The Unified Airway: A Systematic Review of Gene Expression Profiling in Allergic Rhinitis, Asthma, and Chronic Rhinosinusitis

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Objectives
To evaluate molecular overlap in airway gene expression alterations in diseases that constitute the unified airway hypothesis: allergic rhinitis, asthma, and chronic sinusitis.

Study Design
Systematic literature review with pooled data analysis.

Methods
The published literature of high-throughput gene expression studies for allergic rhinitis, asthma, and chronic sinusitis was systematically reviewed. Studies using genome-wide microarray techniques for measurement of nasal, sinus, and bronchial epithelial tissue were evaluated for differentially expressed genes. The gene expression profiles of the three diseases of the unified airway were compared to determine overlap in molecular findings that could support the unified airway hypothesis.

Results
A total of 936 differentially expressed genes were identified in 14 studies of unified airway diseases - chronic sinusitis (8), allergic rhinitis (3), and asthma (3). Overlap was found in 19 differentially expressed genes between at least 2 unified airway diseases. Three genes, CST1, POSTN, and SERPIN B4, were differentially expressed in all three diseases.

Summary of overlap in dysregulated genes

<table>
<thead>
<tr>
<th>Gene</th>
<th>Chromosomal Location</th>
<th>Protein Function</th>
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</thead>
<tbody>
<tr>
<td>CST1</td>
<td>20</td>
<td>Cystatin-BN precursor</td>
</tr>
<tr>
<td>POSTN</td>
<td></td>
<td></td>
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<tr>
<td>SERPIN B4</td>
<td></td>
<td>Serpin peptidase inhibitor</td>
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Discussion
Three differentially expressed genes, cystatin-SN, periostin, and serpin peptidase inhibitor, were common to all three conditions of the unified airway hypothesis. Cystatin-SN is a cysteine proteinase inhibitor found in exocrine glands and is likely representative of the increase in glandular secretions in these diseases. Periostin is involved in extracellular adhesion and migration and may be involved in remodeling seen in airway diseases. An inhibitor of periostin is in clinical trials. Serpin peptidase inhibitor is a regulator of inflammation. The proteins coded by genes common to two of the conditions generally code for proteins involved in immune function, inflammation, and cell adhesion, which are hallmark features seen in the pathogenesis of unified airway diseases.

Conclusion
The unified airway hypothesis has been described on clinical and epidemiological levels to link allergic rhinitis, asthma, and sinusitis. The current study identifies molecular alterations that provide a basis for the common pathogenesis of these airway diseases. Demonstrating overlap between individual genes involved in these conditions will ultimately allow for analyses of functional pathways between these diseases that will further explain the unified airway on a molecular level. Understanding common features of these diseases will allow application of emerging treatments to diseases within the unified airway.

References