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Research Category
Basic Science

Abstract Title
Investigating interferon lambda as a potential antiviral therapy against respiratory syncytial virus infection

Background
Accounting for over 2% of all deaths of children under 5 years old, respiratory syncytial virus (RSV) poses a significant burden to global pediatric health. Despite extensive research efforts, there is still a lack of effective treatments against RSV specifically for children. Interferon lambdas (IFNLs) are secreted following viral infections in mucosal surfaces, and treatment with IFNLs is protective against other respiratory viral infections.

Objective
This study aims to investigate the effect of IFNL3 as an antiviral agent against RSV infection.

Methods
Immortalized bronchial epithelial cells (HBEC3-KT) and monocyte-derived macrophages were cultured and infected with RSV-GFP, which allows for visualization of infection. Cells were treated with different concentrations of IFNL3 or IFNβ at different timepoints to investigate the protective effect of IFNL3 on RSV infection compared to IFNβ. RSV infection was visualized using fluorescence microscopy and replication was quantified with a classical plaque assay. RSV fusion protein expression was assessed with western blot. The expression of interferon-stimulated genes (ISGs) was measured via qPCR.

Results
Prophylactic treatment with IFNL3 significantly inhibited RSV infection HBEC3-KT and macrophages in a concentration-dependent manner, while therapeutic treatment with IFNL3 failed to protect cells from RSV infection. Prophylactic IFNL3 treatment also greatly reduced RSV titre compared with untreated cells. Prophylactic IFNβ treatment confers greater inhibition of RSV infection compared to IFNL3 treatment. Additionally, IFNL3 potently induced baseline IFIT1 and ISG15 expression compared with untreated HBEC3-KT cells. IFNL3 also upregulated IFIT1 and ISG15 expressions during RSV infection compared with untreated infected cells.

Conclusion
These results demonstrate that prophylactic treatment with IFNL3 potently inhibits RSV replication in human airway epithelial cells and promotes baseline ISGs expression, which is likely correlated with lower RSV viral titre in treated cells. This study can potentially introduce IFNL3 as an antiviral agent against RSV in children.

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