4803 Q & A Workshop: Insect Allergy Update
Unique & New Antigens and Difficult Cases
The alpha-gal story and “Longhorn” Ticks

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Disclosures

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Disclosure: Up-to-Date author
What is alpha-gal?

- Carbohydrate synthesized by the glycosylation enzyme alpha-1,3-galactosyltransferase
- Alpha-gal epitope is present on the tissues and cells of all lower mammals
- Humans and apes, however, do not have alpha-gal due to an inactive gene product
### Table 3. Specificity of the IgE Antibodies That Cross-React with Cetuximab.*

<table>
<thead>
<tr>
<th>Type of Reaction and Subject No.</th>
<th>Type of Cetuximab</th>
<th>Galactose-α-1,3-Galactose</th>
<th>Mammalian Allergens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SP2/0‡</td>
<td>CHO‡</td>
<td>Mouse IgG‡</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>international units per milliliter</td>
</tr>
<tr>
<td>Hypersensitivity reaction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anaphylaxis related to cetuximab</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>41.6</td>
<td>0.35</td>
<td>13.8</td>
</tr>
<tr>
<td>2</td>
<td>38.8</td>
<td>0.35</td>
<td>35.2</td>
</tr>
<tr>
<td>3</td>
<td>20.2</td>
<td>0.35</td>
<td>12.6</td>
</tr>
<tr>
<td>4</td>
<td>11.1</td>
<td>0.35</td>
<td>2.9</td>
</tr>
<tr>
<td>5</td>
<td>4.9</td>
<td>0.35</td>
<td>2.0</td>
</tr>
<tr>
<td>6</td>
<td>4.2</td>
<td>0.35</td>
<td>2.7</td>
</tr>
<tr>
<td>Recurrent anaphylaxis unrelated to cetuximab¶</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>131.0</td>
<td>1.89</td>
<td>38.9</td>
</tr>
<tr>
<td>8</td>
<td>69.2</td>
<td>0.35</td>
<td>42.1</td>
</tr>
<tr>
<td>9</td>
<td>55.1</td>
<td>0.35</td>
<td>32.2</td>
</tr>
<tr>
<td>10</td>
<td>43.5</td>
<td>0.35</td>
<td>32.3</td>
</tr>
<tr>
<td>11</td>
<td>81.1</td>
<td>0.35</td>
<td>100.0</td>
</tr>
<tr>
<td>12</td>
<td>13.0</td>
<td>0.35</td>
<td>9.0</td>
</tr>
<tr>
<td>Mean</td>
<td>27.7</td>
<td>NA</td>
<td>25.5</td>
</tr>
<tr>
<td>No hypersensitivity reaction∥</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Chung CH et al. N Engl J Med 2008;358:1109-1117
Delayed anaphylaxis, angioedema, or urticaria after consumption of red meat in patients with IgE antibodies specific for galactose-α-1,3-galactose

Scott P. Commins, MD, PhD, a Shama M. Satinover, MS, a Jacob Hosen, BS, a Jonathan Mozena, MD, b Larry Borish, MD, a Barrett D. Lewis, MD, c Judith A. Woodfolk, MBChB, PhD, a and Thomas A. E. Platts-Mills, MD, PhD a

Charlottesville and Fredericksburg, Va, and Springfield, Mo

24 patients
Virginia & Missouri
Symptoms delayed 3-6 hours after eating mammalian meat
Patients report fewer reactions on red meat avoidance diet
Skin prick test to meats often produces wheal < 4mm
Geographical distribution of cetuximab hypersensitivity reactions

As reported by O’Neil et al, JCO 2007
Distribution of known cases of delayed anaphylaxis to mammalian meat

Dots = single cases
Smaller stars = 5 to 24 cases within a state
Larger stars = states with 25 or more cases

Commins SP, James HR, Kelly LA...Platts-Mills TAE. The relevance of tick bites to the production of IgE ab to the mammalian oligosaccharide galactose-α-1,3-galactose. J Allergy Clin Immunol 2011
Geographical Incidence of Rocky Mountain Spotted Fever

Data from CDC website for 2009; accessed 2/2011
Geographical range of *Amblyomma americanum* population

Data from CDC website; accessed 10/2010
Geographical range of *Amblyomma americanum* population

Data from CDC website; accessed 9/2012
Bites from the larvae of *Amblyomma* or *Dermacentor* ticks and IgE ab to alpha-Gal.

<table>
<thead>
<tr>
<th>Test</th>
<th>10/26/06</th>
<th>5/21/07</th>
<th>10/9/07</th>
<th>11/6/07*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cetuximab (alphaGal)</td>
<td>0.49</td>
<td>16.9</td>
<td>48.3</td>
<td>130</td>
</tr>
<tr>
<td>Total IgE</td>
<td>127</td>
<td>199</td>
<td>350</td>
<td>532</td>
</tr>
</tbody>
</table>

- Multiple bites by seed ticks are not uncommon in the Southeast.

*Titers: Beef 19.2 Pork 10.1, Cat 17.5, Dog 19.8, IU/ml. Chicken, Turkey, Roach, Dust Mite and Ragweed all <0.35 IU/ml.

Time course of IgE antibodies to alpha-gal and total IgE following episodes of multiple tick bites (red arrows)
Time course of IgE antibodies to alpha-gal and total IgE following episodes of multiple tick bites (red arrows)
Time course of IgE antibodies to alpha-gal and total IgE following episodes of multiple tick bites (red arrows)
Prevalence of IgE antibodies to alpha-gal among 125 patients with or without histories of tick bites

Percentage of Patients in Each Category of Tick Bite Report

Titer of IgE to Alpha-Gal (IU/ml)

- No Bites (n=23)
- Bites with short-term reactions (n=71)
- Bites with long-term reactions (n=31)
Total IgE versus IgE to Alpha-Gal

- **R** = 0.78
- **P** < 0.001

Report tick or chigger bite(s)

No history obtained for tick bite(s)

Specifically deny tick bite(s)
References

The relevance of tick bites to the production of IgE antibodies to the mammalian oligosaccharide galactose-α-1,3-galactose. J Allergy Clin Immunol, 2011;127:1286-93.


Relationship between red meat allergy and sensitization to gelatin and galactose-α-1,3-galactose. J Allergy Clin Immunol. 2012; 129:1334-42