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**Background**

Although acute exacerbations, mostly triggered by rhinoviruses (RVs), account for the majority of hospitalizations and life-threatening situations in asthma, there is still very little known about the pathophysiological mechanisms involved.

**Objective**

We sought to investigate the role of plasmacytoid DCs (pDCs) in asthma exacerbations and unwind potential mechanisms involved.

**Methods**

Patients with asthma under stable disease or acute exacerbations, and healthy individuals, were studied for pDC presence in their sputum and their association with various leukocytic populations, cytokines and disease parameters. Animal models of asthma and virus-induced asthma exacerbations were further used to dissect the functional role of pDCs in the disease process.

**Results**

pDCs were markedly increased in the sputum of patients with stable asthma and acute exacerbations. Moreover, increasing pDC numbers were directly linked to the severity of type 2 inflammation, deterioration of lung function and risk for asthmatic attacks. In animal models of allergic asthma and RV-induced exacerbations, pDCs were shown to be key mediators of the immuno-inflammatory response driving asthma; they were recruited to the lung during inflammation and migrated to the lymph nodes to boost Th2-mediated effector responses. Accordingly, pDC depletion post-allergen challenge or during RV infection abrogated disease exacerbation. Central to this was interleukin 25 (IL-25) which conditioned pDCs for pro-inflammatory activation and migration.

**Conclusion**

Our studies uncover a previously unsuspected role of pDCs in asthma exacerbations with major implications in disease diagnosis, prognosis and monitoring. They also propose the therapeutic targeting of pDCs and IL-25 for the treatment of asthma attacks.