Emerging Allergens

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Allergens

- Proteins
- Small mol mass
- Resistant against enzymatic digestion
- Abundancy

These features apply for many proteins - only a minority of those are allergens!!
(Food) Allergens belong to a limited number of protein families – sharing structural determinants and displaying sequence similarity - the molecular basis of cross reactivity!

1092 Allergens (IUUIS Allergen nomenclature database: www.allergen.org)

(Allergens in ALLFAM Database (http://www.meduniwien.ac.at/allergens/allfam/): 995 Allergens from 186 Protein families (out of 12,273 Pfam protein families) – 2% of all known domains)

Protein families of animal food allergens

FIG 1. Distribution of animal food allergens into Pfam families. Allergens were from either version 2.1 of the InformAll (www.foodallergens.ifr.ac.uk; dark bars) or version 5.0 of FARRP (www.allergenonline.com; gray bars) databases. Pfam family names are given apart from very low density lipoprotein (VLDL), arginine kinase, and ovomucin, which represent proteins with multiple different domains. BPTI, Bovine pancreatic trypsin inhibitor.
Protein families of plant food allergens

67% of plant food allergens

Jenkins et al. J Allergy Clin Immunol 2005
Europrevall
The Prevalence, Cost and Basis of Food Allergy across Europe

• **Allergen library: 53 Allergens**
  – Preparation of natural and recombinant allergens
  – Physicochemical characterisation of natural and recombinant allergens
  – Catalogue of harmonized quality criteria of purified food allergens established
  – Range of analytical methods applied

_Sancho et al. Clin Exp Allergy 2010_
## Europrevall
### Physico-chemical Characterization of Allergens

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Methods</th>
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<tr>
<td>Sequence verification</td>
<td>MALDI-TOF, Q-TOF MS, N-terminal sequencing</td>
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<td>Isoforms</td>
<td>2D-PAGE, LC-MS</td>
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<td>Folding</td>
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<td>Aggregation</td>
<td>Size exclusion chromatography (SEC)</td>
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<td>Purity (proteolysis)</td>
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<td>Biological activity</td>
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<td>IgE reactivity</td>
<td>ELISA, RAST, CAP, Chip; Immunoblotting (IB), inhibition assay; (human reference sera), Basophil activation test;</td>
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(purified nat allergen vs extract; Recombinant vs natural allergen)
Dietary proteins from GM-plants

• Soy
• Corn
• Oilseed rape
• Cotton?
Food Allergen Panels
(for improved diagnosis)
Soy Allergens

- Soy (*Glycine max*): 8 allergens identified and listed in IUIS allergen database.
- Gly m 1 – Hydrophobic protein from soy (7 kDa)
- Gly m 2 – Defensin (8 kDa)
- Gly m 3 – Profilin (14 kDa)
- Gly m 4 – PR 10 (Bet v 1 homologue) (16 kDa)*
- Gly m 5 – Vicillin, beta-conglycinin, (7S)**
- Gly m 6 – Glycinin, (11S)
- Gly m 7 – Seed biotinylated protein (76 kDa)
- Gly m 8 – 2S Albumin***

Soy Allergy

20 Patients with anaphylaxis due to soy ingestion (Salzburg, AT)*

Sera tested by: CAP, CHIP, ELISA

**CAP Soy extract**: 17/20 negative

**CHIP**: 14/20 positive to soy allergens

**ELISA**: 14/20 positive

* Berneder et al. IAA 2013
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Allergen recognition pattern

- 19/20 Patients sensitized to Bet v 1
  Reactivity to Bet v 1 Homologue, Gly m 4; BP- associated food allergy
- 1/20 sensitized to 7S and 11S globulin (cross reactive to peanut allergens)
Corn allergens

IUUIS Database:
Corn (Zea mays)
• Zea m 1 – Beta expansin (25 – 35 kDa)
• Zea m 12 – Profilin (14 kDa)
• Zea m 14 – nonspecific lipid transfer protein (8 kDa)*
• Zea m 25 – Thioredoxin

Within Europe food allergic reactions to corn are restricted to certain geographic areas - Italy.

*Pastorello et al. 2000
Oilseed rape

• Oilseed rape (*Brassica napus*)
• *Bra n 1 – 2S Albumin (15 kDa)*

Maybe of future interest if protein isolates are used in food production or as a food additive!!

*Puumalainen et al. 2006*
Conclusions

• A range of analytical and immunological methods are needed to assess allergenicity of (food) proteins. (reassessment of current methodologies)

• A quantitative outcome is preferred.

• For prevalence of food allergies geographic differences and different dietary habits have to be taken into account!

• Food processing can impact on allergenicity.
Conclusions cont.

- Reevaluation of allergen panels may give further information on clinical relevance.

- Existing knowledge is based on known allergens.