TLR3 Signaling Is Required for Human Rhinovirus (HRV)-Induced Airways Neutrophilic Inflammation and Hyperresponsiveness But Not Viral Clearance in Experimentally-Infected Mice

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Introduction: Human rhinovirus (HRV), a single-stranded (ss) RNA virus, causes exacerbation of chronic lower airway diseases including asthma. HRV infection triggers innate immune responses, including the production of interferons (IFNs) and pro-inflammatory chemokines.

Methods: We investigated the requirement of Toll-like receptor (TLR)-3, which recognizes viral double-stranded RNA formed upon viral replication, for HRV-induced airway responses. Wild type (wt) B6129SF2/J and TLR3-deficient (TLR3-/-) mice were inoculated intranasally with HRV1B, a minor group virus which replicates in mouse lungs.

Results: One day after infection with HRV1B, TLR3 -/- mice showed significantly decreased expression of the neutrophil chemoattractants KC/CXCL1 and MIP-2/CXCL2, and decreased whole lung neutrophil counts compared to HRV-infected wt mice. TLR3-/- mice also displayed significantly decreased airway cholinergic responsiveness after HRV infection. However, compared to wt mice, TLR3 -/- mice showed no significant differences in viral titer, viral RNA or type I IFN expression. TLR3 -/- mice showed partial reductions in type II and III IFN expression.

Conclusions: We conclude that TLR3 is required for HRV-induced airways neutrophilic inflammation and hyperresponsiveness but not viral clearance in B6129SF2/J mice. In other words, in this model, TLR3-driven innate immune responses to HRV are paradoxically maladaptive following experimental infection.