Suppression of Influenza virus infection by rhinovirus interference - An Epidemiological and in vitro study

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Introduction: Human rhinovirus (RV) is the most frequent etiologic agent for common cold. The detection rate of RV was as high as 23.4% in paediatric outpatients, followed by influenza A (IVA, 19.6%) and influenza B (IVB, 6.3%) in Hong Kong1. Most of the infections in healthy individuals are mild and self-limiting, and asymptomatic RV infection is common. In contrast, influenza viruses (IV) confer substantial morbidity and mortality worldwide every year. Viral antigenic drift, antigenic shift and vaccine strain-mismatch makes the prediction of flu seasonality difficult. In this study, we observe a significant negative correlation of RV prevalence against that of influenza in paediatric in-patients. To support our findings, primary airway epithelial cells were sequentially infected with RV followed by IVs. A significant suppression of IVs replication is identified in cells with prior exposure to RV. Taken together we evidence viral interference, a phenomenon in which an infection of one virus provide transient protection to secondary viral infection, between RV and IV.

![Graph](image1.png)

**Figure 1:** Detection of respiratory viruses in Hong Kong paediatrics. A) Monthly prevalence of IVA and IVB in comparison to EV/RV from patients admitted to hospitals under New Territories East Clusters. Strong negative correlation of EV/RV against that of the total IVs prevalence is identified \( R^2 = 0.702, \; p<0.001 \). B) Pearson correlation of virus prevalence indicates a negative covariance of EV/RV with IVA, IVB, total IVs, total parainfluenza viruses (PIVs) and Respiratory syncytial virus (RSV) with \( p<0.01 \).

![Graph](image2.png)

**Figure 2:** Suppression of influenza replication upon prior RV infection using in vitro infection experiment. A) Experimental plan of sequential infection. Well-differentiated human bronchial epithelial cells (HBEc) were first infected with RV (RV-A16 or RV-1B) or mock treated for 2 hours before washing. After 48 hours of primary infection, cells were subjected to secondary IV infection and viral supernatants were collected for viral titration. B) Immunohistochemical staining of HBEc. C) Replication kinetics of IVs with or without prior RV infection from HBEc of one representative patient. D) Replication of IVs titer (Seasonal IVA, Oseltamivir-resistant IVA and IVB) upon prior RV infection as compared to sham control using TCID50 assay. Log10 reduction in virus titer was compared with sole IV infection, and statistical analysis was performed using Student’s t-test with \( p<0.05 \), \( p<0.01 \) and \( p<0.001 \).

**Conclusion:** Our data suggests that RV induces a transient protection against pan-influenza virus infection. Identification of this novel correlate to influenza immunity may give new direction for the development of prophylactics.

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