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TLR2-mediated innate immune priming boosts lung anti-viral immunity

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Shareable abstract (@ERSpublications)
TLR2-agonist treatment to the respiratory tract activates airway epithelial cells to prime the innate immune system to rapidly respond to infection and reduce virus-induced inflammation, including in the context of corticosteroid treatment and in asthma https://bit.ly/3g02Q4M

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Abstract

Background We assessed whether Toll-like receptor (TLR)2 activation boosts the innate immune response to rhinovirus infection, as a treatment strategy for virus-induced respiratory diseases.

Methods We employed treatment with a novel TLR2 agonist (INNA-X) prior to rhinovirus infection in mice, and INNA-X treatment in differentiated human bronchial epithelial cells derived from asthmatic-donors. We assessed viral load, immune cell recruitment, cytokines, type I and III interferon (IFN) production, as well as the lung tissue and epithelial cell immune transcriptome.

Results We show, *in vivo*, that a single INNA-X treatment induced innate immune priming characterised by low-level IFN-λ, Fas ligand, chemokine expression and airway lymphocyte recruitment. Treatment 7 days before infection significantly reduced lung viral load, increased IFN-β/λ expression and inhibited neutrophilic inflammation. Corticosteroid treatment enhanced the anti-inflammatory effects of INNA-X. Treatment 1 day before infection increased expression of 190 lung tissue immune genes. This tissue gene expression signature was absent with INNA-X treatment 7 days before infection, suggesting an alternate mechanism, potentially *via* establishment of immune cell-mediated mucosal innate immunity. *In vitro*, INNA-X treatment induced a priming response defined by upregulated IFN-λ, chemokine and anti-microbial gene expression that preceded an accelerated response to infection enriched for nuclear factor (NF)-κB-regulated genes and reduced viral loads, even in epithelial cells derived from asthmatic donors with intrinsic delayed anti-viral immune response.

Conclusion Airway epithelial cell TLR2 activation induces prolonged innate immune priming, defined by early NF-κB activation, IFN-λ expression and lymphocyte recruitment. This response enhanced anti-viral innate immunity and reduced virus-induced airway inflammation.