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| **Virus-induced acute and chronic lower respiratory tract disease is driven by TLR7** |
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| **Introduction/Aim:** Single stranded RNA (ssRNA) viruses such as influenza A virus (IAV) and respiratory syncytial virus (RSV) cause millions of global infections each year. While these viruses typically cause mild upper respiratory tract (URT) illness, a subset of people, including the young, elderly and immunocompromised, develop serious lower respiratory tract (LRT) disease, which can provoke severe respiratory symptoms such as pneumonia, bronchiolitis or even death. Sequalae resulting from severe acute LRT disease from these infections can give rise to chronic respiratory disease, such as asthma. Toll-like receptor 7 (TLR7) recognises ssRNA within the endosome and is critical for establishing innate immune defences against these viruses by activating proinflammatory and antiviral signaling pathways. Immunopathology as a result of hyperinflammation (the “cytokine storm”) can worsen disease. We reasoned that hyperactivation of TLR7-dependent proinflammatory signaling underlines a pathogenic mechanism that promotes LRT disease following viral infection.**Methods:** Wild type C57BL/6 and TLR7 knockout (TLR7 KO) mice were intranasally infected with IAV (Hk-X31 or PR8 strains) or RSV A (Long strain). Flow cytometry and gene expression analysis was used to assess inflammation at acute or chronic timepoints.**Results:** Following infection, inflammation in the URT (nasal compartment) was enhanced in the absence of TLR7 although monocyte and plasmacytoid dendritic cell populations were lower. This was associated with reduced innate and adaptive T cell responses in the LRT, leading to decreased Th1-mediated immunity. Viral clearance in the lungs was not compromised and TLR7 KO mice instead displayed less disease burden as evidenced by reduced acute LRT inflammation and abrogated chronic airway hyperreactivity.**Conclusion:** This research unveils TLR7-mediated hyperinflammation as a potential mechanism utilized by respiratory viruses to drive LRT disease and suggests the compartmentalization of the inflammatory response to the URT may reduce the acute and chronic manifestations of LRT disease.**Grant Support:** This work was supported by The National Health and Medical Research Council of Australia (Project I.D. 1122506, 1128276) |