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In vivo T regulatory cell regulation during Human Rhinovirus infection

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Text:

Rationale: Respiratory infections with human rhinoviruses (HRV) are strongly associated with asthma exacerbations and pose a severe health risk for allergic individuals. How HRV infections and chronic allergic diseases are linked, and which role HRV plays in the breaking of allergen-specific tolerance is unknown. T regulatory cells (Tregs) play an important role in the induction and maintenance of immune tolerance. Therefore, the aim of this study is to investigate the effects of HRV on Tregs during asthma exacerbations. **Methods:** Healthy and asthmatic individuals were experimentally infected with HRV16 in vivo. Peripheral blood mononuclear cells (PBMCs) were obtained before infection and three days after infection. Tregs were sorted from the PBMCs according to their flow cytometric profile CD4⁺CD3⁺CD25⁺CD49d⁺CD127⁻ and were analyzed with next generation sequencing. **Results:** We have found that on baseline there is a clear difference in Tregs from asthmatics compared to healthy individuals. Tregs from asthmatics show a more Th2 type profile with increased expression of IL13, IL4, IL5, PTGDR2 and reduced FOXP3. Three days after intranasal infection with RV16 in both asthmatics and healthy individuals an antiviral response is induced in T regulatory cells, including upregulation of MX1, STAT1, IFI44L, IRF7/9, OAS3. In healthy individuals there is an additional upregulation of FOS and JUN, and the suppressor molecule SOCS3, while this was not altered or even down regulated in asthmatics. Furthermore, in healthy individuals CCL5 was downregulated, while unchanged in asthmatics. **Conclusion:** Tregs from healthy and asthmatic individuals show an anti-viral response after RV infection. However there are clear differences between healthy and asthmatic individuals, upon baseline and in response to rhinovirus infection. These differences in response might affect Treg functions, level of inflammation, chronicity and viral clearance. These data suggest that Treg functions might be altered or impaired during HRV infections, which may contribute to asthma exacerbations.