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Title: IP-10 is selectively produced in the airways upon respiratory virus infection

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Body: Acute respiratory infections (ARIs) represent a challenge in clinical practice. The symptoms of bacterial and viral infections are overlapping, and due to the lack of a specific reliable marker, the physician is left with diagnostic uncertainty. This often leads to an empirical antibiotic (over)treatment, although 60% of ARIs are associated with viral infections. It has been reported that IFN-gamma-inducible protein 10 (IP-10) is produced by the airway epithelium upon infection with respiratory viruses and is measurable in vivo in respiratory secretions and serum. This led us to evaluate the cytokine profile induced by primary airway epithelial cells upon viral and bacterial stimulation. We analysed IP-10, IL-6, and IL-8 responses of primary human nasal and bronchial epithelial cells after stimulation with rhinoviruses (RVs), poly(IC), and bacterial-derived products including LPS, flagellin, and lipopeptides. In addition, we measured IP-10 in nasopharyngeal aspirates (NPAs) obtained from three different groups of children hospitalized for lower respiratory tract infections: children with RV-wheezy bronchitis, RSV bronchiolitis and non-viral ARI. Bronchial and nasal cells produced similar amounts of IL-6 and IL-8 after viral and bacterial stimulation. In contrast, IP-10 was selectively produced upon stimulation with poly(IC) and infection with RVs. In accordance with the in vitro data, IP-10 was found at higher concentrations in NPAs from RV- and RSV-infected children compared to those with non-viral ARI. Our findings suggest a role of IP-10 during antiviral responses of the airways and its possible use as a tool to assist the physician in clinical decision-making when evaluating patients with ARI.