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**Title:** Efficacy of IFN- $\lambda$ 1 to protect human airway epithelial cells against rhinovirus 1B infection

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**Body:** Impaired interferon (IFNs) production has been observed in various respiratory diseases. This contributes to the enhanced sensitivity towards viral infections which ultimately lead to acute exacerbations. To compensate for this impaired host IFN response, there is need to explore new therapeutic strategies, like exogenous administration of IFNs as prophylactic treatment. In the present study, we examined the protective potential of IFN- $\lambda$ 1 and compared it with the previously established protective effect of IFN- $\beta$ . A549 cells and human primary bronchial epithelial cells were first treated with IFN- $\beta$  (500IU/ml) and IFN- $\lambda$ 1 (500ng/ml) for 18h. For infection, two approaches were adopted: i) Continuous scenario: after pretreatment cells were infected with HRV for 24h or 72h in IFNs-containing medium, ii) Pre-treatment scenario: IFNs-containing medium was replaced after 18h cells were infected for 4h and further maintained for another 24h and 72h in HRV and IFNs-free medium. The protective effect was evaluated in terms of a reduction in the number of viral copies/infectious progeny, and an enhanced expression of IFN-stimulated genes (ISGs). In both cell types and in both approaches IFN- $\beta$  or - $\lambda$ 1 treatment resulted in pronounced and long lasting antiviral effects (even in the absence of the IFNs in the culture medium) exemplified by significantly reduced viral copy numbers and diminished infectious progeny. This was associated with strong up-regulation of multiple ISGs. Here we demonstrate that protective potential of IFN- $\lambda$ 1 is comparable to IFN- $\beta$ . Yet, due to the more localized expression of IFN- $\lambda$ 1 receptors (e.g. in the respiratory epithelium), the use of IFN- $\lambda$ 1 may be even more promising than IFN- $\beta$ .