Allergen Data Collection: **Celery** (Apium graveolens)

.....

Authors in alphabetical order [contact information]

Barbara BALLMER-WEBER (Zurich, Switzerland) Matthias BESLER (Hamburg, Germany) Karin HOFFMANN-SOMMERGRUBER (Vienna, Austria) Stefan VIETHS (Langen, Germany) **Brunello WÜTHRICH (Zurich, Switzerland)**

Abstract

IgE mediated reactions to celery are common in food allergic adults in Europe. Sensitization to celery is frequently associated with birch and/or mugwort pollinosis, hence the term "birch- mugwort- celerysyndrome" has been established. There is evidence that birch pollen and celery allergy are highly related in Central Europe, while celery allergy is most frequently related to mugwort pollen in Southern Europe. Moreover, allergies to carrot and spices, predominantly of the umbelliferous family, are highly associated to celery allergy. Celery can induce allergic reactions of immediate type from oral contact urticaria to anaphylactic shock. About 30% of patients with oral allergy syndrome are allergic to celery. Diagnostic tests like skin tests with raw celery and active allergen extracts have high positive predictive values, while the negative predictive values are low. Roots, also called tuber or celeriac, and sticks from the celery plant are used in nutrition and diagnostic procedures. Usually the frequency of sensitization to celery tuber is higher than to celery stick in celery allergic subjects. Celery tuber and stick are consumed as a raw or cooked vegetable and as a spice which is a common hidden allergen in various processed foods. Despite its high allergenic potency and at least partial thermostability celery and celery products are currently not included in mandatory labelling regulations for food allergens. At least three groups of cross- reactive allergens have been identified in celery: 1. Bet v 1 homologous 16

kDa allergen (Api g 1) with IgE cross- reactivity to birch pollen, fruits, and vegetables (eg. apple and carrot), 2. The actin- binding panallergen profilin (Api g 4) with appr. 15 kDa, and 3. Allergens in the range of 30-70 kDa, including the recently described 55/58 kDa isoallergens (Api g 5) cross-reactive to birch pollen and mugwort pollen.

The present data collection reviews detailed information on the prevalence and symptoms of celery allergy as well as cross- reactivities, and molecular biological and allergenic properties of the major celery allergens in tabular form.

(Internet Symposium on Food Allergens 2000, 2(3):145-167)

| <u>Contents</u> | page |
|--|------|
| <u>1 Prevalence of Celery Allergy</u> | 147 |
| 2 Symptoms of Celery Allergy | 149 |
| <u>3 Diagnostic Features of Celery Allergy</u> | 150 |
| <u>4 Therapy of Celery Allergy</u> | 152 |
| 5 Composition of Celery | 153 |
| <u>6 Allergens of Celery</u> | 154 |
| 6.1 Sensitization to Celery Allergens | 154 |
| 6.2 Properties of Bet-v-1-homologous Protein (Api g 1) | 155 |
| 6.3 Properties of Chlorophyll a/b binding Protein | 157 |
| 6.4 Properties of Celery Profilin (Api g 4) | 158 |
| 6.5 Properties of 55/58 kDa Protein (Api g 5) | 159 |
| 7 Isolation & Preparation | 160 |
| 8 Cross-Reactivities | 160 |
| 9 Stability of Celery Allergens | 163 |
| <u>10 Allergen Sources</u> | 164 |
| <u>11 Food Labelling</u> | 164 |
| <u>12 References</u> | 164 |

Disclaimer

The reference lists of the Allergen Data Collections are based mainly on searches of Medline and FSTA (Food Science & Technology Abstracts) databases up to the related dates of publication. The scientific rigor of the studies listed is variable and not subject of critique or evaluation by the authors or the editor of the Allergen Data Collections. The reader should be aware of considerable problems in comparing data from different studies (eg. patient cohorts, diagnostic performances, possible flaws in allergen preparations and methodologies for allergen characterization) and is encouraged to review the original publications.

The information provided by the Internet Symposium on Food Allergens is for educational, communication and information purposes only and is not intended to replace or constitute medical advice or treatments. Neither the authors nor the editorial board of the Internet Symposium on Food Allergens is responsible for use which might be made of the information.



<u>1 Prevalence of Celery Allergy</u>

Prevalence data are based on different diagnostic procedures. While the prevalence of sensitization (sensitivity) can be estimated by SPT, RAST, and immunoblot, a clinical relevant sensitization (allergy) is evaluated by convincing history (anamnesis) or food challenge tests (ideally by DBPCFC).

1.1 Subjects with Atopic or Other Diseases

| Country / Subjects | Allergy / Sensitivity | References |
|--|--|-----------------------------|
| <i>France</i> 80 cases of food- related anaphylaxis (study period 1993-97) | period celery and carrot 7.5% (reported to CICBAA databank) European Commission 1998 | |
| <i>France, Lyon</i> a) 61 patients with mugwort pollen sensitivity b) from which 26 with birch pollen sensitivity | a) celery 59% b) celery 88% (RAST) | Vallier et al. 1988 |
| <i>France, Paris</i> a) 24 patients with latex and pollen allergy b) 20 patients with latex allergy (no pollen allergy) c) 25 patients with pollen allergy (no latex allergy) | clinical symptoms SPT a) celery in 0% and 33% b) celery in 0% and 5% c) celery in 20% and 72% | <u>Levy et al. 2000</u> |
| <i>France, Pierre Benite</i> a) 580 patients with adverse reactions to food b) 60 cases of anaphylaxis (study period 1984-92) | a) celery 30% (RAST) b) celery 30% | Andre et al. 1994 |
| Germany, Berlin 167 pollen and food sensitive patients | celery 70% and 14% (SPT and case history) | Jankiewicz et al. 1996 |
| <i>Italy, Florence</i> 54 episodes of food-dependent anaphylaxis in 44 children (age of 1 month to 16 years) (from 1994- 1996) | celery 1.9% | Novembre et al. 1998 |
| <i>Italy, Genoa</i> 132 pollen and food sensitive patients | celery 0.7% (self-reported) | Troise et al. 1992 |
| <i>Italy, Milan</i> 262 fruit and/or vegetable allergic patients | celery 5-10% (clinical history) | Ortolani et al. 1988 |
| <i>Italy, Milan</i> 100 fruit and/or vegetable allergic patients | celery 5% (clinical history) | Ortolani et al. 1989 |
| <i>Italy, Milan</i> 196 adults with birch pollen allergy and oral allergy syndrome | celery 7% (clinical history) | <u>Asero 1997</u> |
| Netherlands 131 cases of food- induced anaphylaxis (from 1993-1997) | celery 6.1% (survey, reported to the TNO Nutrition and Food Research Institute) | European Commission 1998 |
| Spain, Madrid 29 plant-derived food allergic patients | celery 3.4% (SPT) | Diez-Gomez et al. 1999 |
| Sweden 55 cases of food- induced anaphylaxis (from 1994- 1996) | celery 3.6% (Hospital Reports) | European Commission 1998 |
| Sweden, Halmstad / Malmö | a) celery 2% | |
| a) 380 birch pollen allergic patientsb) 103 patients without birch pollen allergy | b) celery 0% (questionnaire) | <u>Eriksson et al. 1982</u> |
| Switzerland, Bern 22 patients with severe food-induced anaphylaxis (study period 1994-96) | celery 50% | Rohrer et al. 1998 |

| Switzerland, Vaudois 111 patients with pollen- associated food allergy | celery 57% (RAST) | Bircher et al. 1994 |
|--|--|----------------------------|
| Switzerland, Zurich 402 food allergic adults (study period 1978-87) | celery 43% (clinical history, diagnostic tests) | Wüthrich 1993 |
| Switzerland, Zurich 383 food allergic patients (study period 1990-94) | celery 36% celery tuber 20% (spice) (clinical history, diagnostic tests) | Etesamifar & Wüthrich 1998 |
| <i>UK, London</i> 100 patients with food intolerance | celery 1% (repeated challenge) | Lessof et al. 1980 |
| USA, Boston, MA 279 adults with exercise- induced anaphylaxis (study period 1980-98) | celery 7% (reported trigger) | Shadick et al. 1999 |

<u>1.2 Prevalence of Associated Allergies</u>

| Country / Subjects | Sensitivity / Allergy to | | | References |
|--|---|-----------------------|------|---------------------------|
| Austria, Vienna 20 patients with mugwort- birch- celery- spice syndrome | paprika 73% pepper 95% (immunoblot) | | | Leitner et al. 1998a |
| <i>Italy, Milan</i> 196 adults with birch pollen allergy and oral allergy syndrome | celery and carrot 83% (n=103 celery and fennel 73% (n=63) (concordance of allergy, clinic | <u>Asero 1997</u> | | |
| Switzerland, Zurich 31 celery allergic patients (study period 1978-82, follow-up 1983) | mugwort pollen 87% carrots 52% caraway 26% parsley 16% fennel 13% green pepper 10% aniseed 3% (clinically relevant allergy) | Wüthrich & Hofer 1984 | | |
| Switzerland, Zurich 70 patients with celery and pollen allergy (birch and/or mugwort) | Spices from Apiaceae family aniseed, fennel, coriander, an Spices from unrelated familie pepper, ginger, nutmeg, cinna positive in 3 of 11 patients (scratch test) | Stäger et al. 1991 | | |
| | | SPT | RAST | |
| | birch pollen | 91% | 91% | |
| | alder pollen | 86% | | |
| <i>Switzerland, Zurich</i> 22 patients with positive DBPCFC to celery | hazel pollen | 82% | | |
| | grass / rye pollen | 55% | 67% | Ballmer-Weber et al. 2000 |
| | ash pollen | 36% | | |
| | mugwort pollen | 36% | 73% | |
| | carrot | | 77% | |
| | | | | |

| | RAST | a) | b) | c) | d) | e) | |
|---|---|----|-----------|------------|------------|------------|----------------------|
| Switzerland, Zurich | celery stick | 0% | 45% | 0% | 17% | 70% | |
| | celery tuber | 0% | 100% | 0% | 50% | 100% | |
| 41 patients with sensitivity to a) 7 birch pollen sensitive | celery mix | 0% | 100% | 0% | 100% | 100% | |
| a) 7 offer poilen sensitive b) 11 birch pollen and celery c) 7 mugwort pollen d) 6 mugwort pollen and celery e) 10 birch, mugwort pollen and celery | Umbelliferae | 0% | 9-18 % | 14- 28% | 33- 50% | 30- 70% | Wüthrich et al. 1992 |
| | Labiatae | 0% | 9% | 0% | 0% | 20- 30% | |
| | <i>Umbelliferae:</i> aniseed, dill, fennel, lovage <i>Labiatae:</i> basil, majoram, pot majoram, thyme | | | | | | |

<u>2 Symptoms of Celery Allergy</u>

| Symptoms & Case Reports | References |
|--|--|
| systemic reactions | |
| anaphylaxis (1, 4, 5, 6, 7, 9, 10), exercise-induced anaphylaxis (3, 8) | |
| symptoms on skin and mucous membranes angioedema (2, 4, 6, 10, 16, 17), conjunctivitis (17), edema (15), flush (17), itch of ears (17), palmoplantar itch (17), pruritus (10), generalized pruritus (17), urticaria (2, 4, 6, 10, 15, 16, 17), contact urticaria syndrome (4) | (1) Forsbeck & Ros 1979 (2) Kauppinen et al. 1980 (3) Kidd et al. 1983 (4) Kremser & Lindemayr 1983 (5) Dechamp et al. 1984 |
| <u>gastrointestinal symptoms</u> abdominal cramps (17), diarrhea (16), emesis (17), flatulence (17) itching in throat (16, 17), heartburn (17), swelling of lips (16), nausea (16, 17), vomiting (16), oral allergy syndrome* (12, 14, 16, 17) | (6) Pauli et al. 1985 (7) Rose & Altman 1985 (8) Silverstein et al. 1986 (9) Stricker et al. 1986 (10) Pauli et al. 1988 (11) Ortolani et al. 1988 (12) Ortolani et al. 1989 |
| respiratory symptoms asthma (10, 16), cough (17), dyspnoe (17), laryngeal edema (11, 13, 14), rhinitis (17), rhinoconjunctivitis (10, 17), general / not specified (6) | (13) Hoerler & Ukiwe 1992 (14) Jordan-Wagner et al. 1993 (15) Bonnin et al. 1995 (16) Jankiewicz et al. 1996, 1998 (17) Ballmar Wahar et al. 2000 |
| * symptoms, which could be involved in oral allergy syndrome: local symptoms as intra-oral and lip-irritation, angioedema and systemic symptoms as rhino-conjunctivitis, urticaria-angioedema, asthma, and anaphylaxis (11) | (17) Danmer-weber et al. 2000 |

Percentage of Reactions

| Semantana / D f | (1) | | | | | |
|---|------------------|---------------------------------|----------------------|----------------------|-----------------------|-----------------------|
| Symptoms / Ref. | (1) | (2) | (3) | (4) | (5) | (6) |
| Anaphylaxis | 19% | 15% | 2.9% | 20% | | |
| shock tragments | 10% | | 2.9% | | | |
| Lutaneous | | | | | | |
| Angio-oedema | 29% | <u> </u> | 31% | <u> </u> | | 14% |
| Contact urticaria | | | 17% | | | |
| Jrticaria | 10% | | 5.7% | | 17% | |
| Jrticaria / Angio-oedema | | 85% | | 90% | | |
| Jrticaria / flush / pruritus | | | | | | 23% |
| Oral allergy syndrome | | | | | 87% | 55% |
| Gastrointestinal | | | | | 20% | 14% |
| Diarrhea | 6.5% | | 2.9% | | | |
| Respiratory | | 40% | | 35% | | |
| Asthma | 6.5% | | 8.6% | | 10% | |
| Dyspnoe | 10% | | 20% | | | |
| Dyspnoe / cough | | | | | | 14% |
| Rhinitis / conjunctivitis | 10% | | 8.6% | | | 14% |
| No. of patients | 31 | 20 | 35 | 20 | 30 | 22 |
| (1) celery allergic patients (clinical history) (2) patients with celery allergy and concomitant pollen allergy (mugwort, birch) (clinical history) (3) celery allergic patients (clinical history) (4) patients (14-49 years of age) with celery allergy (clinical history) (5) adults with celery and pollen allergy (clinical history) (6) after DBPCFC in celery allergic patients (13-55 years of age) | | | | | | |
| Onset of Symptoms Symptoms occurred after ingestion of celery within 30 min to 1 h in 46%, within 2-3 h in 8%, and >3 h in 46% of 13 celery allergic patients (1) Symptoms of oral itching and eyelid angioedema in 2 patients within 4 and 6 min after open food challenge with 15 g of celery (2) | | | | | | |
| Lineshold for Elicitation Quantities of 700 mg celery in each, 13.3 g in 5%, and 28.5 g DBPCFC (1) | duced a g in 29% | nptom llergic s o of 21 (| symptom selery al | ns in 48 lergic p | %, 1.9 g atients v | ; and 5.6 vith pos |

<u>3 Diagnostic Features of Celery Allergy</u>

| Parameters / Subjects | Outcome | | References | |
|---|---------------|-----------------|------------|--|
| | Allergy to c | elery according | | |
| | years | (1) | (2) | |
| Age at Manifestation 31 celery allergic patients (1) 35 celery allergic patients (2) | <10 | 0% | 0% | |
| | 11-20 | 19% | 23% | (1) W ² (1, $1, 0, 11, 0, 1004$ |
| | 21-30 | 29% | 49% | (1) <u>Wuthrich & Holer 1984</u> (2) Wüthrich & Dietschi 1985 |
| | 31-40 | 32% | 23% | (2) wumen & Dictsem 1965 |
| | 41-50 | 10% | 6% | |
| | >50 | 10% | 0% | |
| | (clinical his | tory) | | |

| Internet Symposium on Food Allergens 2(3):2000 http://www.foo | | | | | | o://www.food-allergens.de | |
|--|---|--|--|--|--|---|---------------------------|
| <i>Gender of Patients</i> 31 celery allergic patients (1) 35 celery allergic patients (2) | 86% and 87% female, respectively $(1, 2)$ | | | | | (1) <u>Wüthrich & Hofer 1984</u> (2) <u>Wüthrich & Dietschi 1985</u> | |
| RAST, Scratch Test 68 pollen allergic patients | 72% concord chamber test | lance of to cel | of RAS ery | ST and | l scratch | 1 | Halmepuro et al. 1984 |
| <i>IgE</i> birch pollen allergic patients with atopic dermatitis: a) responding (n=17) with worsening of atopic dermatitis within 48 h (no immediate symptoms observed) and b) non-responding (n=20) to DBPCFC with birch pollen related foods (carrot, celery, hazelnut, apple) | Celery specific serum IgE (RAST): a) 8.4 kU/L b) 3.1 kU/L (mean values) | | | | | Reekers et al. 1999 | |
| SPT, IgE and Clinical Relevance 31 celery allergic patients | Skin testing bulb was reli sensitive | (scrato able, l | ch or p RAST | rick) was n | with free ot suffic | sh celery eiently | Wüthrich & Hofer 1984 |
| SPT, IgE and Clinical Relevance 35 celery allergic patients | Positivity of SPT with na scratch test v intracutaneo 64%, RAST with o | Positivity of diagnostic tests: SPT with native celery- root 89%, scratch test with celery- salt 71%, intracutaneous test with commercial extract 64%, RAST with celery- sticks 66% | | | | | Wüthrich & Dietschi 1985 |
| a) RAST and Clinical Relevance b) SPT and Clinical Relevance 4 patients with clinical history of celery allergy | a) RAST (specific IgE > 0.7 kU/L): positive results in 75% b) SPT with fresh food: positive results in 100% | | | | | <u>Ortolani et al. 1989</u> | |
| | 69% of patients were positive in DBPCFC, 4 of 8 non-responders reacted in open challenge, and 2 placebo-responders | | | | | | |
| SPT, IgE, and DBPCFC 32 patients with history of celery allergy (13-55 years of age, mean 32 years) | sensitivity specificity PPV NPV | a) 48% 88% 96% 19% | b) 86% 13% 87% 11% | c) 96% 25% 90% 43% | PPT* 96% 0% 88% 0% | RAST 73% 38% 90% 17% | Ballmer-Weber et al. 2000 |
| | a) + b) SPT with commercial extracts c) SPT with self-prepared extract * prick-to-prick test with raw celery tuber | | | | | | |
| <i>IgE and DBPCFC (positive vs.</i> <i>negative)</i> patients with history of celery allergy a) 22 with positive DBPCFC b) 4 with negative DBPCFC and positive open challenge c) 4 with negative DBPCFC and negative open challenge | No obvious differences in sensitization pattern between a) and b) in immunoblot and EAST; only 1 patient of c) had celery specific IgE (Api g 4 and glycoproteins) | | | | | Lüttkopf et al. 2000 | |
| SPT and IgE celery allergic patients | a) Positivity in EAST to native celery: 50% of SPT positive patients (n=34) b) Positivity in EAST to heated celery: 18% of SPT positive patients (n=11) 26% of SPT negative patients (n=35) | | | | | | Jankiewicz et al. 1996 |
| SPT, Extracts 12 (14) patients with OAS after eating celery | Positive reac 58% to fresh 86% to com | tions i celery nercia | n SPT y extra l extra | : cts cts | | | <u>Asero 1997</u> |

| SPT, RAST, Extracts, rApi g 1 a) 24 patients with celery and birch pollen allergy from Davos, Switzerland b) 12 patients with celery allergy and mugwort pollen sensitivity from Montpellier, France | Positive reactions in skin prick and SPT, respectively: a) 100% to fresh celery 100% to commercial extra 100% to recombinant Api b) 92% to fresh celery 25% to commercial extrac 17% to recombinant Api g Positive reactions in RAST:: a) 67% to commercial extractions b) 45% to commercial extractions | <u>Hoffmann-Sommergruber et</u> <u>al. 1999a</u> | | |
|--|---|---|-----------|---------------------------|
| Immunoblot and Clinical Relevance | Sensitivity in SDS-PAGE imm | | | |
| a) 23 patients with celery allergy | 15 kDa allergen | a) 7/1% | D) 73% | Bauer et al. 1996 |
| b) 15 patients with celery sensitivity (RAST) without clinical relevance | 46-60 kD allergens | 30% | 60% | |
| Mugwort Sensitization, Severity of Symptoms 22 patients with positive DBPCFC to celery | Positivity to mugwort pollen (SPT): a) 60% of patients with systemic reactions to celery b) 16% of patients with pure oral allergy syndrome | | | Ballmer-Weber et al. 2000 |

<u>4 Therapy of Celery Allergy</u>

| Treatment * | Outcome | References |
|---|---|-----------------------|
| <i>Oral Desensitization</i> with commercial celery and parsley extracts: 1 adult with celery- carrot- mugwort- spice- syndrome, symptoms of urticaria, dyspnoe, vomiting, and collaps after ingestion of raw fruits and vegetables (especially celery) and spices | Daily administration of diluted mixed extract of increasing doses, maintenance dose administered 3 times per week, length of therapy approximately 3 years, after therapy parsley and celery were tolerated as spices, side effects of earlobe erythema and occasional diarrhea occurred | Wüthrich & Hofer 1986 |
| Subcutaneous Desensitization with 2 commercial extracts (5 grasses, cereals, mugwort and ribwort / birch and alder): 1 adult with suspected celery allergy and symptoms of allergic rhinitis, generalized urticaria, angioedema, and pruritus | After 3 years of subcutaneous desensitization no symptoms of pollinosis or food allergy occurred | Wüthrich & Hofer 1986 |

* Studies may be experimental, unproved, or controversial. Please notice the <u>disclaimer</u> !

<u>5 Composition of Celery Tuber</u>

<u>5.1 Distribution of Nutrients</u> (raw vegetable)

For other celery products see: USDA Nutrient Database

| Nutrients: Content per 100 g | | |
|------------------------------|-------------------------|---------------------|
| Energy 78 kJ (18 kcal) | Selenium 1-10 µg | Thr 45 mg |
| Water 88.6 g | | Trp 12 mg |
| Protein 1.6 g | Vitamins | Tyr 25 mg |
| Lipid 0.3 g | Carotin 15 µg | Val 75 mg |
| Carbohydrate 2.3 g | Vitamin K 100 µg | |
| Fiber 4.2 g | Vitamin B1 35 µg | Carbohydrates |
| Minerals 0.9 g | Vitamin B2 70 µg | Fructose 100 mg |
| | Nicotinamide 900 µg | Sucrose 1710 mg |
| Minerals | Pantothenic acid 510 µg | Starch 440 mg |
| Sodium 75 mg | Vitamin B6 200 µg | |
| Potassium 320 mg | Folic acid 7 µg | Lipids |
| Magnesium 9 mg | Vitamin C 8 mg | Palmitic acid 65 mg |
| Calcium 70 mg | | Stearic acid 4 mg |
| Manganese 150 µg | Amino Acids | Oleic acid 13 mg |
| Iron 530 µg | Arg 45 mg | Linolic acid 155 mg |
| Copper 20 µg | His 25 mg | Linoleic acid 17 mg |
| Zinc 310 µg | Ile 50 mg | |
| Phosphorus 80 mg | Leu 75 mg | Others |
| Chloride 150 mg | Lys 75 mg | Oxalic acid 6800 µg |
| Fluoride 14 µg | Met 18 mg | Purines 30 mg |
| Iodine 3 µg | Phe 45 mg | |

Reference: Deutsche Forschungsanstalt für Lebensmittelchemie, Garching bei München (ed), **Der kleine "Souci-Fachmann-Kraut" Lebensmitteltabelle für die Praxis**, WVG, Stuttgart 1991

5.2 Proteinfraction

| Proteins / Glycoproteins | Amount |
|--------------------------|---|
| Profilin (Api g 4) | 33 μg / 100 g raw celery tuber (yield after 4 step purification) (1) |

References: (1) Vallier et al. 1992

<u>6 Allergens of Celery</u>

| Proteins / Glycoproteins | Allergen Nomenclature | References |
|--|------------------------------|---|
| Bet v 1 - homologous Protein [16 kDa] | Api g 1.0101 Api g 1.0201 | Breiteneder et al. 1995, Ebner et al. 1995, Vieths et al. 1995, Hoffmann-Sommergruber et al. 2000 |
| Chlorophyll a/b Binding Protein ** | Api g 3* | Scheiner et al. 1997 |
| <u>Celery Profilin [</u> 15 kDa] | Api g 4 | Vallier et al. 1992, van Ree et al. 1992, Ebner et al. 1995, Vieths et al. 1995, Scheurer et al. 2000 |
| 55/58 kDa Allergen | Api g 5 | Ganglberger et al. 2000 |
| Allergens: >30 kDa (CCD, cross- reactive carbohydrate determinants) | | Vieths et al. 1994, Jankiewicz et al. 1998, Fötisch et al. 1999, Lüttkopf et al. 2000 |
| 2 Allergens: appr. 15 kDa | | Vallier et al. 1988 |
| Allergens: 15, 25, 36, and 60 kDa | | Jordan-Wagner et al. 1993 |
| Allergens: 15, 46-60 kDa | | Bauer et al. 1996 |
| 60 kDa Allergen | | Heiss et al. 1996, Grote et al. 1998 |

* proposed name not listed in WHO/IUIS Allergen Nomenclature (<u>Larsen & Lowenstein 2000</u>) ** probably a minor allergen, clinical relevance unknown

<u>6.1 Sensitization to Celery Allergens</u>

| Country / Subjects | Sensitization | | | References | |
|---|--|-------|---------------------|--------------------------|----------------------------------|
| <i>Austria, Vienna</i> 17 birch pollen allergic patients with celery sensitivity | 15 kDa allergen (Api g 1) in 76%13-14 kDa allergen (Api g 4) in 24 %(SDS-PAGE immunoblot) | | | <u>Ebner et al. 1995</u> | |
| <i>France, Lyon</i> 36 patients with celery sensitivity | 15 kDa allergen (probably Api g 4) in 58%high Mr bands in 63%any allergen band in 92%(SDS-PAGE immunoblot) | | Vallier et al. 1988 | | |
| | Allergens | imm | unoblot | SPT | |
| | nApi g 1 | in 09 | % | | |
| <i>France, Montpellier</i> 12 patients with celery allergy (clinical history) and mugwort pollen sensitivity (SPT) | rApi g 1 | in 0% | | in 17% | Hoffmann-Sommergruber et |
| | rBet v 1 | in 0% | | | |
| | multiple celery proteins (other than Api g 1)in 67% | | | | |
| | Allergens from celery to | uber: | | | |
| | Allergens | | a) | b) | |
| <i>Germany, Berlin</i> a) 60 celery sensitive patients b) 30 celery and pollen allergic patients | Api g 1 | | in 33% | 80% | |
| | Api g 4 | | in 17% | 23% | a) <u>Jankiewicz et al. 1996</u> |
| | multiple bands (carbohydrate epitopes) | | in 32% | 27% | b) Jankiewicz et al. 1998 |
| | other | | in 10% | | |
| | (SDS-PAGE / immunol | blot) | | | |

| <i>Germany, Berlin</i> 12 apple and celery allergic patients | Carbohydrate epitopes on allergens > 30 kDa (periodate treatment, immunoblot, EAST inhibition) | | | | Vieths et al. 1994 |
|---|--|---------|-------|----------------------------|------------------------------------|
| Netherlands, Amsterdam 401 sera with IgE against pollen and/or vegetable foods | celery profilin (Api g 4) in 18% | | | <u>van Ree et al. 2000</u> | |
| | Allergens | immun | oblot | SPT | |
| | nApi g 1 | in 71% | | | |
| <i>Switzerland, Davos</i> 24 patients with celery and birch pollen | rApi g 1 | in 67% | | 100,00 % | Hoffmann-Sommergruber et al. 1999a |
| allergy (clinical history) | rBet v 1 | in 100% | | | |
| | multiple celery proteins in 83% | | 1 | | |
| | Allergens | | imm | moblot | |
| | Api g 1 | | 59% | | |
| Switzerland, Zurich 22 celery allergic patients (DBPCFC positive) | CCD (cross-reactive carbo- hydrate determinants), >45 kDa | | | | Lüttkopf et al. 2000 |
| | Api g 4 | | 23% | | |

* for patients designated with celery sensitivity the history of celery allergy may be unknown

6.2 Properties of Bet v 1 - homologous Protein (Api g 1)

6.2.1 Molecular Biological Properties

| Bet-v-1-homolo | ogous Protein | | References |
|---|---|--|---|
| Allergen Nome | nclature Api g 1 | | (1) Larsen & Lowenstein 2000 |
| Isoallergens and Variants 2 isoallergens designated Api g 1.0101 and Api g 1.0201 sharing 72% aa similarity (1, 3) (BLAST at NBCI: 49% aa sequence identity and 65% similarity) 4 isoallergens in 2D-PAGE immunoblot (2) | | (1) <u>Breiteneder et al. 1995</u> (2) <u>Schöning et al. 1995</u> (3) <u>Hoffmann-Sommergruber et al. 2000</u> | |
| Molecular Mas | 8 | | |
| Api g 1.0101Api g 1.0201calculated:16.2 kDa (1)17 kDa (5)SDS-PAGE:15 kDa (2), 16 kDa (4)17 kDa (5)2D-PAGE:15.5 kDa (3) | | (1) <u>Breiteneder et al. 1995</u> (2) <u>Ebner et al. 1995</u> (3) <u>Schöning et al. 1995</u> (4) <u>Jankiewicz et al. 1998</u> (5) <u>Hoffmann-Sommergruber et al. 2000</u> | |
| <i>Isoelectric Point</i> 2D-PAGE: major protein pI 4.4-4.6 (1), minor proteins pI 4.9, 5.1, and 6.0 (1) calculated: pI 4.45 (Api g 1.0201) (2) | | | (1) <u>Schöning et al. 1995</u> (2) <u>Hoffmann-Sommergruber et al. 2000</u> |
| Amino Acid Sequence, mRNA, and cDNA | | | |
| Api g 1 | Api g 1.0101 | Api g 1.0201 | |
| SWISS-PROT: GenBank: PIR: | <u>P49372</u> <u>Z48967</u> <u>S63984</u> | <u>Z75662</u> | (1) <u>Breiteneder et al. 1995</u> (2) Hoffmann-Sommergruber et al. 2000 |
| Amino Acids | 154* | 159 | |
| mRNA | 643 bp | 700 bp | |
| cDNA | | | |
| * product 2-154 | | | |

| recombinant Protein Expression in <i>Escherichia coli</i> : cDNA subcloned into expression plasmid j 1 in <i>E.coli</i> BL21DE3 (1, 2) <u>cDNA library:</u> Api g 1.0201 cloned after selection of IgE- expression library (3) Api g 1.0201- cDNA subcloned as a 6xHis and expression in <i>E.coli</i> M15[pREP4] (4) | pMW 175 and e binding clone f s-tagged protein | expression of rApi g rom celery cDNA into plasmid pDS56 | (1) <u>Breiteneder et al. 1995</u> (2) <u>Hoffmann-Sommergruber et al. 1996</u>, <u>1999a</u> (3) <u>Scheiner et al. 1997</u> (4) <u>Hoffmann-Sommergruber et al. 2000</u> |
|--|--|---|---|
| 3D-Structure Model structure of Api g 1.0201 calculated structure prediction using SWISS MODEL | t by homology t from ExPASy) | o Bet v 1 (3D-) (1) | (1) <u>Hoffmann-Sommergruber et al. 2000</u> |
| Biological Function Bet v 1 family of pathogenesis-related prot | eins (PR-family | 7 10) (1) | (1) SWISS-PROT |
| Sequence Homology | | | |
| aa sequence identity | Api g 1.0101 | Api g 1.0201 | |
| Carrot allergen Dau c 1: | 81% | 47% | |
| 2 Parsley pathogenesis-related proteins: | 61% | 60% | |
| Korean ginseng ribonuclease 1: | 56% | 65% | |
| Dandelion pathogenesis-related protein: | 44% | 33% | (1) Breiteneder et al. 1995 |
| Birch pollen allergen Bet v 1: | 42% | 34-37% | (2) <u>Hoffmann-Sommergruber et al. 1998</u> (3) BLAST at NBCI |
| Cherry allergen Pru a 1: | 42% | 39% | (5) BLAST at NDET |
| Apple allergen Mal d 1: | 39% | 36% | |
| Hazelnut allergen Cor a 1: | 38% | 37% | |
| Soybean stress-induced protein: | 38% | 37% | |
| 2 Potato pathogenesis-related proteins: | 35-38% | 32-33% | |

<u>6.2.2 Allergenic Properties</u>

| Bet v 1 - homologous Protein | References |
|--|--|
| Frequency of Sensitization IgE-binding to Api g 1 in 33-100% of patients (1) | (1) see <u>6.1 Sensitization to Celery</u> <u>Allergens</u> |
| Allergenicity of recombinant Api g 1 (1) All 10 sera from celery allergic patients bound to natural and recombinant Api g 1 with comparable intensities (immunoblot); complete inhibition of IgE binding to natural Api g 1 by rApi g 1 and rBet v 1, only reduced inhibition by rApi g 1 to natural Bet v 1 (serum pool, immunoblot inhibition); (2) 24 celery allergic and Api g 1 sensitized patients: a) Equal diagnostic potency (100% positivity) of commercial crude celery extract, native celery tuber and rApi g 1 in skin testing (SPT, skin prick-to-prick test) b) 16 sera showed IgE binding to Api g 1 in SDS-PAGE immunoblot, 2 sera detected native Api g 1 without reactivity to rApi g 1 indicating the presence of additional isoforms in native Api g 1 (3) 22 celery allergic patients (DBPCFC positive): 13 sera bound to natural and rApi g 1 in SDS-PAGE immunoblot (3 sera weaker binding to natural Api g 1 than to rApi g 1) and to rApi g 1 in EAST; inhibition of IgE binding from 1 patient's serum to rApi g 1 by native celery extract and rApi g 1 and to native Api g 1 (immunoblot) | (1) <u>Breiteneder et al. 1995</u> (2) <u>Hoffmann-Sommergruber et al. 1999a</u> (3) <u>Lüttkopf et al. 2000</u> |

| Internet Symposium on Food Allergens 2(3):2000 | http://www.food-allergens.de |
|--|--|
| <i>Allergenicity of recombinant Api g 1 isoforms</i> Purified recombinant isoform Api g 1.0201: recognized by 10 sera from celery allergic patients, yet with weaker IgE-binding capacity as compared to rApi g 1 (Api g 1.0101) (SDS-PAGE immunoblot) (1) In immunoblot inhibition: IgE-binding to Api g 1.0201 not inhibited by rApi g 1 (Api g 1.0101), only weak inhibition by rBet v 1a, complete inhibition by natural Bet v 1 (1) | (1) <u>Hoffmann-Sommergruber et al. 2000</u> |
| Stability of Api g 1 Allergenic activity sensitive to heat treatment of celery tuber | (1) see 9 Stability of Celery Allergens |

6.3 Properties of Chlorophyll a/b Binding Protein

6.3.1 Molecular Biological Properties

| Chlorophyll a/b Binding Prot | ein | References |
|---|---|--|
| Allergen Nomenclature Api g 3 | (proposed name) | (1) <u>Scheiner et al. 1997</u> |
| Molecular Mass 24.8 kDa | | (not published) |
| Isoelectric Point pI 4.87 | | (not published) |
| Amino Acid Sequence, mRNA | , and cDNA | |
| Api g 3 GenBank: Amino Acids mRNA cDNA | <u>Z75663</u> 264 963 bp | (1) Hoffmann-Sommergruber et al. (GenBank) (2) <u>Scheiner et al. 1997</u> |
| recombinant Protein Expression in cDNA library: Api g 3 cloned after selection of IgE- expression library (1) | binding clone from celery cDNA | (1) <u>Scheiner et al. 1997</u> |
| Biological Function / Localization In chloroplasts associated with the light- harvesting complex (1) | | (1) <u>Scheiner et al. 1997</u> |
| Sequence Homology 80-90% aa sequence identities to chlo mustard, tomato, soybean, spinach, p maize, rice, and wheat (1) | prophyll a/b binding proteins from white otato, barley, cucumber, garden pea, | (1) BLAST at NBCI |

<u>6.3.2 Allergenic Properties</u>

| Chlorophyll a/b Binding Protein | References |
|--|--|
| Frequency of Sensitization Probably a minor allergen (IgE-binding in <50% of patients), apart from IgE- screening of the cDNA library the frequency of IgE binding has never been tested in a larger group of patients (2) | (1) see <u>6.1 Sensitization to Celery</u> <u>Allergens</u> (2) <u>Scheiner et al. 1997</u> |

<u>6.4 Properties of Celery Profilin</u>

<u>6.4.1 Molecular Biological Properties</u>

| Celery Profilin | | References |
|---|-------------------------|--|
| Allergen Nomenclature Api g 4 | | (1) Larsen & Lowenstein 2000 |
| Isoallergens and Variants Double band in SDS-PAGE (1, 2) | | (1) <u>Vallier et al. 1992</u> (2) <u>Jankiewicz et al. 1998</u> |
| Molecular Mass calculated: 14.3 kDa (3) SDS-PAGE: 15 kDa (1), 15-16 kDa (2) | | (1) <u>Vallier et al. 1992</u> (2) <u>Jankiewicz et al. 1998</u> (3) <u>Scheurer et al. 2000</u> |
| Isoelectric Point calculated: pI 4.54 (2) 2D-PAGE: pI 5.80 - 5.90 (1) | | (1) <u>Vallier et al. 1992</u> (2) <u>Scheurer et al. 2000</u> |
| Amino Acid Sequence,mRNA, and cDNA Profilin SWISS-PROT: GenBank: | AF129423 | (1) Scheurer et al. 2000 |
| Amino Acids mRNA cDNA (open reading frame) | 133 405 bp 399 bp | (1) <u>Schedrer et al. 2000</u> |
| recombinant Protein <u>Expression in Escherichia coli:</u> PCR amplification of cDNA and expression of rApi g 4 in <i>E.coli</i> BL21DE3 using a modified pET-30a vector (1) | | (1) <u>Scheurer et al. 2000</u> |
| Biological Function Profilin family (1) | | (1) <u>Vallier et al. 1992</u> |
| Profilin family (1) Sequence Homology aa sequence identities to birch pollen profilin (Bet v 2) 80%, soybean profilin (Gly m 3) 78%, wheat profilin 78%, maize profilin 77%, kidney bean 76%, and barley profilin 75% (1, 2) aa sequence identity to human profilin: 33% (2) | | (1) BLAST at NBCI(2) <u>Scheurer et al. 2000</u> |

6.4.2 Allergenic Properties

| Celery Profilin | References |
|---|--|
| Frequency of Sensitization IgE-binding to profilin in appr. 23-58% of patients (1) | (1) see <u>6.1 Sensitization to Celery</u> <u>Allergens</u> |
| IgE-Binding Mimotope A synthetic peptide (CAISGGYPVC) defined by phage display (using random nonapeptide libraries screened with anti- profilin antibodies from an exclusively profilin allergic patient) inhibited IgE binding to celery tuber profilin (immunoblot). This peptide is considered to mimic a common conformational IgE epitope of profilins (1) | (1) <u>Leitner et al. 1998b</u> |

6.5 Properties of 55/58 kDa Proteins (Api g 5)

6.5.1 Molecular Biological Properties

| 55/58 kDa Proteins | References | |
|---|------------------------------------|--|
| Allergen Nomenclature Api g 5 | (1) Larsen & Lowenstein 2000 | |
| Isoallergens and Variants At least 2 isoallergens by SDS-PAGE (1) | (1) Ganglberger et al. 2000 | |
| Molecular Mass SDS-PAGE: 2 allergens: 55 kDa and 58 kDa (1) | (1) Ganglberger et al. 2000 | |
| Isoelectric Point | | |
| Amino Acid Sequence, mRNA, and cDNA | | |
| Api g 5 | | |
| SWISS-PROT: <u>P81943</u> | | |
| GenBank: | (1) Constitution of all 2000 | |
| PIR: | (1) Gangiberger et al. 2000 | |
| Amino Acids 18 N-terminal aa | | |
| mRNA | | |
| cDNA | | |
| <i>Other Properties</i> Reactive to monoclonal mice antibodies against birch pollen and to polyclonal rabbit antibody against a mugwort pollen allergen (formerly Art v 1) (1) | (1) <u>Ganglberger et al. 2000</u> | |

<u>6.5.2 Allergenic Properties</u>

| 55/58 kDa Proteins | References |
|--|--|
| Frequency of Sensitization | (1) see <u>6.1 Sensitization to Celery</u> |
| IgE-binding to 30-70 kDa allergens in 32-63% of patients (1) | Allergens |

7 Isolation & Preparation

| Extract / Purified Allergens | Methods | References |
|---------------------------------|---|--|
| Protein extract | Grinding of raw piece-cut celery tuber in Tris/HCl buffer pH 7.6 (containing benzamidine, EDTA, and phenylmethyl- sulphonyl- fluoride), filtration, centrifugation, and precipitation by adding ammonium sulphate up to 75% saturation; resolubization in Tris/HCl buffer pH 7.6 and dialysis; extract defatted with ethyl ether | Vallier et al. 1992 |
| Protein extract | Low temperature extraction method: raw celery tuber homogenized in acetone (-40°C), precipitates washed, filtered, lyophylized and water extracted | Vieths et al. 1992 |
| Protein extract | Protein extraction from celery tuber with potassium phosphate buffer pH 7.0 (containing polyvinylpyrrolidone, EDTA, and diethyldithiocarbamic acid, sodium azide), centrifugation, filtration and dialysis, storage after lyophylization -20°C | <u>Bauer et al. 1996</u> |
| Protein extract | Celery tuber ground in liquid nitrogen (1) or frozen in liquid nitrogen and homogenized (2), protein extraction with potassium phosphate buffer (1) or phosphate buffered saline pH 7.4 (2) at 4°C, centrifugation, filtration, dialysis, and lyophylization | (1) <u>Ganglberger et al. 2000</u> (2) <u>Ballmer-Weber et al. 2000</u> |
| Profilin (Api g 4) | Isolation from protein extract by 4 chromatographic steps: IEC (with DEAE) followed by SEC (with Sephacryl S200), and preparative anion exchange HPLC (DEAE) followed by exclusion- diffusion HPLC (Protein PAK SW 300) | Vallier et al. 1992 |
| Profilin (Api g 4) | Isolation from protein extract by affinity chromatography with a poly- L-prolin column | Vallier et al. 1992 Vieths et al. 1995 |
| 55/58 kDa allergen (Api g 5) | Separation of celery extract by IEC (Mono Q HR column) | Ganglberger et al. 2000 |
| 63 kDa allergen (Api g 5) | Preparative SDS-PAGE of celery extract followed by gel elution | Ganglberger et al. 2000 |

<u>8 Cross-Reactivities</u>

| Cross-Reacting Allergens | Subjects / Methods | References |
|---|--|--|
| Celery: (pollen) mugwort and birch pollen | 13 celery allergic patients: Cross- reactivity between stick celery and mugwort and birch pollen (RAST inhibition) | Kremser & Lindemayr 1983 |
| <i>Celery: (pollen, apple)</i> mugwort and birch pollen, apple | Cross- reactivity between celery tuber, birch pollen, and apple (RAST inhibiton) | Halmepuro et al. 1984 |
| Celery: (pollen) mugwort and birch pollen | 20 celery and pollen allergic patients: Cross- reactivity in RAST inhibiton | <u>Pauli et al. 1985</u> |
| Celery: (pollen, fennel) significant associations: celery and mugwort pollen, celery and fennel * | 262 fruit and/or vegetable allergic patients (clinical history, SPT, RAST) | <u>Ortolani et al. 1988</u> |
| Celery, Profilin: (pollen) birch and mugwort profilin (15 kDa) | Sera reactive to 15 kDa celery allergen: Inhibition of IgE binding to birch and mugwort pollen profilins (15 kDa each) by celery extract (1) and celery profilin (2) and to celery profilin by recombinant birch pollen profilin (2) (immunoblot inhibition) | Vallier et al. 1988 Vallier et al. 1992 |

| Celery: (pollen) rye grass profilin (12 kDa) | Serum from 1 patient with allergic rhinitis and atopic dermatitis related to vegetable foods and pollen: inhibition of IgE-binding to rye grass profilin by celery extract (RAST), detection of celery profilin at 12 kDa (SDS-PAGE immunoblot) | van Ree et al. 1992 |
|---|--|-----------------------------------|
| <i>Celery (Api g 1): (birch pollen)</i> birch pollen (Bet v 1) | 7 Bet v 1 and Bet v 2 sensitive patients (pooled serum): significant inhibition of IgE- binding to 15 kDa allergen (Api g 1) by rBet v 1, no inhibition of binding to 14 kDa allergen (Api g 4) (immunoblot inhibition) | <u>Ebner et al. 1995</u> |
| Celery (Api g 4): (birch pollen) birch pollen (Bet v 2 profilin) | 7 Bet v 1 and Bet v 2 sensitive patients (pooled serum): complete inhibition of IgE- binding to 14 kDa allergen (Api g 4) by rBet v 2, no inhibition of binding to 15 kDa allergen (Api g 1) (immunoblot inhibition) | <u>Ebner et al. 1995</u> |
| Celery allergens: (pollen) birch and mugwort pollen, Api g 1, Api g 4 | 16 kDa celery allergen (Api g 1) cross- reactive to Bet v 1 detected by 6/8 of patients with a birch pollen / celery sensitivity; 15 to 16 kDa double band (celery profilin, Api g 4) detected by 6/16 patients with mugwort pollen / celery and birch pollen / mugwort pollen / celery sensitivities (SDS-PAGE immunoblot, immunoblot inhibition) | <u>Vieths et al. 1995</u> |
| Celery: (pollen) birch and mugwort pollen | Pooled sera from patients with celery allergy: Inhibition of IgE binding to 46-60 kD celery allergens by birch and mugwort pollen (immunoblot inhibition) | <u>Bauer et al. 1996</u> |
| Celery: (pollen) 60 kDa mugwort allergen (formerly Art v 1) | Patients with food and pollen allergy: inhibition of IgE- binding to appr. 40-70 kDa celery allergens by 60 kDa mugwort allergen in 2 of 3 patients (SDS-PAGE inhibition), 2-40% reduction of IgE-binding to celery proteins by 60 kDa mugwort allergen in 3 patients (RAS T inhibition) | <u>Heiss et al. 1996</u> |
| Celery: (birch pollen) 35 kDa birch pollen allergen and Bet v 1 | Sera from birch pollen allergic patients reactive to 35 kDa allergen: IgE binding to celery extract inhibited by 35 kDa allergen and Bet v 1 from birch pollen (EAST inhibition) | Wellhausen et al. 1996 |
| Celery extract, rApi g 1: (<i>pollen</i>) birch pollen, rBet v 1, rBet v 2 profilin, timothy grass pollen extract; 21 patients with clinical relevant allergy to pollen and plant- derived food | Mixture of rBet v 1 and rBet v 2 inhibited IgE-binding to 10-14 kDa (profilin related) and 17-21 kDa (Bet v 1 related) celery allergens, timothy grass pollen inhibited IgE-binding to 10-14 kDa and 30-100 kDa allergens from celery; only weak inhibition of IgE-binding to Bet v 1 by rApi g 1 (immunoblot inhibition); 79% (2-100%) inhibition of IgE-binding to celery extract by mixture of rBet v 1 and rBet v 2 and 89% (4-100%) by mixture of rBet v1, rBet v 2, and timothy pollen extract (9 sera) (RAST inhibition) | <u>Kazemi-Shirazi et al. 2000</u> |
| <i>Celery: (pollen, fruits)</i> birch pollen, apple and cherry extracts; rBet v 1 (birch pollen), and Bet v 1 homologous allergens rApi g 1 (celery), rMal d 1 (apple), and rPru a 1 (cherry) | a) 4 birch pollen and cherry allergic patients: No inhibition of IgE-binding by rApi g 1 to neither of the extracts or rBet v 1 and rPru a 1 (immunoblot inhibition estimated according to band intensities) b) Max. inhibition of IgE binding to rApi g 1 by rMal d 1 and rPru a 1 <20% and by rBet v 1 >90%, estimated allergenic potencies: rBet v 1 >> rMal d 1, rPru a 1 > rApi g 1 (EAST inhibition, 10 cherry and/or celery allergic patients) c) Results indicate different epitopes of Api g 1 and fruit allergens (Mal d 1, Pru a 1) | Scheurer et al. 1999 |

| <i>Celery: (pollen, fruits)</i> a) birch pollen b) mugwort pollen c) lychee fruit d) carbohydrate moieties | IgE binding to celery extract in celery allergic patients (DBPCFC positive): a) >90% max. inhibition (3 sera, EAST inhibition) b) >75% max. inhibition in 2 from 3 sera (EAST inhibition) c) About 90% max. inhibition in 2 from 3 sera (EAST inhibition) d) Complete inhibition of IgE binding to celery allergens >40 kDa by bromelain glycopeptide MXF (2 sera, immunoblot inhibition) | Lüttkopf et al. 2000 |
|--|--|---|
| <i>Celery: (carrot)</i> stick celery, carrot | Cross- reactivity between stick celery and raw carrot; detection of 17 kDa allergen in celery and carrot (RAST inhibition, immunoblot inhibition) | Helbling et al. 1993 |
| <i>Celery: (carrot)</i> Dau c 1 from carrot, Api g 1 | Pooled sera from 6 carrot allergic patients: Reduction of IgE-binding to native Dau c 1 and complete inhibition to rDau c 1.2 by rApi g 1 from celery (immunoblot inhibition) | <u>Hoffmann-Sommergruber et</u> <u>al. 1999b</u> |
| <i>Celery: (fruits, vegetables)</i> carrot, cucumber, watermelon | 6 patients sensitive to celery, carrot, cucumber and/or watermelon (SPT, EAST): Cross- reactivity between all 4 foods; detection of 15 kDa allergen in all foods (RAST inhibition, immunoblot inhibition) | Jordan-Wagner et al. 1993 |
| Celery: (tomato) tomato | 6 Pollen and tomato sensitized patients: 51-85% inhibition of IgE binding to tomato extract by celery extract (EAST inhibition) | Petersen et al. 1996 |
| <i>Celery: (apple)</i> apple | 16 celery and/or apple allergic patients: Detection of Bet v 1 and Bet v 2 homologous allergens in celery and apple extracts; inhibition of IgE binding to celery extract by apple extract and vice versa, allergenic potencies: apple > celery (ELISA and immunoblot inhibition) | Steurich & Feyerabend 1996 |
| <i>Celery: (spices)</i> pepper and paprika | Pooled sera from 5 patients with celery- birch- mugwort- spice syndrome: Significant inhibition of IgE binding to pepper and paprika allergens by celery tuber extract and vice versa; no inhibition to pepper and paprika allergens by rBet v 1 and rBet v 2 (immunoblot inhibition) | Leitner et al. 1998a |
| Celery: (carbohydrate epitopes) glycopeptide bromelain | Pooled serum from 5 celery allergic patients: 78% and 8.6% inhibition of IgE binding to bromelain by celery extracts and rApi g 1, respectively (ELISA inhibition) | Jankiewicz et al. 1998 |
| Celery: (carbohydrate epitopes) N-glycan from bromelain | 7 celery allergic patients with IgE binding to N-glycan from bromelain: 22-100% maximal inhibition of IgE binding to celery by bromelain glycan (EAST inhibition); Inhibition of IgE binding to multiple bands >40 kD from celery by bromelain glycan (immunoblot inhibition); alpha 1,3-fucose key structure for IgE binding (chemical defucosylation) | Fötisch et al. 1999 |

* multiple sensitization (not proven by inhibition-tests)

9 Stability of Celery Allergens

| Treatment / Ripening | Effects | References |
|---|--|--|
| Celery (Heat) cooking | Sensitivity to raw and cooked celery (scratch chamber test, 13 celery allergic patients) | Kremser & Lindemayr 1983 |
| <i>Celery (Heat)</i> boiled celery tubers (30 min), boiling water | 70 patients with celery and pollen sensitivity (birch and/or mugwort) in SPT or intracutaneous test, positivity in SPT: 94% to raw celery tuber, 36% to cooked celery tuber, 8/13 to cooking water Celery-birch sensitive patients (n=13): negative or low RAST to heated celery extracts and to stick celery Celery-mugwort sensitive patients (n=6): positive RAST to heated celery extracts and high RAST values to stick celery | Wüthrich et al. 1990 |
| <i>Celery (Heat)</i> microwaved celery tubers (750 W, 100°C) | a) Reactivity of 46 celery sensitive patients (1): 78% to raw celery, 43% to celery heated for 30 min (SPT and/or EAST); b) Reactivity of 30 celery and pollen allergic patients in EAST (2): 100% to raw celery, 67% to celery heated for 10 min, 57% to celery heated for 30 min; c) Api g 1 abolished after 10 min, profilin (Api g 4) after 30 min, and carbohydrate epitopes (allergens >30 / >35 kDa) were heat resistant (SDS-PAGE immunoblot) (1, 2) | (1) <u>Jankiewicz et al. 1996</u> (2) <u>Jankiewicz et al. 1998</u> |
| Celery (Heat) microwaved celery tubers (30 min, 100°C) | Heating of celery tuber reduced allergenic activity of Api g 1, while semipurified heated Api g 1 retained immunoreactivity (SDS-PAGE immunoblot) | Vieths et al. 1998 |
| <i>Celery (Heat)</i> celery tubers (30 min, 100°C) | a) 22 celery allergic patients (DBPCFC positive): 68% of sera bound to allergens from native celery and 27% to heated celery allergens (EAST) b) Api g 1 monosensitized patient: strong inhibition of IgE binding to native celery extract by rApi g 1, native celery extract, and birch pollen; no inhibition by heated celery extract (EAST inhibition) c) CCD (cross-reactive carbohydrate determinants) monosensitized patients: >75% max. inhibition of IgE binding to celery extract by heated celery extract (EAST inhibition) | <u>Lüttkopf et al. 2000</u> |
| Celery (preservation) preservation methods a) gamma-irradiation (total dose of 10 kGy) b) ultra high pressure (600 mPa / 20°C) c) commercially dried celery powder d) a high voltage impulse treatment | 3 sera from celery sensitive patients with different specificity (to Api g 1, profilin or glycoproteins >30 kDa, respectively): Little changes (slight increase or decrease) in IgE binding for all 4 methods, none of the treatments resulted in loss of IgE binding (EAST); new allergen band with 18-19 kDa detected in irradiated celery tuber (SDS-PAGE immunoblot) | Jankiewicz et al. 1997 Vieths et al. 1997 |

| Celery (Enzymic Hydrolysis) a) digestion with artificial gastric fluid (pepsin, cathepsin, and mucin, 2 h, 37°C) b) followed by hydrolysis with pancreatic enzymes (45 min, 37°C) | 3 sera from celery sensitive patients: a) loss of celery bands >40kDa, strong IgE binding to hydrolyzed proteins (immunoblot) b) other proteins degraded with the exception of proteins at <20kDa and 38 kDa, strong reduction of IgE binding (immunoblot) | <u>Vieths et al. 1997</u> |
|--|---|---|
| <i>Celery Extract</i> (<i>Deglycosylation</i>) deglycosylation by periodate treatment | Celery allergic patients: Strong reduction of IgE binding to allergens > 30 / 35 kDa indicating carbohydrate epitopes, no difference in IgE binding to Api g 1 and Api g 4 (SDS-PAGE immunoblot, EAST inhibition) 8 from 12 sera showed IgE binding to bromelain glycopeptide (ELISA) (3) | (1) <u>Vieths et al. 1994</u> (2) <u>Jankiewicz et al. 1996</u> (3) <u>Jankiewicz et al. 1998</u> |
| Celery Extract (Deglycosylation) deglycosylation by periodate treatment | Celery allergic patients: No difference in IgE binding (SDS-PAGE immunoblot) | <u>Bauer et al. 1996</u> |

10 Allergen Sources

| Reported Adverse Reactions | References |
|--|---|
| Food / Food additives After ingestion of vegetable and as spice (1) | (1) see <u>2 Symptoms of Celery</u> <u>Allergy</u> |
| Canned Celery Local and systemic allergic reactions in 1 patient after ingestion of canned celery preparation, positive SPT to raw celery and negative SPT to cooked celery | Bauer et al. 1996 |

<u>11 Food Allergen Labelling</u>

| Food Allergen | Labelling / Regulation Status | References |
|--|------------------------------------|--|
| <i>International Regulations</i> Celery and products of these | not demanded / advisary status (1) | (1) <u>Codex Alimentarius</u> Commission 1999 |
| <i>European Regulations</i> Celery and celery products | not demanded / recommendation (1) | (1) <u>Bousquet et al. 1998</u> |

<u>12 References</u>

- Andre F, Andre C, Colin L, Cacaraci F, Cavagna S (1994) Role of new allergens and of allergens consumption in the increased incidence of food sensitizations in France *Toxicology* 93:77-83
- Asero R (1997) Relevance of pollen-specific IgE levels to the development of Apiaceae hypersensitivity in patients with birch pollen allergy Allergy 52:560-4
- Ballmer-Weber BK, Vieths S, Lüttkopf D, Heuschmann P, Wüthrich B (2000) Celery allergy confirmed by DBPCFC. A clinical study in 32 subjects with a history of adverse reactions to celery root J Allergy Clin Immunol 106:373-8
- Bauer L, Ebner C, Hirschwehr R, Wüthrich B, Pichler C, Fritsch R, Scheiner O, Kraft D (1996) IgE cross- reactivity between birch pollen, mugwort pollen and celery is due to at least three distinct cross- reacting allergens: immunoblot investigation of the birch- mugwort- celery syndrome *Clin Exp Allergy 26:1161-70*
- Bircher AJ, Van Melle G, Haller E, Curty B, Frei PC (1994) IgE to food allergens are highly prevalent in patients allergic to pollens, with and without symptoms of food allergy *Clin Exp Allergy 24:367-74*
- Bonnin JP, Grezard P, Colin L, Perrot H (1995) A very significant case of allergy to celery cross- reacting with ragweed Allerg Immunol (Paris) 27:91-3 (in French)

- Bousquet J, Björkstén B, Bruijnzeel-Koomen CAFM, Huggett A, Ortolani C, Warner JO, Smith M (1998) Scientific criteria and the selection of allergenic foods for product labelling *Allergy* 53:3-21
- Breiteneder H, Hoffmann-Sommergruber K, O'Riordain G, Susani M, Ahorn H, Ebner C, Kraft D, Scheiner O (1995)
 Molecular characterization of Api g 1, the major allergen of celery (*Apium graveolens*), and its immunological and structural relationships to a group of 17-kDa tree pollen allergens *Eur J Biochem 233:484-9*
- Codex Alimentarius Commission (1999) Food labelling complete texts Joint FAO/WHO Food Standards Programme, FAO/WHO, Rome
- Dechamp C, Michel J, Deviller P, Perrin LF (1984) Anaphylactic shock to celery and sensitization to ragweed and mugwort. Crossed or concomitant allergy? Presse Med 13:871-4 (in French)
- Diez-Gomez ML, Quirce S, Cuevas M, Sánchez-Fernández C, Baz G, Moradiellos FJ, Martinez A (1999) Fruit-pollenlatex cross-reactivity: implication of profilin (Bet v 2) Allergy 54:951-61
- Ebner C, Hirschwehr R, Bauer L, Breiteneder H, Valenta R, Ebner H, Kraft D, Scheiner O (1995) Identification of allergens in fruits and vegetables: IgE cross-reactivities with the important birch pollen allergens Bet v 1 and Bet v 2 (birch profilin) J Allergy Clin Immunol 95(5Pt1):962-9
- Etesamifar M, Wüthrich B (1998) IgE- mediated food allergies including oral allergy syndrome in 383 patientsAllergologie 21:451-7 (in German)
- European Commission (1998) Reports on tasks for scientific cooperation. The occurrence of severe food allergies in the EU European Commission, Directorate-General III, SCOOP/NUTR/REPORT/2, Brussels
- Forsbeck M, Ros AM (1979) Anaphylactoid reaction to celery Contact Dermatitis 5:191
- Fotisch K, Altmann F, Haustein D, Vieths S (1999) Involvement of carbohydrate epitopes in the IgE response of celery- allergic patients Int Arch Allergy Immunol 120:30-42
- Ganglberger E, Radauer C, Grimm R, Hoffmann-Sommergruber K, Breiteneder H, Scheiner O, Jensen-Jarolim E (2000)
 N-terminal sequences of high molecular weight allergens from celery tuber *Clin Exp Allergy 30(4):566-570*
- Grote M, Fischer S, Muller WD, Valenta R (1998) In situ localization of a high molecular weight cross- reactive allergen in pollen and plant- derived food by immunogold electron microscopy J Allergy Clin Immunol 101(2Pt1):250-7
- Halmepuro L, Vuontela K, Kalimo K, Bjorksten F (1984) Cross- reactivity of IgE antibodies with allergens in birch pollen, fruits and vegetables Int Arch Allergy Appl Immunol 74:235-40
- Heiss S, Fischer S, Muller WD, Weber B, Hirschwehr R, Spitzauer S, Kraft D, Valenta R (1996) Identification of a 60 kd cross-reactive allergen in pollen and plant-derived foodJ Allergy Clin Immunol 98(5Pt1):938-47
- Helbling A, Lopez M, Schwartz HJ, Lehrer SB (1993) Reactivity of carrot-specific IgE antibodies with celery, apiaceous spices, and birch pollen Ann Allergy 70:495-9
- Hoerler S, Ukiwe J (1992) Laryngeal edema from celery allergic reaction Am J Emerg Med 10:613
- Hoffmann-Sommergruber K, Vanek-Krebitz M, Ferris R, O'Riordain G, Susani M, Hirschwehr R, Ebner C, Ahorn H, Kraft D, Scheiner O, Breiteneder H (1996) Isolation and cloning of Bet v 1- homologous food allergens from celeriac (Api g 1) and apple (Mal d 1) Adv Exp Med Biol 409:219-24
- Hoffmann-Sommergruber K, Demoly P, Crameri R, Breiteneder H, Ebner C, Laimer Da Camara Machado M, Blaser K, Ismail C, Scheiner O, Bousquet J, Menz G (1999a) IgE reactivity to Api g 1, a major celery allergen, in a Central European population is based on primary sensitization by Bet v 1 J Allergy Clin Immunol 104(2Pt1):478-84
- Hoffmann-Sommergruber K, O'Riordain G, Ahorn H, Ebner C, Laimer Da Camara Machado M, Puhringer H, Scheiner O, Breiteneder H (1999b) Molecular characterization of Dau c 1, the Bet v 1 homologous protein from carrot and its cross-reactivity with Bet v 1 and Api g 1 Clin Exp Allergy 29:840-7
- Hoffmann-Sommergruber K, Ferris R, Pec M, Radauer C, O'Riordain G, Laimer da Camara Machado M, Scheiner O, Breiteneder H (2000) Characterization of Api g 1.0201, a new member of the Api g 1 family of celery allergens Int Arch Allergy Immunol 122:115-23
- Jankiewicz A, Aulepp H, Baltes W, Bogl KW, Dehne LI, Zuberbier T, Vieths S (1996) Allergic sensitization to native and heated celery root in pollen- sensitive patients investigated by skin test and IgE binding Int Arch Allergy Immunol 111:268-78
- Jankiewicz A, Baltes W, Bögl KW, Dehne LI, Jamin A, Hoffmann A, Haustein D, Vieths S (1997) Influence of food processing on the immunochemical stability of celery allergens J Sci Food Agric 75:359-70
- Jankiewicz A, Aulepp H, Altmann F, Fötisch K, Vieths S (1998) Serological investigation of 30 celery- allergic patients with particular consideration of the thermal stability of IgE- binding celery allergens Allergo J 7:87-95
- Jordan-Wagner DL, Whisman BA, Goetz DW (1993) Cross- allergenicity among celery, cucumber, carrot, and watermelon Ann Allergy 71:70-9
- Kazemi-Shirazi L, Pauli G, Purohit A, Spitzauer S, Fröschl R, Hoffmann-Sommergruber K, Breiteneder H, Scheiner O, Kraft D, Valenta R (2000) Quantitative IgE inhibition experiments with purified recombinant allergens indicate pollen-derived allergens as the sensitizing agents responsible for many forms of plant food allergy J Allergy Clin Immunol 105:116-125

- Kauppinen K, Kousa M, Reunala T (1980) Aromatic plants a cause of severe attacks of angio-edema and urticaria Contact Dermatitis 6:251-4
- Kidd JM 3d, Cohen SH, Sosman AJ, Fink JN (1983) Food- dependent exercise-induced anaphylaxis J Allergy Clin Immunol 71:407-11
- Kremser M, Lindemayr W (1983) Celery allergy (celery contact urticaria syndrome) and relation to allergies to other plant antigens *Wien Klin Wochenschr 95:838-43* (in German)
- Larsen JN, Lowenstein H (2000) Official list of allergens: IUIS Allergen Nomenclature Subcommittee ftp://biobase.dk / pub / who-iuis / allergen.list
- Leitner A, Jensen-Jarolim E, Grimm R, Wüthrich B, Ebner H, Scheiner O, Kraft D, Ebner C (1998a) Allergens in pepper and paprika. Immunologic investigation of the celery- birch- mugwort- spice syndrome Allergy 53:36-41
- Leitner A, Vogel M, Radauer C, Breiteneder H, Stadler BM, Scheiner O, Kraft D, Jensen-Jarolim E (1998b) A mimotope defined by phage display inhibits IgE binding to the plant panallergen profilin Eur J Immunol 28:2921-7
- Lessof MH, Wraith DG, Merrett TG, Merrett J, Buisseret PD (1980) Food allergy and intolerance in 100 patients local and systemic effects Q J Med 49(195):259-71
- Levy DA, Mounedji N, Noirot C, Leynadier F (2000) Allergic sensitization and clinical reactions to latex, food and pollen in adult patients *Clin Exp Allergy 30:270-275*
- Lüttkopf D, Ballmer-Weber BK, Wüthrich B, Vieths S (2000) Celery allergens in patients with positive double- blind placebo- controlled food challenge J Allergy Clin Immunol 106:390-9
- Much T, Wüthrich B, Tondury T Clinical aspects, diagnosis and therapy of food hypersensitivity Z Hautkr 53:141-9 (in German)
- Novembre E, Cianferoni A, Bernardini R, Mugnaini L, Caffarelli C, Cavagna G, Giovane A, Vierucci A (1998)
 Anaphylaxis in children: clinical and allergological features *Pediatrics 101(4):e8*
- Store of the oral allergy syndrome Ann Allergy 61(6Pt2): 47-52
- Ortolani C, Ispano M, Pastorello EA, Ansaloni R, Magri GC (1989) Comparison of results of skin prick tests (with fresh foods and commercial food extracts) and RAST in 100 patients with oral allergy syndrome J Allergy Clin Immunol 83(3):683-90
- Pauli G, Bessot JC, Dietemann-Molard A, Braun PA, Thierry R (1985) Celery sensitivity: clinical and immunological correlations with pollen allergy *Clin Allergy 15:273-9*
- Pauli G, Bessot JC, Braun PA, Dietemann-Molard A, Kopferschmitt-Kubler MC, Thierry R (1988) Celery allergy: clinical and biological study of 20 cases Ann Allergy 60:243-6
- Reekers R, Busche M, Wittmann M, Kapp A, Werfel T (1999) Birch pollen- related foods trigger atopic dermatitis in patients with specific cutaneous T-cell responses to birch pollen antigens J Allergy Clin Immunol 104:466-72
- Rohrer CL, Pichler WJ, Helbling A (1998) Anaphylaxie: Klinik, Ätiologie und Verlauf bei 118 Patienten Schweiz Med Wochenschr 128:53-63
- Rose MH, Altman LC (1985) Anaphylaxis after ingestion of raw celery Ann Allergy 54:166
- Scheurer S, Son DY, Boehm M, Karamloo F, Franke S, Hoffmann A, Haustein D, Vieths S (1999) Cross- reactivity and epitope analysis of Pru a 1, the major cherry allergen *Mol Immunol 36:155-67*
- Scheurer S, Wangorsch A, Haustein D, Vieths S (2000) Cloning of the minor allergen Api g 4 profilin from celery (Apium graveolens) and its cross- reactivity with birch pollen profilin Bet v 2 Clin Exp Allergy 30:962-71
- Scheiner O, Aberer W, Ebner C, Ferreira F, Hoffmann-Sommergruber K, Hsieh LS, Kraft D, Sowka S, Vanek-Krebitz M, Breiteneder H (1997) Cross- reacting allergens in tree pollen and pollen-related food allergy: implications for diagnosis of specific IgE Int Arch Allergy Immunol 113:105-8
- Schöning B, Vieths S, Petersen A, Baltes W (1995) Identification and characterisation of allergens related to Bet v I, the major birch pollen allergen, in apple, cherry, celery and carrot by two- dimensional immunoblotting and Nterminal microsequencing J Sci Food Agric 67:431-40
- Shadick NA, Liang MH, Partridge AJ, Bingham C, Wright E, Fossel AH, Sheffer AL (1999) The natural history of exercise-induced anaphylaxis: Survey results from a 10-year follow-up study *J Allergy Clin Immunol* 104:123-7
- Silverstein SR, Frommer DA, Dobozin B, Rosen P (1986) Celery- dependent exercise-induced anaphylaxis J Emerg Med 4:195-9
- Stäger J, Wüthrich B, Johansson SG (1991) Spice allergy in celery-sensitive patients Allergy 46:475-8
- Steurich F, Feyerabend R (1996) Kreuzreaktivität von Sellerie- und Apfelallergenen Allergologie 19:361-6 (in German)
- Stricker WE, Anorve-Lopez E, Reed CE (1986) Food skin testing in patients with idiopathic anaphylaxis J Allergy Clin Immunol 77:516-9
- Troise C, Voltolini S, Delbono G, Negrini AC (1992) Allergy to pollens from Betulaceae and Corylaceae in a Mediterranean area (Genoa, Italy) - a ten-year retrospective J Investig Allergol Clin Immunol 2:313-7
- Vallier P, Dechamp C, Vial O, Deviller P (1988) A study of allergens in celery with cross- sensitivity to mugwort and

birch pollens Clin Allergy 18:491-500

- Vallier P, DeChamp C, Valenta R, Vial O, Deviller P (1992) Purification and characterization of an allergen from celery immunochemically related to an allergen present in several other plant species. Identification as a profilin *Clin Exp Allergy 22(8):774-82*
- van Ree R, Voitenko V, van Leeuwen WA, Aalberse RC (1992) Profilin is a cross- reactive allergen in pollen and vegetable foods Int Arch Allergy Immunol 98:97-104
- van Ree R, Akkerdaas JH, van Leeuwen WA, Fernández-Rivas M, Asero R, Knul-Brettlova V, Knulst A, Aalberse RC (2000) New perspectives for the diagnosis of food allergy ACI Int 12:7-12
- Vieths S, Schöning B, Brockmann S, Aulepp H (1992) Untersuchungen zur Allergie gegen Lebensmittel pflanzlicher Herkunft: Herstellung von Obst- und Gemüseextrakten für serologische Untersuchungen Deutsche Lebensmittel-Rundschau 88:239-43, 272-9 (in German)
- Vieths S, Mayer M, Baumgart M (1994) Food allergy: specific binding of IgE antibodies from plant food sensitized individuals to carbohydrate epitopes Food Agric Immunol 6:453-63
- Vieths S, Jankiewicz A, Wüthrich B, Baltes W (1995) Immunoblot study of IgE binding allergens in celery roots Ann Allergy Asthma Immunol 75:48-55
- Vieths S, Jankiewicz A, Aulepp H, Haustein D (1997) Allergy to heated and processed foods in: 8th International Paul-Ehrlich-Seminar, Vol. 91, pp 250-62, Gustav Fischer Stuttgart
- Vieths S, Hoffmann A, Holzhauser T, Muller U, Reindl J, Haustein D (1998) Factors influencing the quality of food extracts for in vitro and in vivo diagnosis Allergy 53(46 Suppl):65-71
- Wellhausen A, Schöning B, Petersen A, Vieths S (1996) IgE binding to a new cross- reactive structure: a 35 kDa protein in birch pollen, exotic fruit and other plant foods Z Ernährungswiss 35:348-55
- Wüthrich B, Dietschi R (1985) The celery- carrot- mugwort- condiment syndrome: skin test and RAST results Schweiz Med Wochenschr 115:358-64 (in German)
- Wüthrich B, Hofer T (1984) Food allergy: the celery- mugwort- spice syndrome. Association with mango allergy? Dtsch Med Wochenschr 109:981-6 (in German)
- Wüthrich B, Hofer TH (1986) Nahrungsmittelallergien III. Therapie: Eliminationsdiät, symptomatische medikamentöse Prophylaxe und spezifische Hyposensibilisierung Schweiz Med Wschr 41:1401-10 + 1446-9 (in German)
- Wüthrich B, Stäger J, Johansson SG (1990) Celery allergy associated with birch and mugwort pollinosisAllergy 45:566-71
- Wüthrich B, Stöger P, Johansson SG (1992) RAST- spezifische IgE auf Gewürze bei Sensibilisierung gegen Birke-, Beifußpollen und Sellerie Allergologie 11:380-3 (in German)

copyright © 2000 by matthias besler - ONLINE PUBLISHER