Food Allergies and Safety Considerations for Biotechnology

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Goals

- Define food allergy

- Discuss prevalence, pathogenesis and key difficulties in assessing allergenicity

- Allergenicity considerations for foods derived from biotechnology
  - Novel food proteins – new allergenic risk?
  - Modification of known allergens in food
Adverse reactions to food

- Immunological (Hypersensitivities)
  - IgE Mediated
  - Food Allergy
  - Non-IgE Mediated
    - Celiac Disease

- Non-Immunological (Intolerances)
  - Toxicological Example: Scombroid Poisoning
  - Metabolic Example: Lactose Intolerance

- Microbial
  - Infections Example: Salmonellosis
  - Toxins Example: Staphylococcal enterotoxins

Peanuts, egg, milk, soy, etc.
Food allergy

- “Adverse reaction to food mediated by IgE antibody”
- Typical symptoms - immediate and life-threatening!
- Over 150 foods – most commonly consumed in diet
  - **US**: peanut, soy, egg, milk, wheat, tree nuts, fish, shellfish
  - **Europe**: ... sesame, mustard, celery
  - **Japan**: ... buckwheat
- Genetic AND environmental
- No effective treatment – Labeling/ avoidance is key!
- Lifetime risk for many
### Food allergy prevalence

- 4% of total population: Infants (6-8%) >> adults (2%)
- **Anaphylaxis**: 30,000 cases, 2000 hospitalizations, 150 deaths/yr

<table>
<thead>
<tr>
<th>Food</th>
<th>Children</th>
<th>Adults</th>
<th>Outgrown?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk</td>
<td>2.5%</td>
<td>0.3%</td>
<td>80%</td>
</tr>
<tr>
<td>Egg</td>
<td>1.3%</td>
<td>0.2%</td>
<td>60-70%</td>
</tr>
<tr>
<td>Peanut</td>
<td>0.8%</td>
<td>0.6%</td>
<td>20%</td>
</tr>
<tr>
<td>Tree nut</td>
<td>0.2%</td>
<td>0.5%</td>
<td>No</td>
</tr>
<tr>
<td>Fish</td>
<td>0.1%</td>
<td>0.4%</td>
<td>No</td>
</tr>
<tr>
<td>Shellfish</td>
<td>0.1%</td>
<td>2.0%</td>
<td>No</td>
</tr>
<tr>
<td>Other (Fruit)</td>
<td>6%</td>
<td>3.7%</td>
<td>-</td>
</tr>
</tbody>
</table>

Sampson, JACI, 2004
ALLERGY

Sensitization

B cell  T cell

IgE Antibody

Food protein/ pollen

Challenge and Elicitation

Anaphylaxis

- Skin - itchiness, flushing, hives, swelling, eczema
- GI - nausea, vomiting, abdominal pain, diarrhea
- Respiratory - runny nose, wheezing, throat closing/swelling
- Vascular - dizziness, faintness, arrhythmias, shock

Mast cell/ Basophil
Difficulties in allergenicity assessment

- Allergenic food << proteins <<<< epitopes
  - Not all allergenic proteins nor epitopes identified
  - Concentrations vary between foods/ products
  - Heterogeneous sensitized population
- Sensitization (i.e. IgE) and elicitation can be mutually exclusive
- Reactivity is amplified – severity is unpredictable
- No known allergen threshold level or minimum amount to trigger reactivity
- No validated animal models
Biotechnology and food allergy

- Transgenic modification of crops and/or introduction of uncommon proteins derived through biotechnology
  - **Novel food protein** exposures
    - Transferring an existing allergen or cross-reactive protein from one crop to another
    - Creating *de novo* food allergens
  - Modification of **known food allergens**
    - Altering or quantitatively increasing an endogenous (existing) allergen in the food crop
    - Increase exposure to allergenic protein previously consumed at low concentrations
    - Transgenic manipulation to make “allergen-free” foods
**Novel food proteins**

- Does the transgenic protein have allergenic characteristics or bind IgE? (it is assumed they will then elicit reactions)

- 2003 Codex Alimentarius approach:
  - Source of protein
  - Amino acid sequence homology
  - Pepsin resistance
  - Specific serum screening

- Crossreactivity(?): plant-derived proteins/ pollen allergy
  - Identification of allergenic protein families
  - Targeted serum studies
  - Other protein modifications/ glycosylation?
Modification of known food allergens

- Will it ↑ or ↓ reactions in sensitized individuals? ↓ reactions easier to assess; absence of reactions difficult to confirm

- Serum studies provide limited data; human food challenge data provides most confirmatory evidence

- Assessment considerations:
  - Type of food protein or crop
  - What are the relative concentrations of existing allergenic proteins in food? How modified?
    - Depends on good analytical methods – limitations?
  - Use in more sensitive populations (i.e. infants)?
  - What is the final exposure to protein concentrations per meal? Evidence of prior human exposure? How does exposure compare to food challenge “thresholds”

- Animal dose-response models?