Asthma Development is Associated with an Aberrant IL-10 Response to Viruses in Early Life

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**Background**: Viral infection is a common trigger of severe respiratory illnesses in early life and a risk factor for later asthma development. The mechanism leading to asthma could involve an aberrant airway immune response to viral infections, but this has rarely been studied in a human setting.

**Objectives**: To investigate *in situ* virus-specific differences in upper airway immune mediator levels during viral episodes of respiratory illnesses and the association with later development of asthma.

**Methods**: We included 493 episodes of acute respiratory illnesses in 277 children aged 0-3 years from the COPSAC2010 mother-child cohort. Levels of 18 different immune mediators were assessed in nasal epithelial lining fluid and compared between children with and without viral PCR-identification (nasopharyngeal sample). Finally, we investigated whether the virally associated immune response was associated with development of asthma by age 6 years.

**Results**: Viral detection during respiratory illnesses was associated with upregulation of several Type 1 and T regulatory  immune mediators, including IFN-ɣ, TNF-α, CCL4, CXCL10 and IL-10, and downregulation of Type 2 and Type 17 immune mediators, including CCL13, CCL26 and CXCL8  (FDR<0.05). Children who developed asthma by age 6 years had decreased levels of IL-10 (FDR<0.05), and nominal significantly decreased levels of IL-2 and IFN-ɣ, and increased levels of CCL4 and CXCL10 during viral episodes compared to children who did not develop asthma.

**Conclusion**: We described the airway immune mediator profile during viral respiratory illnesses in early life and showed that children developing asthma by age 6 years have an aberrant response, particularly characterized by a reduced regulatory (IL-10) response. This provides insight into the interplay between early-life viral infections and asthma, and pinpoints IL-10 as a potential target for the prevention of childhood asthma.