# Human rhinovirus infection of airway epithelial cells induces tenascin-C release

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Introduction: Viral infections are the cause of 75% of all asthma exacerbations, with human rhinovirus (HRV) being the most common. Tenascin-C (TNC) is an ECM protein that is present in small quantities in the airway of healthy individuals, but in high quantities in asthma sufferers; however, the inflammatory potential of TNC in asthma has yet to be investigated. We hypothesise that HRV infection induces the upregulation of TNC expression in the airway, contributing to increased inflammatory cytokine production.

Materials and Methods: C57BL/6 mice were intranasally administered with the viral mimic Poly(I:C) and bronchoalveolar lavage fluid (BALF) analysed for TN-C. BEAS-2B cell line and primary human bronchial epithelial cells (PBECs) were stimulated with Poly(I:C) or infected with HRV and assayed for TN-C mRNA, protein expression and release. Finally, recombinant TN-C was added exogenously to BEAS-2B cells and extracellular vesicles (EVs) were isolated following stimulation, analysed for TN-C expression and used to stimulate BEAS-2B cells and macrophages.

Results: TNC expression in the mice BALF was significantly upregulated following Poly(I:C) stimulation, and in vitro Poly(I:C) and HRV treatment induced TN-C mRNA and TN-C release in PBECs and BEAS-2B cells, highlighting a novel relationship between HRV infection and airway TN-C expression. Viral-induced TN-C release was significantly higher from asthmatic PBECs compared to non-asthmatic PBECs, demonstrating an increased prominence in a disease setting. Furthermore, Poly(I:C) stimulation also induced EV release and EV-associated TNC expression in BEAS-2B cells. EVs derived from Poly(I:C) stimulation induced cytokine release from BEAS-2B cells and macrophages, as did stimulation with recombinant TN-C, demonstrating the inflammatory potential of EVs and TN-C in the airway following viral treatment.

Discussion: Further work to determine the effects of TNC on inflammation in the airway is ongoing. The current data support a potential link between TNC release following HRV infection and inflammatory cytokine production in the airway, potentially through the release of EVs.