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Pulmonary type-2 innate lymphoid cells in paediatric severe asthma: phenotype and response to steroids

Prasad Nagakumar[1,2,3], Franz Puttur[1,3], Lisa G. Gregory[1], Laura Denney[1], Louise Fleming[2], Andrew Bush[2], Clare M. Lloyd[1,4] and Sejal Saglani[1,2,4]

Affiliations: [1]National Heart and Lung Institute, Imperial College London, London, UK. [2]Respiratory Paediatrics, Royal Brompton Hospital and National Heart and Lung Institute, Imperial College London, London, UK. [3]Both authors contributed equally. [4] Both authors contributed equally.

Correspondence: Sejal Saglani, Inflammation, Repair and Development, National Heart and Lung Institute, Sir Alexander Fleming Building, Imperial College London, Exhibition Road, London, SW7 2AZ, UK. E-mail: s.saglani@imperial.ac.uk

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Children with severe asthma have a distinct type-2 airway molecular phenotype with higher ILC2s, Th2 cells and eosinophils than difficult asthma, while IL-17$^+$ cells are similar. ILC2s are sensitive to systemic steroids whereas IL-17$^+$ cells are unchanged. bit.ly/2JMtW1R

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ABSTRACT Children with severe therapy-resistant asthma (STRA) have poor control despite maximal treatment, while those with difficult asthma (DA) have poor control from failure to implement basic management, including adherence to therapy. Although recognised as clinically distinct, the airway molecular phenotype, including the role of innate lymphoid cells (ILCs) and their response to steroids in DA and STRA is unknown.

Immunophenotyping of sputum and blood ILCs and T-cells from STRA, DA and non-asthmatic controls was undertaken. Leukocytes were analysed longitudinally pre- and post-intramuscular triamcinolone in children with STRA. Cultured ILCs were evaluated to assess steroid responsiveness *in vitro*.

Airway eosinophils, type 2 T-helper (Th2) cells and ILC2s were significantly higher in STRA patients compared to DA and disease controls, while IL-17$^+$ lymphoid cells were similar. ILC2s and Th2 cells were significantly reduced *in vivo* following intramuscular triamcinolone and *in vitro* with steroids. Furthermore, asthma attacks and symptoms reduced after systemic steroids despite persistence of steroid-resistant IL-17$^+$ cells and eosinophils.

Paediatric STRA and DA have distinct airway molecular phenotypes with STRA characterised by elevated type-2 cells. Systemic corticosteroids, but not maintenance inhaled steroids resulted in improved symptom control and exacerbations concomitant with a reduction in functional ILC2s despite persistently elevated IL-17$^+$ lymphoid cells.