

# **Extracellular nucleoprotein exacerbates influenza viral pathogenesis by activating Toll-like receptor 4 and NLRP3 inflammasome**

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## **Abstract**

Activation of pattern recognition receptors (PRRs) by viral components is critical for viral clearance, but it also increases the viral pathogenesis. However, the role of viral proteins in the activation of PRRs and viral pathogenesis is not very well understood. In this study, we showed that influenza virus nucleoprotein (NP) is released from the infected cells and exacerbates viral pathogenesis by stimulating Toll-like receptor (TLR) 4 and the NLR family pyrin domain containing 3 (NLRP3) inflammasome. Extracellular NP induced monocytic cells to produce interleukin (IL)-1 $\beta$  and IL-6 which led to a subsequent increase in the level of trypsin in the lungs, resulting in the increased viral infectivity and pathology. These results reveal the role of released NP in influenza pathogenesis and highlight the importance of the interaction of internal viral proteins with PRRs in the extracellular compartment in viral pathogenesis.