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Abstract Title

Intranasal Interferon-lambda Protects Mice against Respiratory Syncytial Virus Infection

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Background

RSV is a major cause of respiratory tract infections and hospitalization in infants and young children. Current maternal vaccination offers only time-limited protection to infants, while targeted antiviral therapies remain unavailable. Consequently, there is an urgent need for alternative approaches to enhance host antiviral immunity. Interferon-lambda (IFN- λ) is predominantly an epithelial cell-produced cytokine that promotes antiviral defences at mucosal surfaces while limiting systemic inflammation. Building on its demonstrated efficacy against COVID-19 and other respiratory viral pathogens, we hypothesized that intranasal IFN- λ administration will provide localized, effective protection against RSV infection in mice.

Objective

To evaluate the protective effects of intranasal IFN- λ administration against RSV infection in mice.

Methods

Six to seven-week-old BALB/c mice received intranasal IFN- λ either 24 h prior to (prophylactic treatment) or 24 h post-RSV infection (therapeutic treatment). At 5 days post-infection, bronchoalveolar lavage (BAL) and lung tissue were collected. BAL was used to assess pulmonary inflammation through protein quantification using ELISA, differential leukocyte counting using Giemsa staining, and immune cell phenotyping using flow cytometry. The right lung lobe was used to quantify pro-inflammatory gene expression using RT-qPCR and viral burden using a plaque assay. The left lung lobe was processed for histopathological evaluation using hematoxylin and eosin staining.

Results

Prophylactic IFN- λ treatment significantly reduced neutrophil infiltration in RSV-infected mice compared to vehicle-treated mice. Prophylactic treatment with IFN- λ significantly suppressed pro-inflammatory gene expression (IL-1 β , IL-6, CXCL1, and TNF- α), while therapeutic IFN- λ significantly reduced IL-1 β expression in RSV-infected mice. Lung viral titre and NS-1 gene expression were reduced in both treatment regimens compared to vehicle-treated mice. Lung tissue inflammation was significantly attenuated in both IFN- λ treatment regimens.

Conclusion

Prophylactic intranasal IFN- λ treatment conferred greater protection against RSV infection in mice than therapeutic intranasal treatment by attenuating neutrophil infiltration, and proinflammatory gene expression in the lung tissue