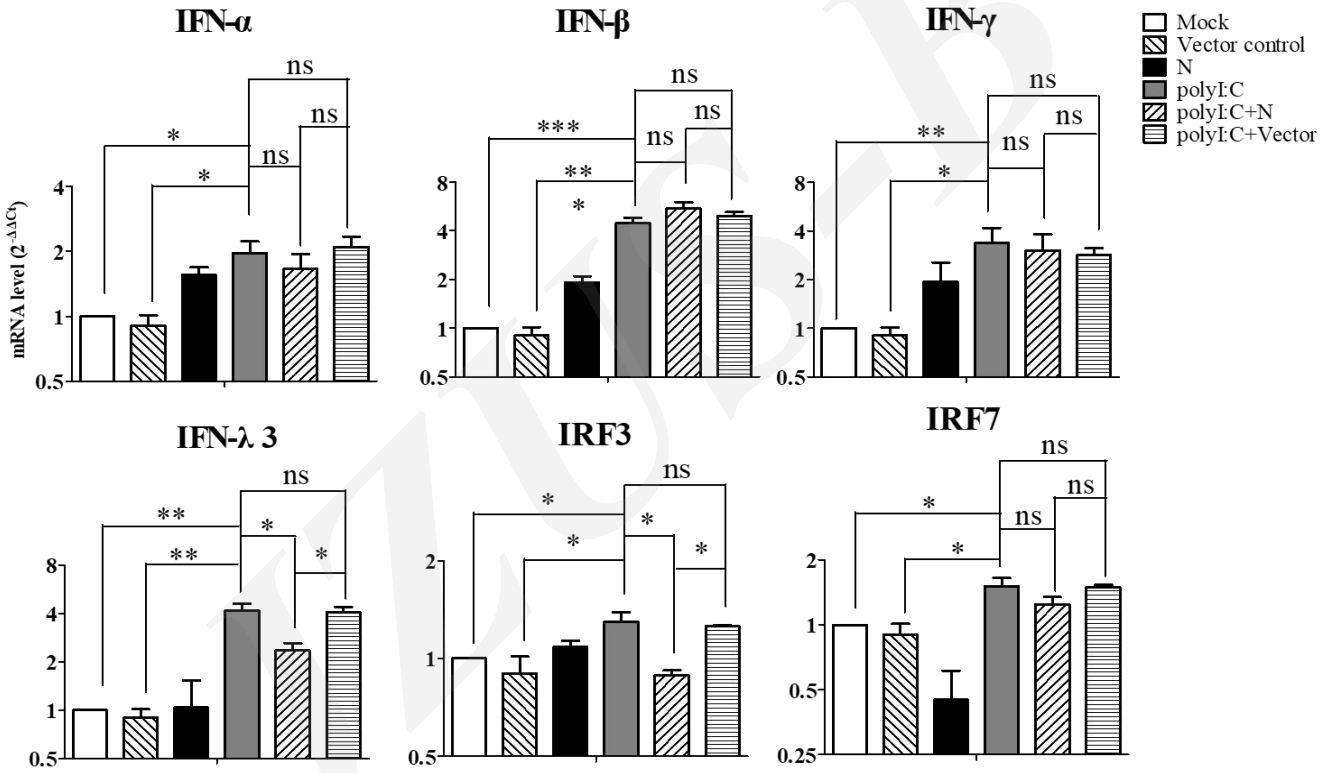




Wack A, Terczyńskadyla E, Hartmann R. Guarding the frontiers: the biology of type III interferons[J]. Nature Immunology, 2015, 16(8):802-809.

Research Summary

The N protein of the epidemic strain could antagonize type III IFN, but not type I or type II IFN expression induced by poly (I: C) in IPEC-J2 cells.

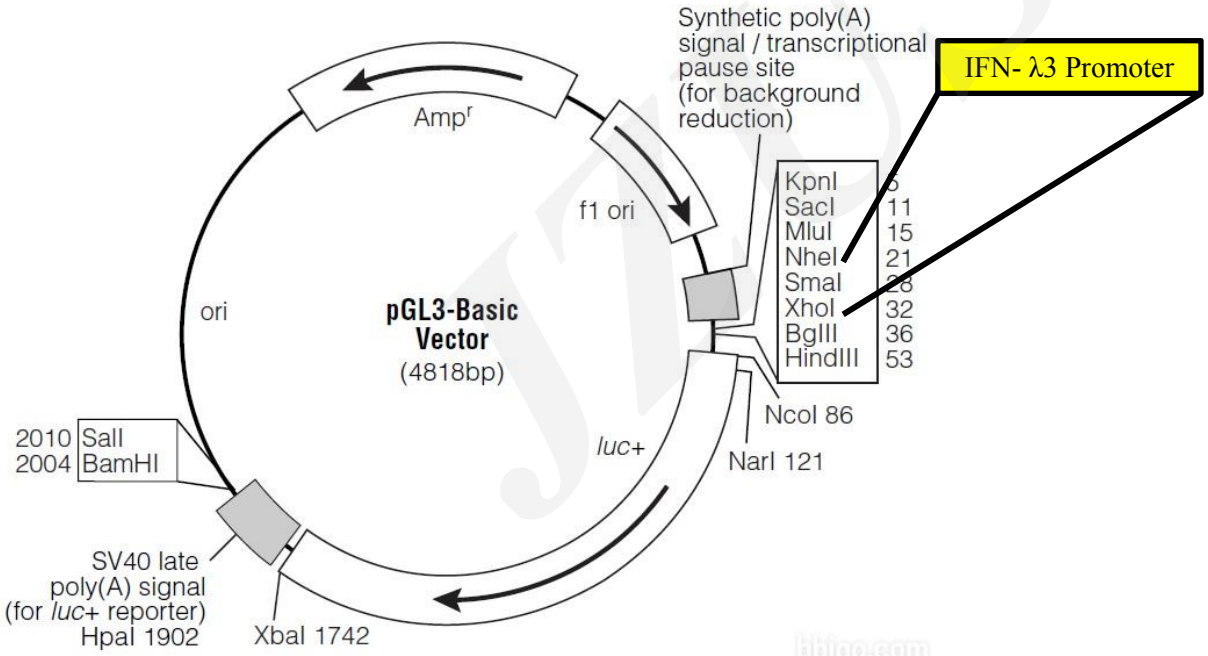


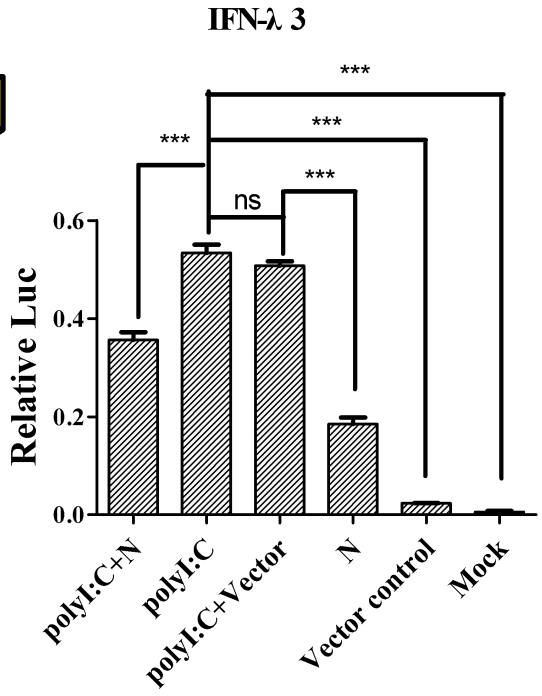
- The three types of IFNs, IFN-α, IFN-β, IFN-γ and IFN-λ3, were notably increased after treatment with poly (I: C) as determined by qPCR.

- The mRNA levels of IFN-α, IFN-β and IFN-γ in poly (I: C)-treated cells were similar to those in poly (I: C) and pcDNA3-N co-transfected cells, whereas the mRNA level of IFN-λ3 was significantly reduced.

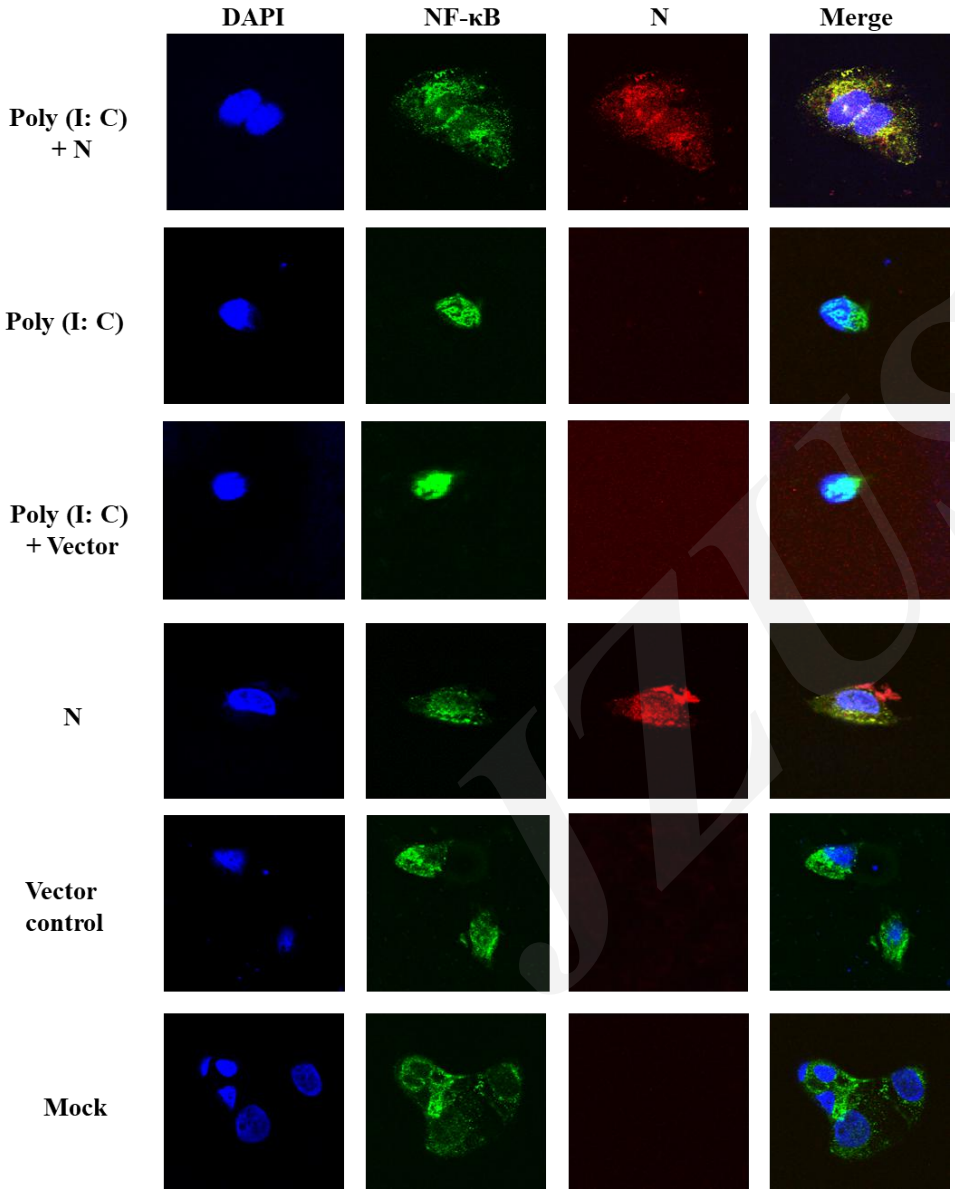
Research Summary

- To confirm IFN-λ3 inhibition by PEDV N protein, we constructed a luciferase reporter vector containing firefly luciferase under the control of the IFN-λ3 promoter.
- Poly (I: C)-induced relative luciferase activity was significantly reduced after PEDV N protein was expressed in IPEC-J2 cells, while it remained induced after the pcDNA3.1 vector was transfected.





Research Summary



- To further investigate the IFN-λ3 inhibitory mechanism of PEDV N protein, NF-κB, the key cellular transcription factor in the IFN pathway, was examined.
- Immunofluorescence showed that NF-κB was distributed mostly in the cytoplasm of unstimulated cells. After the induction of poly (I: C), it was translocated into the nuclei.
- When PEDV N protein was expressed, the NF-κB distribution returned to normal.
- These results showed that NF-κB failed to translocate into the nuclei, leading to IFN-λ3 inhibition, and suggest that PEDV N protein blocks IFN-λ production by preventing the activation of NF-κB in IPEC-J2 cells.