Abstract

The clinical manifestations of asthma are thought to result from the effects of environmental factors superimposed on genetic contributions. Environmental factors are often associated with both prevalent and new onset asthma. SurroMed’s proof-of-principle study includes high-throughput technologies that allow the identification, characterization, and enumeration of over 200 unique populations of cells, including subsets of lymphocytes, granulocytes, monocytes, and B cells. A better understanding of the response to corticosteroids will spearhead the development of beneficial drugs with fewer side effects. Biomarker discovery at SurroMed includes a panel of effects of glucocorticosteroids on cell surface and soluble factors

Phenotypic Profiling in Asthma/Allergy Study Design
- SurroMed proof of principle study
- 80 Subjects
  - asthma/allergy (mild asthma), allergy, healthy controls
  - Prednisone vs. placebo
  - oral, 20 mg, 2x/day
  - Two blood samples per subject

Phenotypic Profiling in Asthma/Allergy Methodology
- Cell populations and intensities: MLSC
  - Subsets of T cells, B cells, NK cells, Granulocytes, Eosinophils, Monocytes
  - Markers of activation, adhesion, costimulation, naive/memory cells, HLA class II, etc.
- Soluble factors: ELISA
  - Cytokines, chemokines, Ig, Acute phase proteins, MMPs, TIMPs, RF, soluble cell adhesion molecules, etc.

Microvolume Laser Scanning Cytometry (MLSC)
- Proprietary instrumentation, reagents, consumables and software for quantification of cell populations in small volumes of whole or processed blood = integrated solution

Phenotypic Profiling in Asthma/Allergy Statistics
- 725 unique variables
  - Cell populations: 250
  - Cell surface intensities: 408
  - Soluble factors: 67
- Conservative (step-down Bonferroni) method to protect against false positive errors
- Paired comparisons, pre & post treatment

Significant Measures

<table>
<thead>
<tr>
<th>Drug or Placebo</th>
<th>Prednisone</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 0</td>
<td>188</td>
<td>1</td>
</tr>
<tr>
<td>Day 1</td>
<td>87</td>
<td>0</td>
</tr>
<tr>
<td>Day 2</td>
<td>72</td>
<td>0</td>
</tr>
<tr>
<td>Day 3</td>
<td>63</td>
<td>0</td>
</tr>
</tbody>
</table>

Significant differences post prednisone
- Expected results based on literature
- Adjusted p-value < 0.05
- No differences observed for placebo group

Conclusions
- Robust data collection: 160 samples, 725 variables
- Big drug vs. placebo effect
  - Broad spectrum anti-inflammatory and immunosuppressive agent
- Significant differences observed in all types of bioanalytical measurements
  - Absolute cell counts
  - Relative cell types
  - Cell surface antigen expression
  - Soluble factors
- Some disease group differences
  - Total IgE higher in allergic subjects
  - Eosinophils higher in asthmatic subjects

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