Are all Th2 inflammations the same?

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PREDOMINANT T_{H2} -LIKE BRONCHOALVEOLAR T-LYMPHOCYTE POPULATION IN ATOPIC ASTHMA

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Humbert et al JACI 1997
Variable Th2 gene expression in asthma

Woodruff et al AJRCCM 2009
ILC2 cells

Endotypes of asthma?

Lloyd and Hessel Nat Rev Immunol 2010
Subtypes of asthma

Discordant Symptoms

EARLY SYMPTOM PREDOMINANT
Early onset, atopic. Normal BMI. High symptom expression.

OBSESE NON-EOSINOPHILIC
Later onset, female preponderance. High symptom expression.

EARLY ONSET ATOPIC ASTHMA
Concordant symptoms. Inflammation & airway dysfunction.

Primary Care Asthma
Monitoring inflammation allows down-titration of corticosteroids.

Concordant Disease
Symptom-based approach to therapy titration may be sufficient.

Secondary Care Asthma

Discordant Inflammation

BENIGN ASTHMA

INFLAMMATION PREDOMINANT
Late onset, greater proportion of males. Few daily symptoms but active eosinophilic inflammation.

Eosinophilic Inflammation

Asthma: from immunopathology to treatment

Robinson DS
J. Allergy Clin. Immunol
2010;126:1081-91
Type 2 directed biologics in asthma

**IgE**

- 0.88
- 0.66

**IL-5**

- Cumulative No. of Asthma Exacerbations
- Placebo
- Mepolizumab 75 mg, intravenously
- Mepolizumab 100 mg, subcutaneously

**IL-13**

- 1.01
- 0.40

Periostin-high (≥50 ng/mL)

**References**

- Hanania et al 2013 AmJRCCM
- Ortega et al NEJM 2014
- Corren et al NEJM 2011
Biomarkers within Type 2 asthma

Type 2 cytokines are released as part of the inflammatory response

IL-13

IL-13

IL-5

IL-13

EOSINOPHILS

Eosinophils migrate into the airway lumen and can be measured in sputum

Eosinophils can be measured in the blood

IL-5 induces eosinophil maturation

Periostin is secreted basolateraly and enters the blood stream

Induction of iNOS, leading to increases in FeNO that can be measured in the breath

FeNO

Periostin

Secretion of periostin

Airway lumen

Bronchial epithelium

Subepi. space

Exacerbations Rates

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Low FeNO at baseline</th>
<th>High FeNO at baseline</th>
<th>Low eosinophils at baseline</th>
<th>High eosinophils at baseline</th>
<th>Low periostin at baseline</th>
<th>High periostin at baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omalizumab</td>
<td>0.60</td>
<td>0.50</td>
<td>0.65</td>
<td>0.70</td>
<td>0.73</td>
<td>0.66</td>
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<tr>
<td>Placebo</td>
<td>0.71</td>
<td>1.07</td>
<td>0.72</td>
<td>1.03</td>
<td>0.72</td>
<td>0.93</td>
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Questions (and opinions!)

• Is all Type 2 asthma the same: are there subgroups with allergic (IgE) disease, eosinophil predominant (IL-5) or IL-13 driven?
  – Possibly, but likely overlap

• Is Type 2 allergic inflammation the same in different sites (lung, nose, skin)
  – Similarities but tissue specific differences (microbiome)

• How much allergic inflammation in non-Type 2?
  – Probably less than we think!
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