Building handprints of complex diseases – severe asthma as a proof of concept

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Rationale

*U-BIOPRED hypothesis*

Revisiting disease stratification using molecular information
Integrating omics data using an innovative systems biology methodology
Methods

Framework developed during U-BIOPRED and eTRIKS projects

Data hosted in tranSMART

Data fusion: SNF (Wang et al, Nature methods, 2011)

Clustering: Consensus clustering with spectral clustering (Wilkerson et al, Bioinformatics, 2010)

Deviation from ideal stability (Lefaudeux et al, JACI, 2016)

Pathway analysis: g:Profiler (Reimand et al, NAR 2016)

Prediction: mixOmics DIABLO (Singh et al, 2016)
Clusters

<table>
<thead>
<tr>
<th>Cluster</th>
<th>Clinical</th>
<th>Biological</th>
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</thead>
<tbody>
<tr>
<td>2</td>
<td>Low FEV1 and FVC, high macrophages, high ICS and low OCS</td>
<td>Type-1 interferon signaling, cytokine signaling in immune system</td>
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<tr>
<td>3</td>
<td>Female, high FVC, low neutrophils, no OCS</td>
<td>Histone demethylation, dioxygenase activity</td>
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<tr>
<td>5</td>
<td>Younger, early onset, high macrophages, high medication</td>
<td>Interleukin 3, 5 and GM-CSF signaling, platelet activation, response to oxygen compounds</td>
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<tr>
<td>6</td>
<td>Older, high BMI, high OCS</td>
<td>Influenza infection, Selenocysteine synthesis, regulation of macrophages</td>
</tr>
</tbody>
</table>
Predictive modelling

Prediction based on clinical variables alone is not concluent

Prediction based on omics variables:

- Selecting necessary and sufficient predictors of groups
- Across several omics platforms
- Exploring the correlations between features

Example for cluster 2