Immune Response to Rhinoviruses and Their Link to Asthma Exacerbations

Alar Aab,1,2 Willem van de Veen1, Stefan Söllner1, Oliver Wirz1, Barbara Stanic1, Can Altunbulakli, Sebastian Johnston, Ana Rebane, Cezmi A. Akdis1 and Mübeccel Akdis1

Background

Respiratory infections with human rhinoviruses (HRV) pose severe health risks for patients with asthma or chronic obstructive pulmonary disease and represent the leading cause for their exacerbations. Here, we studied the effect of HRV1B, HRV14, HRV16 and HRV29 infections to human immune system cells to investigate their roles in allergy and asthma exacerbations and chronicity.

METHODS:

Peripheral blood mononuclear cells (PBMC) from healthy and allergic individuals were stimulated with HRV1B, HRV14, HRV16 and HRV29, and PBMC proliferation, cytokine profile, viral mRNA expression, virus uptake and cell morphology and viral persistence were investigated by [3H] thymidine incorporation, CFSE staining, luminometric bead array, PCR, in-situ hybridisation, and multispectral imaging flow cytometry.

RESULTS: When PBMC from allergic and nonallergic individuals were stimulated with different types of HRVs, a virus dose-related cellular proliferation was observed, which was particularly confined to B cells. Different serotypes of HRV induced proliferation of plasmablasts (CD19+, CD27++ and CD38++), but not the CD4(+) and CD8(+) T-cells. HRV induced cytokine profiles were more characteristic to innate immune response with elevated IL-6 and IL-8 production. This effect was not observed with UV inactivated RVs. We also found that from CD20+ B-cells could be infected by HRV1B in vitro. We developed the in-situ hybridization method for detection of HRV1B, HRV16 and HRV29 with combination of immunofluorescence staining for anti-CD20mAb. Our findings demonstrate that B cells express HRV RNAs at day 5, particularly in dividing B cells.

CONCLUSION:

HRVs have a unique ability to directly infect and proliferate human B-cells and activate human plasmablasts leading to a proinflammatory cytokine profile. This could explain the strong association and role for HRV with the exacerbation of airway diseases.