Katrine Lindholm Bøgh - DTU Orbit (19/05/2018)
Katrine Lindholm Bøgh

Organisations

Division of Toxicology and Risk Assessment
25/02/2012 → 19/05/2015 Former
VIP

Senior Researcher, National Food Institute
07/03/2008 → present
kalb@food.dtu.dk
VIP

Research Group for Gut Microbiology and Immunology
19/05/2015 → present
VIP

Publications:

Milk allergy prevention and treatment
The invention provides a new strategy for achieving desensitisation or induction of tolerance to milk protein allergens, e.g. BLG, in humans or animals, comprising formulating and using a composition comprising a purified intact expressed milk protein together with one or more purified peptides from said intact milk protein.

General information
State: Published
Organisations: National Food Institute, Research Group for Gut Microbiology and Immunology
Authors: Bøgh, K. L. (Intern), Madsen, C. B. (Intern)
Publication date: 31 Aug 2017

Publication information
IPC: G01N 33/ 68 A I
Patent number: WO2017144730
Date: 31/08/2017
Priority date: 26/02/2016
Priority number: EP20160157602
Original language: English
Electronic versions:
WO2017144730A1.pdf
Main Research Area: Technical/natural sciences
Source: espacenet
Source-ID: WO2017144730
Publication: Research › Patent – Annual report year: 2017

A review of animal models used to evaluate potential allergenicity of genetically modified organisms (GMOs)
Food safety regulators request prediction of allergenicity for newly expressed proteins in genetically modified (GM) crops and in novel foods. Some have suggested using animal models to assess potential allergenicity. A variety of animal models have been used in research to evaluate sensitisation or elicitation of allergic responses. However, protocols for sensitisation and challenge, animal species and strains, diets and other environmental factors differ widely. We present a comprehensive review of published, peer-reviewed experimental animal models used for the evaluation of allergenicity of genetically modified organisms (GMOs).

General information
State: Published
Organisations: National Food Institute, Research Group for Gut Microbiology and Immunology, University of Nebraska, Medical University of Vienna
Authors: Marsteller, N. (Ekstern), Bøgh, K. L. (Intern), Goodman, R. E. (Ekstern), Epstein, M. M. (Ekstern)
Number of pages: 8
Pages: 81-88
Publication date: 2017
Main Research Area: Technical/natural sciences
Correlation of the allergenicity and tolerogenicity of two cow's milk protein products with intestinal uptake

General information
State: Published
Organisations: National Food Institute, Research Group for Gut Microbiology and Immunology, Technical University of Denmark, Utrecht University, Arla Foods
Authors: Graversen, K. (Intern), Hornslet, S. E. (Ekstern), Smit, J. J. (Ekstern), Heydenreich Jensen, L. (Intern), Christoffersen, H. F. (Ekstern), Jacobsen, L. N. (Ekstern), Bøgh, K. L. (Intern)
Pages: 320-320
Publication date: 2017
Conference: European Academy of Allergy and Clinical Immunology Congress 2017, Helsinki, Finland, 17/06/2017 - 17/06/2017
Main Research Area: Technical/natural sciences

Publication information
Journal: Drug Discovery Today: Disease Models
Volume: 17-18
ISSN (Print): 1740-6757
Ratings:
BFI (2018): BFI-level 1
BFI (2017): BFI-level 1
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 0.74 SJR 0.391 SNIP 0.242
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.278 SNIP 0.122 CiteScore 0.55
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.35 SNIP 0.194 CiteScore 0.72
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.274 SNIP 0.23 CiteScore 0.62
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.226 SNIP 0.171 CiteScore 0.61
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.363 SNIP 0.197 CiteScore 0.8
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 0.313 SNIP 0.15
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 0.254 SNIP 0.143
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 0.193 SNIP 0.119
Scopus rating (2007): SJR 0.202 SNIP 0.096
Scopus rating (2006): SJR 0.176 SNIP 0.084
Scopus rating (2005): SJR 0.13 SNIP 0.029
Original language: English
DOIs:
10.1016/j.ddmod.2016.11.001
Source: FindIt
Source-ID: 2349064696
Publication: Research - peer-review » Review – Annual report year: 2017
Correlation of the allergenicity and tolerogenicity of two cow's milk protein products with their intestinal uptake – a study in Brown Norway (BN) rats
Correlation of the allergenicity and tolerogenicity of two cow’s milk protein products with their intestinal uptake – a study in Brown Norway rats

General information
State: Published
Organisations: National Food Institute, Research Group for Gut Microbiology and Immunology, Technical University of Denmark, Utrecht University, Arla Foods Ingredients Group P/S
Authors: Graversen, K. (Intern), Asukowit, C. (Ekstern), Reholt, J. (Ekstern), Homslet, S. E. (Ekstern), Jensen, L. H. (Intern), Smit, J. (Ekstern), Christoffersen, H. F. (Ekstern), Jacobsen, L. N. (Ekstern), Beogh, K. L. (Intern)
Number of pages: 1
Pages: 35-35
Publication date: 2017

Host publication information
Title of host publication: Proceedings of the 3rd International ImpARAS Conference
Place of publication: Helsingør, Denmark
Article number: 016
Main Research Area: Technical/natural sciences
Conference: 3rd International ImpARAS Conference, Helsingør, Denmark, 10/10/2017 - 10/10/2017
Electronic versions:
Proceeding book
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2017

Food allergy skin sensitization: A comparative study with three different gluten products in Brown Norway rats

General information
State: Published
Organisations: National Food Institute, Research Group for Gut Microbiology and Immunology, Technical University of Denmark, Arla Foods Ingredients Group P/S, Utrecht University
Authors: Castan, L. (Ekstern), Ballegaard, A. R. (Intern), Bouchaud, G. (Ekstern), Bøgh, K. L. (Intern)
Number of pages: 1
Pages: 58-58
Publication date: 2017

Host publication information
Title of host publication: Proceedings of the 3rd International ImpARAS Conference
Place of publication: Helsingør, Denmark
Article number: F05
Main Research Area: Technical/natural sciences
Conference: 3rd International ImpARAS Conference, Helsingør, Denmark, 10/10/2017 - 10/10/2017
Electronic versions:
Proceeding book
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2017

IgE - the main player of food allergy
Food allergy is a growing problem worldwide, presently affecting 2-4% of adults and 5-8% of young children. IgE is a key player in food allergy. Consequently huge efforts have been made to develop tests to detect either the presence of IgE molecules, their allergen binding sites or their functionality, in order to provide information regarding the patient's food
allergy. The ultimate goal is to develop tools that are capable of discriminating between asymptomatic sensitization and a clinically relevant food allergy, and between different allergic phenotypes in an accurate and trustworthy manner. This may generate better diagnostic, prognostic and therapeutic monitoring tools for the future.

General information
State: Published
Organisations: National Food Institute, Research Group for Gut Microbiology and Immunology, University Medical Centre Utrecht, Hospital for Sick Children
Authors: Broekman, H. C. H. (Ekstern), Eiwegger, T. (Ekstern), Upton, J. (Ekstern), Bøgh, K. L. (Intern)
Number of pages: 8
Pages: 37-44
Publication date: 2017
Main Research Area: Technical/natural sciences

Publication information
Journal: Drug Discovery Today: Disease Models
Volume: 17-18
ISSN (Print): 1740-6757
Ratings:
BFI (2018): BFI-level 1
BFI (2017): BFI-level 1
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 0.74 SJR 0.391 SNIP 0.242
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.278 SNIP 0.122 CiteScore 0.55
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.35 SNIP 0.194 CiteScore 0.72
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.274 SNIP 0.23 CiteScore 0.62
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.226 SNIP 0.171 CiteScore 0.61
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.363 SNIP 0.197 CiteScore 0.8
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 0.313 SNIP 0.15
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 0.254 SNIP 0.143
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 0.193 SNIP 0.119
Scopus rating (2007): SJR 0.202 SNIP 0.096
Scopus rating (2006): SJR 0.176 SNIP 0.084
Scopus rating (2005): SJR 0.13 SNIP 0.029
Original language: English
Molecular Medicine, Drug Discovery
DOIs:
10.1016/j.ddmod.2016.07.001
Source: FindIt
Source-ID: 2347943439
Publication: Research - peer-review › Journal article – Annual report year: 2017

Sensitising capacity of five different wheat products through the skin

General information
State: Published
Organisations: National Food Institute, Research Group for Gut Microbiology and Immunology, Fujita Health University, National Institute of Health Sciences Tokyo
Number of pages: 1
Sensitising capacity of unmodified and acid hydrolysed gluten through the skin—a comparative study in naïve vs tolerant Brown Norway rats

General information
State: Published
Organisations: National Food Institute, Research Group for Gut Microbiology and Immunology
Authors: Ballegaard, A. R. (Intern), Madsen, C. B. (Intern), Bøgh, K. L. (Intern)
Pages: 316-316
Publication date: 2017
Conference: European Academy of Allergy and Clinical Immunology Congress 2017, Helsinki, Finland, 17/06/2017 - 17/06/2017
Main Research Area: Technical/natural sciences

Publication information
Journal: Allergy: European Journal of Allergy and Clinical Immunology
Volume: 72
Issue number: S103
Article number: 0445
ISSN (Print): 0105-4538
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 6.23 SJR 2.724 SNIP 2.475
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 3.13 SNIP 2.127 CiteScore 5.73
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 2.464 SNIP 2.121 CiteScore 5.51
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 2.195 SNIP 1.902 CiteScore 4.91
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 2.008 SNIP 1.818 CiteScore 4.81
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 2.328 SNIP 1.781 CiteScore 4.89
Tarmens bakterier og fødevareallergi

General information
State: Published
Organisations: National Food Institute, Research Group for Gut Microbiology and Immunology
Authors: Bøgh, K. L. (Intern)
Pages: 17-21
Publication date: 2017
Main Research Area: Technical/natural sciences

Publication information
Journal: Miljø og sundhed
Volume: 23
Issue number: Suppl. 1
ISSN (Print): 1601-4146
Ratings:
ISI indexed (2013): ISI indexed no
ISI indexed (2012): ISI indexed no
ISI indexed (2011): ISI indexed no
Original language: Danish
Electronic versions:
Temanummer_Miljø_Og_Sundhed_2017.pdf
Publication: Research - Journal article – Annual report year: 2017

The effect of Akkermansia muciniphilia on house dust mite induced allergic airway inflammation

General information
State: Published
Organisations: National Food Institute, Research Group for Gut Microbiology and Immunology, University of Zurich
Current challenges facing the assessment of the allergenic capacity of food allergens in animal models

Food allergy is a major health problem of increasing concern. The insufficiency of protein sources for human nutrition in a world with a growing population is also a significant problem. The introduction of new protein sources into the diet, such as newly developed innovative foods or foods produced using new technologies and production processes, insects, algae, duckweed, or agricultural products from third countries, creates the opportunity for development of new food allergies, and this in turn has driven the need to develop test methods capable of characterizing the allergenic potential of novel food proteins. There is no doubt that robust and reliable animal models for the identification and characterization of food allergens would be valuable tools for safety assessment. However, although various animal models have been proposed for this purpose, to date, none have been formally validated as predictive and none are currently suitable to test the allergenic potential of new foods. Here, the design of various animal models are reviewed, including among others considerations of species and strain, diet, route of administration, dose and formulation of the test protein, relevant controls and endpoints measured.
Food Allergens: Is There a Correlation between Stability to Digestion and Allergenicity?

Food allergy is a major health problem in the Western countries, affecting 3-8% of the population. It has not yet been established what makes a dietary protein a food allergen. Several characteristics have been proposed to be shared by food allergens. One of these is resistance to digestion. This paper reviews data from digestibility studies on purified food allergens and evaluates the predictive value of digestibility tests on the allergenic potential. We point out that food allergens do not necessarily resist digestion. We discuss how the choice of in vitro digestibility assay condition and the method used for detection of residual intact protein as well as fragments thereof may greatly influence the outcome as well as the interpretation of results. The finding that digests from food allergens may retain allergenicity, stresses the importance of using immunological assays for evaluating the allergenic potential of food allergen digestion products. Studies assessing the allergenicity of digestion products, by either IgE-binding, elicitation or sensitizing capacity, shows that digestion may abolish, decrease, have no effect, or even increase the allergenicity of food allergens. Therefore, the predictive value of the pepsin resistance test for assessing the allergenic potential of novel proteins can be questioned.
Gluten, Enzymatic or Acid hydrolysed gluten does not induce sensitisation by the oral route in contrast to i.p. dosing: A study in gluten-tolerant Brown Norway rats.

General information
State: Published
Organisations: National Food Institute, Research Group for Gut Microbiology and Immunology
Authors: Madsen, C. B. (Intern), Bøgh, K. L. (Intern)
Number of pages: 1
Publication date: 2016
Event: Abstract from 4th Food Allergy and Anaphylaxis Meeting, Rome, Italy.
Main Research Area: Technical/natural sciences

Publication: Research - peer-review › Journal article – Annual report year: 2016

DOI: 10.1080/10408398.2013.779569
Source: FindIt
Source-ID: 2263192047
Linear epitope mapping of peanut allergens demonstrates individualized and persistent antibody-binding patterns
Characterization of the Immunogenicity and Allergenicity of Two Cow's Milk Hydrolysates – A Study in Brown Norway Rats

Hypoallergenic infant formulas based on hydrolysed milk proteins are used in the diet for cow's milk allergic infants. For a preclinical evaluation of the immunogenicity and allergenicity of new protein ingredients for such hypoallergenic infant formulas as well as for the investigation of which characteristics of hydrolysates that contribute to allergenicity, in vivo models are valuable tools. In this study, we examine the immunogenicity and allergenicity of two hydrolysates in a Brown Norway (BN) rat model, using i.p. dosing, which allows for the use of small quantities. Intact BLG, hydrolysed BLG and a hydrolysed whey product suitable for use in extensively hydrolysed formulas were thoroughly characterized for protein chemical features and administered to BN rats by i.p. immunization with or without adjuvant. Sera were analysed for specific IgG and IgE for evaluation of sensitizing capacity, immunogenicity and antibody-binding capacity. For evaluation of eliciting capacity a skin test was performed. The study showed that the hydrolysates had no residual allergenicity, lacking the capacity to sensitize and elicit reactions in the BN rats. Dosing with or without adjuvant induced a large difference in immunogenicity. Only antibodies from rats sensitized to intact BLG with adjuvant were able to bind the hydrolysates, and the whey-based hydrolysate only showed immunogenicity when dosed with adjuvant. This study showed that hydrolysates can be evaluated by an i.p. animal model, but that the choice of in vitro tests used for evaluation of antibody responses may greatly influence the result as well as may the use of adjuvant.

General information
State: Published
Organisations: National Food Institute, Division of Toxicology and Risk Assessment, Department of Systems Biology, Enzyme and Protein Chemistry
Authors: Bağh, K. L. (Intern), Barkholt, V. (Intern), Madsen, C. B. (Intern)
Development of two Brown Norway rat models for the assessment of primary prevention and desensitising capacity of cow's milk based hydrolysates

General information
State: Published
Organisations: National Food Institute, Research Group for Gut Microbiology and Immunology, Arla Foods
Authors: Bøgh, K. L. (Intern), Laursen, R. R. (Ekstern), Jacobsen, L. N. (Ekstern), Madsen, C. B. (Intern)
Number of pages: 1
Pages: 498-498
Publication date: 2015
Conference: European Academy of Allergy and Clinical Immunology Congress 2015, Barcelona, Spain, 06/06/2015 - 06/06/2015
Main Research Area: Technical/natural sciences

Publication information
Journal: Allergy
Volume: 70
Issue number: Supplement S101
Article number: 1224
ISSN (Print): 0105-4538
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 6.23 SJR 2.724 SNIP 2.475
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 3.13 SNIP 2.127 CiteScore 5.73
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 2.464 SNIP 2.121 CiteScore 5.51
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 2.195 SNIP 1.902 CiteScore 4.91
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 2.008 SNIP 1.818 CiteScore 4.81
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 2.328 SNIP 1.781 CiteScore 4.89
ISI indexed (2011): ISI indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.826 SNIP 1.845
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 1.681 SNIP 0.958
High-throughput sequencing enhanced phage display enables the identification of patient-specific epitope motifs in serum

Phage display is a prominent screening technique with a multitude of applications including therapeutic antibody development and mapping of antigen epitopes. In this study, phages were selected based on their interaction with patient serum and exhaustively characterised by high-throughput sequencing. A bioinformatics approach was developed in order to identify peptide motifs of interest based on clustering and contrasting to control samples. Comparison of patient and control samples confirmed a major issue in phage display, namely the selection of unspecific peptides. The potential of the bioinformatic approach was demonstrated by identifying epitopes of a prominent peanut allergen, Ara h 1, in sera from patients with severe peanut allergy. The identified epitopes were confirmed by high-density peptide micro-arrays. The present study demonstrates that high-throughput sequencing can empower phage display by (i) enabling the analysis of complex biological samples, (ii) circumventing the traditional laborious picking and functional testing of individual phage clones and (iii) reducing the number of selection rounds.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Fluidic Array Systems and Technology, Department of Systems Biology, Center for Biological Sequence Analysis, National Food Institute, Regulatory Genomics, Roche NimbleGen, Institute of Food Research, Medical University of Vienna
Number of pages: 13
Publication date: 2015
Main Research Area: Technical/natural sciences

Publication information
Journal: Scientific Reports
Volume: 5
Article number: 12913
ISSN (Print): 2045-2322
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 4.63 SJR 1.625 SNIP 1.401
Antibodies are molecules of tremendous importance. In their primary role, they protect our bodies against disease. However, in recent decades, scientists have harnessed the binding capabilities of antibodies and have applied them widely in research, diagnostics and therapeutics. Consequently, it is important to characterize antibodies thoroughly. In parallel to the characterization of antibodies, it is also important to characterize the binding area that is recognized by the antibody, known as an epitope. With the development of new technologies, such as high-throughput sequencing (HTS), it is important to determine how these methods can improve our understanding of antibodies and their epitopes. The overall objective of the presented studies was to investigate how emerging technologies (specifically HTS coupled with phage display and next-generation peptide microarrays) could be used for epitope mapping.

In Chapter 1, it was examined whether combining phage display, a traditional epitope mapping approach, with HTS would improve the method. The developed approach was successfully used to map Ara h 1 epitopes in sera from patients with peanut allergy. Notably, the sera represented difficult biological samples due to the rarity of the relevant antibodies and the polyclonal nature of serum. The inclusion of control samples enabled the development of a bioinformatic approach that identified peptide motifs of interest based on clustering and contrasting. A widespread problem in phage display, which is the unintended selection of peptides that are target-unspecific, was examined by comparing patient and control samples. The experiments highlighted that HTS can potentially improve on phage display by enabling the analysis of complex biological samples. Coupling the two methods furthermore has the capacity to omit traditional clone picking and functional testing which is a laborious part of phage display.

In the following study, Chapter 2, it was described how the approach developed in Chapter 1 could be utilized for a different application of phage display, specifically the identification of peptide binders. In this study, phage display screenings were used to identify peptides that could inhibit a major toxin in cobra snake venom, α-cobratoxin. Peptide inhibitors were successfully identified. Importantly, HTS enabled the identification of toxin inhibitors that were not discovered by traditional phage display.

Phage display coupled with HTS was again used in Chapter 3 in an attempt to map the epitopes of a therapeutic target injected into animals. The animals were immunized with a therapeutic target and the expectation was that they develop antibodies, which can be used in therapy. While no epitopes could be definitively identified, the study demonstrated the potential of the MiSeq HTS platform. Sequencing of the phage library also showed that many of the target-unspecific phages identified in the previous chapters, were frequent in the original library, thus indicating that they held proliferation advantages.

Finally, in Chapter 4, a different emerging technology, next-generation peptide microarrays, was applied for epitope mapping of major peanut allergens using sera from allergic patients. New developments in the peptide microarray have...
enabled a greatly increased throughput. In this study, these improvements were utilized to characterize epitopes at high resolution, i.e. determine the importance of each residue for antibody binding, for all major peanut allergens. Epitope reactivity among patients often converged on known epitope hotspots, however the binding patterns were somewhat heterogeneous when examined at the residue level. A high degree of correlation between IgE and IgG4 epitope binding patterns were observed, possibly indicating a common clonal origin. Finally, since the patients had been sampled over time it could be confirmed that the epitope binding patterns were stable over multiple years.

Taken together, the presented studies demonstrated new applications for the investigated techniques focusing on their utilization in epitope mapping. In the process, new insights were obtained into how antibodies recognize their targets in a major disease, i.e. food allergy.

The impact of processing and matrix on the antibody level, specificity and avidity raised against the peanut allergen Ara h 1

The presented studies demonstrated new applications for the investigated techniques focusing on their utilization in epitope mapping. In the process, new insights were obtained into how antibodies recognize their targets in a major disease, i.e. food allergy.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Fluidic Array Systems and Technology, National Food Institute, Research Group for Gut Microbiology and Immunology
Authors: Christiansen, A. (Intern), Dufva, M. (Intern), Bøgh, K. L. (Intern)
Number of pages: 149
Publication date: 2015

Publication information
Publisher: DTU Nanotech
Original language: English
Main Research Area: Technical/natural sciences
Electronic versions:
PhD_thesis_Anders_Christiansen.pdf
Source: PublicationPreSubmission
Source-ID: 119089162
Publication: Research › Ph.D. thesis – Annual report year: 2015

The impact of processing and matrix on the antibody level, specificity and avidity raised against the peanut allergen Ara h 1

The presented studies demonstrated new applications for the investigated techniques focusing on their utilization in epitope mapping. In the process, new insights were obtained into how antibodies recognize their targets in a major disease, i.e. food allergy.

General information
State: Published
Organisations: National Food Institute, Research Group for Gut Microbiology and Immunology, Institute of Food Research, University of Copenhagen
Authors: Jensen, L. H. (Intern), Madsen, C. B. (Intern), Kroghsbo, S. (Intern), Rigby, N. M. (Ekstern), Pozdnyakova, I. (Ekstern), Mills, E. N. C. (Ekstern), Bøgh, K. L. (Intern)
Number of pages: 1
Pages: 494-494
Publication date: 2015
Conference: European Academy of Allergy and Clinical Immunology Congress 2015, Barcelona, Spain, 06/06/2015 - 06/06/2015
Main Research Area: Technical/natural sciences

Publication information
Journal: Allergy
Volume: 70
Issue number: Supplement S101
Article number: 1213
ISSN (Print): 0105-4538
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 6.23 SJR 2.724 SNIP 2.475
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 3.13 SNIP 2.127 CiteScore 5.73
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
The influence of physico-chemical properties of cow's milk based hydrolysates on the allergenic versus primary preventive capacity.

General information
State: Published
Organisations: National Food Institute, Research Group for Gut Microbiology and Immunology, Arla Foods Ingredients Group P/S
Authors: Jensen, L. H. (Intern), Laursen, R. R. (Forskerdatabase), Madsen, C. B. (Intern), Neergaard Jacobsen, L. (Ekstern), Bøgh, K. L. (Intern)
Number of pages: 1
Publication date: 2015
Event: Abstract from 1st ImpARAS congress, Belgrade, Serbia.
Main Research Area: Technical/natural sciences
Publication: Research - peer-review > Conference abstract for conference – Annual report year: 2015
The influence of various forms of processing on the sensitising capacity of cow’s milk and peanut allergens

General information
State: Published
Organisations: National Food Institute, Research Group for Gut Microbiology and Immunology, Division of Food Chemistry, Technical University of Denmark, Institute of Food Research
Authors: Bøgh, K. L. (Intern), Kroghsbo, S. (Intern), Jensen, L. H. (Intern), Madsen, J. L. (Ekstern), Andreasen, M. S. (Intern), Rigby, N. M. (Ekstern), Mills, E. N. C. (Ekstern), Madsen, C. B. (Intern)
Number of pages: 1
Publication date: 2015
Event: Abstract from 1st ImpARAS congress, Belgrade, Serbia.
Main Research Area: Technical/natural sciences
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2015

The use of aluminum hydroxide as adjuvant modulates the antibody response to food allergens

General information
State: Published
Organisations: Division of Toxicology and Risk Assessment, National Food Institute, Research Group for Gut Microbiology and Immunology, Division of Food Chemistry
Authors: Bøgh, K. L. (Intern), Andreasen, M. S. (Intern), Madsen, C. B. (Intern)
Number of pages: 1
Publication date: 2015
Event: Food Allergy and Anaphylaxis Meeting 2014, Dublin, Ireland, 09/10/2014 - 09/10/2014
Main Research Area: Technical/natural sciences
Publication information
Journal: Clinical and Translational Allergy
Volume: 5
Issue number: Suppl 3
ISSN (Print): 2045-7022
Ratings:
Web of Science (2018): Indexed yes
Web of Science (2017): Indexed Yes
Scopus rating (2016): SJR 0.4 SNIP 0.441 CiteScore 1.13
Web of Science (2016): Indexed yes
Scopus rating (2015): SJR 0.377 SNIP 0.308 CiteScore 0.78
Web of Science (2015): Indexed yes
Scopus rating (2014): SJR 0.294 SNIP 0.164 CiteScore 0.62
Scopus rating (2013): SJR 0.269 SNIP 0.177 CiteScore 0.5
ISI indexed (2013): ISI indexed no
Scopus rating (2012): SJR 0.101 SNIP 0
ISI indexed (2012): ISI indexed no
Original language: English
Electronic versions:
DOIs: 10.1186/2045-7022-5-S3-P100
Source-ID: 108451951
Source: PublicationPreSubmission
Publication: Research - peer-review › Conference article – Annual report year: 2015

Transgenic DQ2 mice on a total knock out background have a suboptimal humoral immune response to gluten

General information
State: Published
Organisations: National Food Institute, Research Group for Gut Microbiology and Immunology, Odense University Hospital, Hvidovre Hospital
Authors: Madsen, C. B. (Intern), Kroghsbo, S. (Intern), Barington, T. (Forskerdatabase), Hansen, T. P. (Ekstern), Bøgh, K. L. (Intern), Sabir, H. J. (Forskerdatabase), Husby, S. (Ekstern), Toft-Hansen, H. (Forskerdatabase)
Ultra-high density peptide arrays demonstrate unique patient-specific IgE and IgG4 epitope patterns for peanut allergens that persist over multiple years

Clinicians are seeing a growing number of cashew nut allergic patients. One of the peculiarities of this allergy is that a minimal amount of cashew nut allergen may cause severe allergic reactions, suggesting high potency of the allergen comparable to other tree nuts and peanuts. The double blind placebo controlled food challenge (DBPCFC) test is currently the gold standard to establish cashew nut allergy. The development of predictive tools in diagnosing cashew nut allergy is needed and research should be done on cross-sensitization between cashew nut and other botanically related allergens.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Fluidic Array Systems and Technology, Department of Systems Biology, Center for Biological Sequence Analysis, National Food Institute, University of Vienna, Roche NimbleGen
Authors: Christiansen, A. (Intern), Hansen, C. S. (Intern), Eiwegger, T. (Ekstern), Sullivan, E. (Ekstern), Patel, J. (Ekstern), Kringleum, J. V. (Intern), Lund, O. (Intern), Szepfalusi, Z. (Ekstern), Bøgh, K. L. (Intern), Dufva, M. (Intern)
Number of pages: 1
Pages: 90-90
Publication date: 2015
Conference: European Academy of Allergy and Clinical Immunology Congress 2015, Barcelona, Spain, 06/06/2015 - 06/06/2015
Main Research Area: Technical/natural sciences

Publication information
Journal: Allergy
Volume: 70
Issue number: Suppl. 101
Article number: 183
ISSN (Print): 0105-4538
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 6.23 SJR 2.724 SNIP 2.475
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 3.13 SNIP 2.127 CiteScore 5.73
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 2.464 SNIP 2.121 CiteScore 5.51
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 2.195 SNIP 1.902 CiteScore 4.91
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 2.008 SNIP 1.818 CiteScore 4.81
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 2.328 SNIP 1.781 CiteScore 4.89
ISI indexed (2011): ISI indexed yes
A novel approach for characterisation of conformational allergen epitopes combining phage display and high-throughput sequencing

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Fluidic Array Systems and Technology, Department of Systems Biology, Center for Biological Sequence Analysis, Immunological Bioinformatics, National Food Institute, Division of Toxicology and Risk Assessment
Authors: Christiansen, A. (Intern), Hansen, C. S. (Intern), Kringelum, J. V. (Intern), Lund, O. (Intern), Bøgh, K. L. (Intern), Dufva, M. (Intern)
Pages: P27
Publication date: 2014

Main Research Area: Technical/natural sciences

Publication information
Journal: Clinical and Translational Allergy
Volume: 4
Issue number: Suppl 2
ISSN (Print): 2045-7022
Ratings:
Web of Science (2018): Indexed yes
Web of Science (2017): Indexed Yes
Scopus rating (2016): SJR 0.4 SNIP 0.441 CiteScore 1.13
Web of Science (2016): Indexed yes
Scopus rating (2015): SJR 0.377 SNIP 0.308 CiteScore 0.78
Web of Science (2015): Indexed yes
Scopus rating (2014): SJR 0.294 SNIP 0.164 CiteScore 0.62
Assessment of the Sensitizing Potential of Processed Peanut Proteins in Brown Norway Rats: Roasting Does Not Enhance Allergenicity

Background
IgE-binding of process-modified foods or proteins is the most common method for examination of how food processing affects allergenicity of food allergens. How processing affects sensitization capacity is generally studied by administration of purified food proteins or food extracts and not allergens present in their natural food matrix.

Objectives
The aim was to investigate if thermal processing increases sensitization potential of whole peanuts via the oral route. In parallel, the effect of heating on sensitization potential of the major peanut allergen Ara h 1 was assessed via the intraperitoneal route.

Methods
Sensitization potential of processed peanut products and Ara h 1 was examined in Brown Norway (BN) rats by oral administration of blanched or oil-roasted peanuts or peanut butter or by intraperitoneal immunization of purified native (N-), heated (H-) or heat glycated (G-)Ara h 1. Levels of specific IgG and IgE were determined by ELISA and IgE functionality was examined by rat basophilic leukemia (RBL) cell assay.

Results
In rats dosed orally, roasted peanuts induced significant higher levels of specific IgE to N ARA h 1 and 2 than blanched peanuts or peanut butter but with the lowest level of RBL degranulation. However, extract from roasted peanuts was found to be a superior elicitor of RBL degranulation. Process-modified Ara h 1 had similar sensitizing capacity as N ARA h 1 but specific IgE reacted more readily with process-modified Ara h 1 than with native.

Conclusions
Peanut products induce functional specific IgE when dosed orally to BN rats. Roasted peanuts do not have a higher sensitizing capacity than blanched peanuts. In spite of this, extract from roasted peanuts is a superior elicitor of RBL cell degranulation irrespectively of the peanut product used for sensitization. The results also suggest that new epitopes are formed or disclosed by heating Ara h 1 without glucose.

General information
State: Published
Organisations: National Food Institute, Division of Toxicology and Risk Assessment, Institute of Food Research, National Institute for Agronomic Research
Authors: Kroghsbo, S. (Intern), Rigby, N. M. (Ekstern), Johnson, P. L. F. (Ekstern), Adel-Patient, K. (Ekstern), Bøgh, K. L. (Intern), Salt, L. J. (Ekstern), Mills, E. N. C. (Ekstern), Madsen, C. B. (Intern)
Number of pages: 11
Publication date: 2014
Main Research Area: Technical/natural sciences

Publication information
Journal: P L o S One
Volume: 9
Issue number: 5
Article number: e96475
ISSN (Print): 1932-6203
Characterisation of the Ara h 1-specific IgE repertoire in peanut allergic patients using phage display technology and next generation sequencing

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Fluidic Array Systems and Technology, National Food Institute, Division of Toxicology and Risk Assessment, Department of Systems Biology, Center for Biological Sequence Analysis, Immunological Bioinformatics, Institute of Food Research, Medical University of Vienna
Authors: Christiansen, A. (Intern), Begh, K. L. (Intern), Kringelum, J. V. (Intern), Hansen, C. S. (Intern), Rigby, N. M. (Ekstern), Eiwegger, T. (Ekstern), Szepfalusi, Z. (Ekstern), Lund, O. (Intern), Dufva, M. (Intern)
IgE versus IgG4 epitopes of the peanut allergen Ara h 1 in patients with severe allergy

Background: Development and maintenance of tolerance to food allergens appears to be associated with alterations in antigen specific IgE and IgG4 responses. Previous studies have focused only on comparing IgE and IgG4 linear epitope recognition patterns but take no account of conformational epitopes. Objective: The aim of this study was to compare Ara h 1-specific IgE and IgG4 epitope recognition patterns in patients with severe peanut allergy, applying a method allowing for identification of both linear and conformational epitopes. Methods: Polyclonal sera from three individual patients, suffering from severe allergic reaction to peanuts, including anaphylaxis, were used to analyse the IgE and IgG4 epitope recognition patterns of the major peanut allergen Ara h 1. Epitope identification was conducted by competitive immuno-screening of a phage-displayed random heptamer peptide library. Resulting epitope-mimicking sequences were aligned for identification of consensus sequences and localised on the surface of the Ara h 1 molecule by a computer-based algorithm. Results: All epitope-mimicking sequences identified were found to correspond to conformational epitopes. Each individual patient had his/her own distinct IgE as well as IgG4 epitope recognition profile, though some important IgE epitopes were common to all patients. In general the IgG4 epitope pattern was more heterogeneous than the IgE pattern, did not coincide with IgE epitopes and had a lower affinity than IgE. Conclusions: This study demonstrated the usefulness of the phage-display technology in distinguishing between the epitope pattern of IgE and IgG4, giving detailed information on fine specificity and affinity. Competitive immuno-screening of phage-display random peptide libraries could be a future valuable tool to study the balance and dynamics of the IgE and IgG4 epitope recognition repertoire and provide a diagnostic tool giving information on the associated allergic phenotype. (C) 2013 Elsevier Ltd. All rights reserved.
Linear versus conformational epitopes of three cow's milk allergens

General information
State: Published
Organisations: National Food Institute, Division of Toxicology and Risk Assessment, Department of Systems Biology, Enzyme and Protein Chemistry, Technical University of Denmark

Amino Acid Sequence, Antigens, Plant, Epitope Mapping, Epitopes, Glycoproteins, Humans, Immunoglobulin E, Immunoglobulin G, Molecular Mimicry, Peanut Hypersensitivity, Plant Proteins, Sequence Alignment, Ara h 1 protein, Arachis hypogaea, 37341-29-0 Immunoglobulin E, peanut allergy Peanut Hypersensitivity (MeSH) immune system disease, Primates Mammalia Vertebrata Chordata Animalia (Animals, Chordates, Humans, Mammals, Primates, Vertebrates) - Hominidae [86215] human common, IgE, IgE epitope, IgG4, IgG4 epitope, peanut allergen Ara h 1 allergen , 10006, Clinical biochemistry - General methods and applications, 10064, Biochemistry studies - Proteins, peptides and amino acids, 13502, Food technology - General and methods, 15002, Blood - Blood and lymph studies, 15004, Blood - Blood cell studies, 34502, Immunology - General and methods, 34508, Immunology - Immunopathology, tissue immunology, 35500, Allergy, Allied Medical Sciences, Clinical Immunology, Human Medicine, Medical Sciences, serum blood and lymphatics, computer-based algorithm mathematical and computer techniques, phage-display technology laboratory techniques, genetic techniques, Allergy, Clinical Chemistry, Foods, BIOCHEMISTRY, IMMUNOLOGY, COWS MILK ALLERGY, PEPTIDE MICROARRAY IMMUNOASSAY, EFFECTOR CELL DEGRANULATION, E-BINDING EPITOPES, FOOD ALLERGY, SEQUENTIAL EPITOPES, ORAL IMMUNOTHERAPY, IMMUNOGLOBULIN-E, DOUBLE-BIND, SUBLINGUAL IMMUNOTHERAPY, Peanut allergy, Ara h 1, Phage-display, epitope, food allergen, immunoglobulin G4, peanut allergen Ara h 1, unclassified drug, amino acid composition, amino acid sequence, antibody affinity, antibody response, antigen purification, antigen recognition, article, biopanning, consensus sequence, controlled study, enzyme linked immunosorbent assay, epitope mapping, human, human tissue, peanut allergy , peptide library, phage display, priority journal, sequence alignment, IMMUNOGLOBULIN E

DOIs:
10.1016/j.molimm.2013.11.014

Source: FindIt
Source-ID: 258739268
Publication: Research - peer-review › Journal article – Annual report year: 2014
Mælkeproteiner og allergi: Kan modernærlserstatninger forebygge mælkeallergi?

General information
State: Published
Organisations: National Food Institute, Division of Toxicology and Risk Assessment
Authors: Bøgh, K. L. (Intern), Madsen, C. B. (Intern)
Pages: 10-11
Publication date: 2014
Main Research Area: Technical/natural sciences

Publication information
Journal: Mælkeritidende
Issue number: 11
ISSN (Print): 0024-9645
Ratings:
ISI indexed (2013): ISI indexed no
ISI indexed (2012): ISI indexed no
ISI indexed (2011): ISI indexed no
Original language: Danish
Electronic versions:
Moderm_lkserstatninger_og_allergiMT11.pdf
Publication: Research › Journal article – Annual report year: 2014
The impact of structural integrity and route of administration on the antibody specificity against three cow's milk allergens - a study in Brown Norway rats.

This study showed that the three-dimensional (3D) structure has a significant impact on the antibodies raised for both systemic and orally administered allergens. A remarkable difference in the antibody binding patterns against linear and conformational epitope was seen between the allergens, indicating that the structural characteristics of proteins may heavily affect the induced antibody response.

General information
State: Published
Organisations: National Food Institute, Division of Toxicology and Risk Assessment, Department of Systems Biology, Enzyme and Protein Chemistry, Technical University of Denmark, University of Copenhagen
Authors: Madsen, J. L. (Ekstern), Kroghsbo, S. (Intern), Madsen, C. B. (Intern), Pozdnyakova, I. (Ekstern), Barkholt, V. (Intern), Bøgh, K. L. (Intern)
Number of pages: 11
Publication date: 2014
Main Research Area: Technical/natural sciences

Experimental approaches to predict allergenic potential of novel food

There are many unanswered questions relating to food allergy sensitization in humans. We don't know under what circumstances sensitization takes place i.e. route (oral, dermal, respiratory), age, dose, frequency of exposure, infection or bystander effect of other allergens. In addition we don't know under what circumstances oral tolerance develops.

With all these unanswered questions, it is a big challenge to design an animal model that, with relatively few animals, is able to predict if a food protein is a potential allergen. An even larger challenge is to predict its potency, a prerequisite for risk evaluation. Attempts have been made to rank proteins according to their allergenic potency based on the magnitude of the IgE response in experimental animals. This ranking has not included abundance as a parameter. We may be able to predict potential allergenicity i.e. hazard but our lack of understanding of the significance of dose for the development of food allergy or its counterpart oral tolerance makes risk assessment very difficult. In addition route of exposure and digestibility are relevant variables. Examples of the use and limitations of animal models for predicting the allergenicity of food proteins will be given. Possibilities and pitfalls will be discussed.

General information
State: Published
Organisations: National Food Institute, Division of Toxicology and Risk Assessment
IgE vs IgG4 epitopes of the peanut allergen Ara h 1 in patients with severe allergy

Background: Development and maintenance of tolerance to food allergens may be associated with increased levels of specific IgG4. It has been suggested that co-localisation of IgG4 and IgE binding epitopes may be of great significance for the tolerance, where IgG4 may act by blocking IgE binding to the allergen. However, recent studies have demonstrated the very importance of the IgG4-epitope affinity for the blocking ability. Studies comparing IgE and IgG4 binding epitopes mainly focus on the identification of linear epitopes.

Peanut allergy is one of the most severe and persistent forms of food allergy. The importance of conformational epitopes, of the major peanut allergen Ara h 1, has been demonstrated. The aim of this study was to compare Ara h 1-specific epitope patterns for IgE and IgG4 in patients with severe peanut allergy applying a method suitable to identify both linear and conformational epitopes.

Methods: Ara h 1-specific IgE and IgG4 epitope patterns were examined by competitive immunoscreening of a phage-displayed random 7-mer peptide library using polyclonal IgE and IgG4 from three individual patients suffering from severe peanut allergy. The resulting peptide sequences were mapped on the surface of a 3D model of the Ara h 1 molecule to mimic epitopes by the use of a computer-based algorithm.

Results: All identified epitope mimics corresponded to conformational epitopes. Each individual peanut allergic patient had his/her own distinct IgE as well as IgG4 epitope binding profile. Although three motifs were identified for all three patients and accounted for half of all identified IgE epitope mimics, no consensus motifs were identified for IgG4. Even though the epitopes overlapped, the IgG4 binding epitope mimics were more heterogeneous than the IgE binding epitope mimics. In addition a higher epitope binding affinity for IgE than IgG4 was indicated.

Conclusion: This preliminary study using competitive immunoscreening of a phage-displayed peptide library successfully distinguished IgE binding patterns from IgG4 binding patterns. The method allows an identification of both, linear and conformational epitopes and gives information on the specificity, diversity and affinity of the identified epitope mimics. This could be a valuable tool to study the balance and dynamics of the antibody IgE- and IgG4-repertoire, and increase the knowledge and understanding of the mechanisms involved in the development of allergy and tolerance.

General information
State: Published
Organisations: National Food Institute, Division of Toxicology and Risk Assessment, Novozymes A/S, Medical University of Vienna, Institute of Food Research
Authors: Bøgh, K. L. (Intern), Nielsen, H. (Ekstern), Eiwegger, T. (Ekstern), Madsen, C. B. (Intern), Mills, E. N. C. (Ekstern), Szépfalusi, Z. (Ekstern), Roggen, E. L. (Ekstern)
Pages: 88-89
Publication date: 2013
Conference: European Academy of Allergy and Clinical Immunology & World Allergy Organization World Allergy & Asthma Congress, Milan, Italy, 22/06/2013 - 22/06/2013
Main Research Area: Technical/natural sciences
The Sensitising Capacity of Intact β-Lactoglobulin Is Reduced by Co-Administration with Digested β-Lactoglobulin

Background: It is generally believed that protein hydrolysis in the gastrointestinal tract decreases the allergenicity of food allergens. However, it remains unknown if specific properties of digestion products determine whether a sensitisation or tolerogenic immune response will develop. We sought to examine the sensitising capacity of the cow’s milk allergen β-lactoglobulin (BLG) and digestion products thereof in a Brown Norway (BN) rat model. Methods: Intact BLG was digested in an in vitro model simulating the gastro-duodenal digestion process and subsequently fractionated by gel permeation chromatography. BN rats were dosed with either PBS, 200 μg of intact BLG, 30 μg of intact BLG, 200 μg of partially digested BLG, 200 μg of digested BLG, or with 200 μg of a fraction of large complexes or a fraction of small complexes.
Sera from BN rats were analysed for specific antibodies and avidity was measured. Results: BLG partly resisted the digestion process. However, the BLG molecules that did not survive the digestion process were rapidly broken down to peptides of sizes less than Mr 4,500. Specific antibody responses revealed that both 200 and 30 μg of intact BLG had immunogenic as well as sensitising capacity, while digested BLG could not induce any specific antibodies. Most importantly, while intact BLG showed a significant sensitising capacity when administered alone, this sensitising capacity was significantly reduced when co-administered with digested BLG. Conclusions: Co-immunisation of intact BLG with digested BLG reduces the sensitising capacity of intact BLG, which could result from tolerogenic mechanisms induced by the digestion products.
Digested Ara h 1 Loses Sensitizing Capacity When Separated into Fractions

The major peanut allergen Ara h 1 is an easily digestible protein under physiological conditions. The present study revealed that pepsin digestion products of Ara h 1 retained the sensitizing potential in a Brown Norway rat model, while this sensitizing capacity was lost by separating the digest into fractions by gel permeation chromatography. Protein chemical analysis showed that the peptide composition as well as the aggregation profiles of the fractions of Ara h 1 digest differed from that of the whole pool. These results indicate that the sensitizing capacity of digested Ara h 1 is a consequence of the peptides being in an aggregated state resembling the intact molecule or that most peptides of the digests need to be present in the same solution, having a synergistic or adjuvant effect and thereby augmenting the immune response against other peptides.

General information
State: Published
Organizations: National Food Institute, Division of Toxicology and Risk Assessment, Department of Systems Biology, Enzyme and Protein Chemistry, Institute of Food Research
Authors: Bøgh, K. L. (Intern), Barkholt, V. (Intern), Rigby, N. M. (Ekstern), Mills, E. N. C. (Ekstern), Madsen, C. B. (Intern)
Pages: 2934-2942
Publication date: 2012
Main Research Area: Technical/natural sciences

Publication information
Journal: Journal of Agricultural and Food Chemistry
Volume: 60
Issue number: 11
ISSN (Print): 0021-8561
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 3.45 SJR 1.291 SNIP 1.344
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 1.236 SNIP 1.253 CiteScore 3.23
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 1.278 SNIP 1.421 CiteScore 3.25
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 1.423 SNIP 1.479 CiteScore 3.44
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 1.43 SNIP 1.471 CiteScore 3.2
Digested BLG can induce tolerance when co-administered with intact BLG in Brown Norway rats

Background: Milk is a major constituent of small children’s diet. Milk allergy is also one of the most common allergies in small children. Prevention, treatment and general understanding of this allergy are therefore important.

Methods: Intact BLG was digested in an in vitro model simulating the human gastro-duodenal digestion process. Four different fractions of BLG-digesta were made, based on sizes of peptides or aggregates hereof. Intact BLG and the four fractions of BLG-digesta were characterized by protein chemical analyses. Brown Norway (BN) rats were immunised i.p. three times without the use of adjuvant with either PBS (control), 200 µg of intact BLG, 30 µg of intact BLG, 200 µg of digested BLG (with 30 µg of intact BLG), 200 µg of digested BLG, 200 µg of a fraction of large complexes or 200 µg of a fraction of small complexes (all three without intact BLG). Sera from BN rats were analysed for specific IgG and IgE responses and avidity of specific antibodies was measured.

Results: Native BLG is relatively resistant to digestion. However, when first broken down to larger fragments these are rapidly digested to smaller peptides of sizes ≤ 4.5 kDa. The small peptides did aggregate to complexes of larger sizes. Specific antibody responses revealed that both the high (200 µg) and low (30 µg) amount of intact BLG had both immunogenic and allergenic sensitising capacity, while digested BLG had no sensitizing capacity. In contrast digested
BLG and the fraction of large complexes retained their antibody binding capacity. Most importantly, while intact BLG showed a significant sensitising capacity when administered alone, the sensitising capacity of the intact BLG was significantly reduced when co-administered with digested BLG.

Conclusion: Co-administration of intact and digested BLG reduced sensitising capacity of intact BLG, indicating induction of tolerance or other protective mechanism by the digested BLG.

General information
State: Published
Organisations: National Food Institute, Division of Toxicology and Risk Assessment, Department of Systems Biology
Authors: Bøgh, K. L. (Intern), Barkholt, V. (Intern), Madsen, C. B. (Intern)
Number of pages: 1
Publication date: 2012
Event: Abstract from 2th Pediatric Allergy & Asthma Meeting, Barcelona, Spain.
Main Research Area: Technical/natural sciences
Electronic versions:
11.pdf
Source: dtu
Source-ID: u::5548
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2012

Food allergen digestibility: The influence on allergenicity
Food allergy is a major health problem in the Western countries, affecting 3-8% of the population. What makes a dietary protein a food allergen has not yet been established, though several characteristics have been proposed to be shared by the food allergens. One of the features believed to be a general characteristic is resistance to digestion. This is based on studies showing that allergenic dietary proteins in general were more resistant to digestion than dietary proteins with no proven allergenicity, leading to the conclusion, that a correlation between stability to digestion and allergenic potential exist. Resistance to digestion is therefore a test parameter included in the safety assessment of the allergenic potential of novel proteins in genetically modified foods. In recent years, the association between resistance to digestion and allergenic potential has been challenged.

When reviewing existing data from digestibility studies on known food allergens, it becomes evident that food allergens do not necessarily resist digestion. However, the choice of assay conditions, the method used for detection of residual intact protein as well as fragments hereof greatly influences the outcome. Studies assessing the allergenicity of digestion products, by either IgE-binding, elicitation or sensitising capacity, shows that digestion may abolish, decrease, have no effect, or even increase the allergenicity of food allergens. However, this dependents on the given allergen.

In conclusion, reviewing existing digestibility data shows that no absolute correlation between resistance to digestion and allergenic potential exist. Therefore stability to digestion may not necessarily be a good parameter for assessing the allergenic potential of novel proteins. Even very small peptides from food allergens may retain both IgE-binding, eliciting and sensitising capacity. As a consequence immunological studies should be performed when evaluating the digestibility of protein allergens.

General information
State: Published
Organisations: National Food Institute, Division of Toxicology and Risk Assessment
Authors: Bøgh, K. L. (Intern), Madsen, C. B. (Intern)
Number of pages: 2
Publication date: 2012
Main Research Area: Technical/natural sciences
Electronic versions:

Bibliographical note
Oral presentation
Source: dtu
Source-ID: u::5545
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2012

IgE epitopes of intact and digested Ara h 1: A comparative study in humans and rats
Background Allergen epitope characterization provides valuable information useful for the understanding of proteins as food allergens. It is believed that IgE epitopes in general are conformational, nevertheless, for food allergens known to sensitize through the gastrointestinal tract linear epitopes have been suggested to be of great importance. ObjectiveThe aim of this study was to identify IgE specific epitopes of intact and digested Ara h 1, and to compare epitope patterns between humans and rats. MethodsSera from five peanut allergic patients and five Brown Norway rats were used to identify intact and digested Ara h 1-specific IgE epitopes by competitive immunoscreening of a phage-displayed random hepta-mer peptide library using polyclonal IgE from the individual sera. The resulting peptide sequences were mapped on
the surface of a three-dimensional structure of the Ara h 1 molecule to mimic epitopes using a computer-based algorithm. Results Patients as well as rats were shown to have individual IgE epitope patterns. All epitope mimics were conformational and found to cluster into three different areas of the Ara h 1 molecule. Five epitope motifs were identified by patient IgE, which by far accounted for most of the eluted peptide sequences. Epitope patterns were rather similar for both intact and digested Ara h 1 as well as for humans and rats. Conclusions Individual patient specific epitope patterns have been identified for the major allergen Ara h 1. IgE binding epitopes have been suggested as biomarkers for persistency and severity of food allergy, wherefore recognition of particular epitope patterns or motifs could be a valuable tool for prevention, diagnosis, and treatment of food allergy.

General information
State: Published
Organisations: National Food Institute, Division of Toxicology and Risk Assessment, Novozymes A/S, Institute of Food Research, Medical University of Vienna
Pages: 337-346
Publication date: 2012
Main Research Area: Technical/natural sciences

Publication information
Journal: Molecular Immunology
Volume: 51
Issue number: 3-4
ISSN (Print): 0161-5890
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Web of Science (2016): Indexed yes
Scopus rating (2016): CiteScore 3.2 SJR 1.523 SNIP 0.961
BFI (2015): BFI-level 1
Web of Science (2015): Indexed yes
Scopus rating (2015): SJR 1.572 SNIP 0.928 CiteScore 3.16
BFI (2014): BFI-level 1
Web of Science (2014): Indexed yes
Scopus rating (2014): SJR 1.474 SNIP 0.916 CiteScore 2.89
BFI (2013): BFI-level 1
Web of Science (2013): Indexed yes
Scopus rating (2013): SJR 1.46 SNIP 0.94 CiteScore 2.89
ISI indexed (2013): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2012): BFI-level 1
ISI indexed (2012): ISI indexed yes
Scopus rating (2012): SJR 1.406 SNIP 0.862 CiteScore 2.94
BFI (2011): BFI-level 1
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
Scopus rating (2011): SJR 1.403 SNIP 0.874 CiteScore 3.01
BFI (2010): BFI-level 1
ISI indexed (2010): ISI indexed yes
Web of Science (2010): Indexed yes
Scopus rating (2010): SJR 1.39 SNIP 0.861
BFI (2009): BFI-level 1
Web of Science (2009): Indexed yes
Scopus rating (2009): SJR 1.482 SNIP 0.905
BFI (2008): BFI-level 2
Web of Science (2008): Indexed yes
Scopus rating (2008): SJR 1.556 SNIP 0.929
Scopus rating (2007): SJR 1.944 SNIP 1.075
Limitations and possibilities of animal models for human allergenic risk evaluation

There are many unanswered questions relating to food allergy sensitization in humans. We don't know under what circumstances sensitization takes place i.e. route (oral, dermal, respiratory), age, dose, frequency of exposure, infection or bystander effect of other allergens. In addition we don't know under what circumstances oral tolerance develops. With all these unanswered questions, it is a big challenge to design an animal model that, with relatively few animals, is able to predict if a food allergen is not only a potential allergen but also predict its potency, a prerequisite for risk evaluation.

One of the pitfalls may be the premise that an animal model needs to mimic the disease. Chemical contact sensitizers may be predicted in an animal test, the Local Lymph Node Assay (LLNA). This assay is based on detailed mechanistic knowledge of contact sensitization including knowledge on dose-response relationship. The outcome of the test is sensitization measured as cell proliferation in the regional lymph node.

Animal models in food allergy can be used to increase our understanding of food allergens and food allergy sensitization e.g. the influence of digestion or processing or to compare closely related allergens. Examples of this will be given.

General information
State: Published
Organisations: National Food Institute, Division of Toxicology and Risk Assessment
Authors: Madsen, C. B. (Intern), Kroghsbo, S. (Intern), Bøgh, K. L. (Intern)
Number of pages: 1
Pages: 11-11
Publication date: 2012

Host publication information
Title of host publication: The 7th meeting of the Immunotoxicology and Chemical Allergy Speciality Section ITCASS
Place of publication: Kgs. Lyngby
Publisher: Technical University of Denmark (DTU)
Main Research Area: Technical/natural sciences
Conference: 7th Meeting of the Immunotoxicology and Chemical Allergy Speciality Section, Helsingør, Denmark, 30/08/2012 - 30/08/2012
Electronic versions:
Limitations_and_possibilities_of_animal_models_for_human_allergenic_risk_evaluation.pdf

Relations
Activities:
7th Meeting of the Immunotoxicology and Chemical Allergy Speciality Section
Publication: Research - peer-review » Conference abstract in proceedings – Annual report year: 2013
Sensitising capacity of peptides from food allergens

Food allergy is a major health problem in the Western countries, affecting 3-8% of the population. What makes a dietary protein a food allergen has not yet been established, though several characteristics have been proposed to be shared by food allergens. One of the features believed to be a general characteristic of food allergens is resistance to digestion. This is based on studies showing that allergenic dietary proteins in general are more resistant to digestion than dietary proteins with no proven allergenicity, concluding that a correlation between stability to digestion and allergenic potential exist. Resistance to digestion is for this reason a test parameter included in the safety assessment of the allergenic potential of novel proteins in genetically modified foods. The association between resistance to digestion and allergenic potential has though been challenged in recent years. This PhD project aimed to investigate the sensitising potential of digestion products from the peanut allergen Ara h 1 and the cow’s milk allergen β-lactoglobulin (BLG) in a Brown Norway (BN) rat model. Further the project aimed to compare the IgE binding epitopes of intact and digested Ara h 1. This was done by digesting Ara h 1 and BLG in an in vitro model simulating the human gastric or gastro-duodenal digestion process. Simulated gastric digestion was performed with immobilised pepsin for 120 min at pH 2.5, while simulated duodenal digestion was performed with immobilised trypsin and chymotrypsin for 15 min at pH 6.5. Fractions of digestion products were made by separating the peptide fragments according to sizes in gel permeation chromatography (GPC). The intact allergens as well as digestion products hereof were thoroughly characterised by reverse phase high-performance liquid chromatography, MALDI-TOF mass spectrometry, amino acid analysis and GPC. To study the sensitising capacity groups of BN rats were immunised with the intact allergen or digestion products hereof by i.p. immunisation and specific antibody responses were examined by ELISAs, RBL-assay or avidity measurements. Comparison of intact and digested Ara h 1-specific IgE binding epitopes were performed by competitive immunoscreening using a random phage-displayed peptide library followed by mapping the identified IgE-binding epitope mimics on the surface of the Ara h 1 molecule. In addition to sera from the sensitised BN rats, sera from peanut allergic patients were used. Both the gastric as well as the gastro-duodenal digestes of the peanut allergen Ara h 1 were found to be very efficient for sensitising the BN rats. While gastric digest consisted of peptide fragments of up to Mr 4,000 the duodenal digest consisted of peptide fragments of up to Mr 2,000, yet both the peptide fragments in the gastric as well as in the gastro-duodenal digestes were aggregated to complexes of larger sizes. After separation of the digested Ara h 1 into fractions the sensitising capacity was lost, though the IgE-binding capacity was retained. Epitope mapping of intact and digested Ara h 1 showed IgE binding epitopes of Ara h 1 to be conformational in origin and at least to some extent surviving the digestion process. For the peanut allergic patients five motifs were found to account for more than 65% of all identified epitope mimics and were found for both the intact as well as the digested Ara h 1. Digested BLG with peptide sizes of up to Mr 4,500 could on the other hand not induce any sensitisation response in the BN rats. They were instead suggested to possess tolerogenic capacity when co-administered together with intact BLG. The results presented in the current thesis demonstrate that even very small peptide fragments, originally thought to be too small to act as a food allergens may indeed possess all features of a ‘complete’ allergen. This implies that an association between allergenicity and resistance to digestion is not an absolute feature of food allergens. The presented work indicates that peptide fragments may either possess sensitising capacity per se or that the observed allergenic capacity could be a result of the small peptide fragments aggregating to complexes of larger sizes. The importance of formation of aggregates is suggested by the epitope mapping study, where survival of conformational epitopes is demonstrated. This together with the findings, that fractionation of digestion products leads to a loss of the sensitising potential, reveals that the allergenicity had to be more than simply a result of the small peptide fragments aggregating, and more a result of them being in an aggregated state resembling the intact Ara h 1 molecule. While small peptide fragments derived from one food allergen may retain sensitising capacity this is not necessarily the truth for other food allergens. This was demonstrated with the cow’s milk allergen BLG, from which peptide fragments were shown not to be efficient for inducing any specific antibodies. Instead the results indicated that the peptide fragments derived from BLG had tolerogenic capacity, demonstrating that while some mixtures of peptides may guide the immune system in one direction, other mixtures of peptides may guide the immune system in another direction. Together these results demonstrate that several characteristics of digestion products from food allergens may collectively contribute the allergenic potential, where more than just peptide sizes and structures may contribute. In conclusion, the experimental data presented in this PhD thesis contribute to the understanding of induction of allergy by investigating the sensitising potential of peptides derived from a food allergen. It add knowledge to our
understanding of the mechanisms underlying the sensitisation, but at the same time points to the difficulties, if not
infeasibilities, in identifying features that can be used as an ubiquitous marker for allergenicity of a dietary protein.

**General information**
State: Published
Organisations: National Food Institute, Division of Toxicology and Risk Assessment, Department of Systems Biology, Enzyme and Protein Chemistry
Authors: Bøgh, K. L. (Intern), Madsen, C. B. (Intern), Barkholt, V. (Intern)
Number of pages: 139
Publication date: 2012

**Publication information**
Place of publication: Søborg
Publisher: DTU Food
ISBN (Electronic): 978-87-92763-28-0
Original language: English
Main Research Area: Technical/natural sciences
Electronic versions:
Source: dtu
Source-ID: u::4992
Publication: Research › Ph.D. thesis – Annual report year: 2012

The influence of digestibility on the allergenicity of food allergens

Food allergy is a major health problem in the Western countries, affecting 3-8% of the population. What makes a dietary protein a food allergen has not yet been established, though several characteristics have been proposed to be shared by the food allergens. One of the features believed to be a general characteristic is resistance to digestion. This is based on studies showing that allergenic dietary proteins in general were more resistant to digestion than dietary proteins with no proven allergenicity, leading to the conclusion, that a correlation between stability to digestion and allergenic potential exist. Resistance to digestion is therefore a test parameter included in the safety assessment of the allergenic potential of novel proteins in genetically modified foods. In recent years, the association between resistance to digestion and allergenic potential has been challenged.

When reviewing existing data from digestibility studies on known food allergens, it becomes evident that food allergens do not necessarily resist digestion. However, the choice of assay conditions, the method used for detection of residual intact protein as well as fragments hereof greatly influences the outcome. Studies assessing the allergenicity of digestion products, by either IgE-binding, elicitation or sensitising capacity, shows that digestion may abolish, decrease, have no effect, or even increase the allergenicity of food allergens. However, this dependents on the given allergen.

In conclusion, reviewing existing digestibility data shows that no absolute correlation between resistance to digestion and allergenic potential exist. Therefore stability to digestion may not necessarily be a good parameter for assessing the allergenic potential of novel proteins. Even very small peptides from food allergens may retain both IgE-binding, eliciting and sensitising capacity. As a consequence immunological studies should be performed when evaluating the digestibility of protein allergens.

**General information**
State: Published
Organisations: National Food Institute, Division of Toxicology and Risk Assessment
Authors: Bøgh, K. L. (Intern), Madsen, C. B. (Intern)
Number of pages: 1
Pages: 9-9
Publication date: 2012

**Host publication information**
Title of host publication: The 7th meeting of the Immunotoxicology and Chemical Allergy Speciality Section ITCASS
Place of publication: Kgs. Lyngby
Publisher: Technical University of Denmark (DTU)
Main Research Area: Technical/natural sciences
Conference: 7th Meeting of the Immunotoxicology and Chemical Allergy Speciality Section, Helsingør, Denmark, 30/08/2012 - 30/08/2012
Electronic versions:
The_influence_of_digestibility_on_the_allergenicity_of_food_allergens.pdf

**Relations**
Activities:
7th Meeting of the Immunotoxicology and Chemical Allergy Speciality Section
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2013
Milk hydrolysis products may retain their allergenic reactivity

Background: Milk allergy is one of the most common allergies in small children. Extensively hydrolyzed milk formulas are therefore an important source of nutrients for infants being predisposed for allergy and not being breastfeed and to infants with cows milk allergy. The aim of this study was to investigate some extensively hydrolyzed milk whey products for their ability to retain sensitizing and reacting activity in a Brown Norway (BN) rat model.

Method: BN rats were immunized i.p. three times without the use of adjuvant with 200 µg of either PBS (control), intact β-lactoglobulin (BLG), enzyme hydrolyzed BLG or the enzyme hydrolysis product PEPTIGEN IF-3080 from Arla, Denmark. There was no intact BLG left in the two hydrolysates. Sera from BN rats were analyzed for specific IgG and IgE.

Result: The study showed that while intact BLG had a significant sensitizing capacity, both hydrolyzed BLG and PEPTIGEN had no sensitizing capacity. However, antibodies from all rats immunized with the intact BLG could still react with both hydrolyzed BLG and PEPTIGEN in a manner that was statistically significant.

Conclusion: The extensively hydrolyzed milk whey products investigated in this study showed no sensitizing capacity, but could bind to antibodies raised in rats immunized with intact BLG. The results in this study resemble observations seen in humans where infants sensitized to cow’s milk may react to extensively hydrolyzed infant formulas. These observations should lead to the development of new standards for extensively hydrolyzed infant formulas based on peptide sizes rather than degree of hydrolysis (DH).
allergens, they induce antibodies with different antigen-binding characteristics. Peanut 7S induces IgE of a higher avidity than hazelnut and pea 7S which, again, has a higher avidity than IgE induced by soy 7S. We also show that soy tolerance influences the function of antibodies to peanut 7S. These findings may help explain how antibodies of different clinical significances can develop in different individuals sensitized to the same allergen.

**General information**

*State:* Published  
*Organisations:* Division of Toxicology and Risk Assessment, National Food Institute, Institute of Food Research, Neogen Europe  
*Authors:* Kroghsbo, S. (Intern), Bøgh, K. L. (Intern), Rigby, N. M. (Ekstern), Mills, E. C. (Ekstern), Rogers, A. (Ekstern), Madsen, C. B. (Intern)  
*Pages:* 212-224  
*Publication date:* 2011  
*Main Research Area:* Technical/natural sciences

**Publication information**

*Journal:* International Archives of Allergy and Immunology  
*Volume:* 155  
*Issue number:* 3  
*ISSN (Print):* 1018-2438  
*Ratings:*  
BFI (2018): BFI-level 1  
Web of Science (2018): Indexed yes  
BFI (2017): BFI-level 1  
Web of Science (2017): Indexed Yes  
BFI (2016): BFI-level 1  
Scopus rating (2016): SJR 0.985 SNIP 1.072 CiteScore 2.61  
BFI (2015): BFI-level 1  
Scopus rating (2015): SJR 1.202 SNIP 1.058 CiteScore 2.48  
BFI (2014): BFI-level 1  
Scopus rating (2014): SJR 0.948 SNIP 1.044 CiteScore 2.57  
BFI (2013): BFI-level 1  
Scopus rating (2013): SJR 0.872 SNIP 1.092 CiteScore 2.36  
ISI indexed (2013): ISI indexed yes  
Web of Science (2013): Indexed yes  
BFI (2012): BFI-level 1  
Scopus rating (2012): SJR 0.832 SNIP 0.923 CiteScore 2.28  
ISI indexed (2012): ISI indexed yes  
BFI (2011): BFI-level 1  
Scopus rating (2011): SJR 1.022 SNIP 1.015 CiteScore 2.47  
ISI indexed (2011): ISI indexed yes  
Web of Science (2011): Indexed yes  
BFI (2010): BFI-level 1  
Scopus rating (2010): SJR 0.835 SNIP 0.963  
Web of Science (2010): Indexed yes  
BFI (2009): BFI-level 1  
Scopus rating (2009): SJR 0.856 SNIP 0.946  
BFI (2008): BFI-level 1  
Scopus rating (2008): SJR 0.902 SNIP 0.943  
Scopus rating (2007): SJR 0.93 SNIP 0.957  
Scopus rating (2006): SJR 0.991 SNIP 1.037  
Web of Science (2006): Indexed yes  
Scopus rating (2005): SJR 0.903 SNIP 1.013  
Web of Science (2005): Indexed yes  
Scopus rating (2004): SJR 0.861 SNIP 0.746  
Web of Science (2004): Indexed yes  
Scopus rating (2003): SJR 0.772 SNIP 0.892
Can soy tolerance protect against peanut allergy?

General information
State: Published
Organisations: Division of Toxicology and Risk Assessment, National Food Institute, Institute of Food Research, Gen-Probe
Authors: Kroghsbo, S. (Intern), Bøgh, K. L. (Intern), Rigby, N. (Ekstern), Rogers, A. (Ekstern), Mills, E. C. (Ekstern), Madsen, C. B. (Intern)
Publication date: 2010
Event: Abstract from The XXIX Congress of the European Academy of Allergy and Clinical Immunology, London, United Kingdom
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 271932
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2010

Digested Ara h 1 has sensitizing capacity in Brown Norway rats

General information
State: Published
Organisations: Division of Toxicology and Risk Assessment, National Food Institute, Enzyme and Protein Chemistry, Department of Systems Biology, Technical University of Denmark, Institute of Food Research
Authors: Bøgh, K. L. (Intern), Kroghsbo, S. (Intern), Dahl, L. (Ekstern), Rigby, N. M. (Ekstern), Barkholt, V. (Intern), Mills, E. N. C. (Ekstern), Madsen, C. B. (Intern)
Pages: 1611-1621
Publication date: 2009
Main Research Area: Technical/natural sciences

Publication information
Journal: Clinical and Experimental Allergy
Volume: 39
Issue number: 10
ISSN (Print): 0954-7894
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 2.117 SNIP 1.46 CiteScore 4.26
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 2.193 SNIP 1.454 CiteScore 4.15
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.9 SNIP 1.667 CiteScore 4.1
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.629 SNIP 1.517 CiteScore 3.95
ISI indexed (2013): ISI indexed yes
Food processing affects the immunogenic and allergenic potential of peanut and soy allergens in an oral rat model

General information
State: Published
Organisations: Division of Toxicology and Risk Assessment, National Food Institute, Institute of Food Research
Authors: Kroghsbo, S. (Intern), Rigby, N. (Ekstern), Mackie, A. (Ekstern), Mills, C. (Ekstern), Salt, L. (Ekstern), Bøgh, K. L. (Intern), Madsen, C. B. (Intern)
Pages: 373-374
Publication date: 2009
Main Research Area: Technical/natural sciences

Publication information
Journal: Allergy. European Journal of Allergy and Clinical Immunology
Volume: 64
Issue number: Suppl 90
ISSN (Print): 0105-4538
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Comparison of sensitisation potential of 7S globulins from peanut, hazelnut, soy and pea

General information
State: Published
Organisations: Division of Toxicology and Risk Assessment, National Food Institute
Authors: Kroghsbo, S. (Intern), Rigby, N. M. (Ekstern), Mills, E. N. C. (Ekstern), Bøgh, K. L. (Intern), Madsen, C. B. (Intern)
Publication date: 2008
Event: Abstract from Immunotoxicology and Chemical Allergy Specialty Section meeting, Oslo, Norway.
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 238616
Publication: Research › Conference abstract for conference – Annual report year: 2008

**Digested Ara h 1 retains its sensitising capacity in Brown Norway rats**

**General information**
State: Published
Organisations: Division of Toxicology and Risk Assessment, National Food Institute, Enzyme and Protein Chemistry, Department of Systems Biology
Authors: Bøgh, K. L. (Intern), Kroghsbo, S. (Intern), Dahl, L. (Ekstern), Barkholt, V. (Intern), Rigby, N. M. (Ekstern), Mills, E. N. C. (Ekstern), Madsen, C. B. (Intern)
Publication date: 2008
Event: Abstract from 8th Nordic Symposium on Allergy, Sønderborg, .
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 234773
Publication: Research › Conference abstract for conference – Annual report year: 2008

**Mælkeproteiner og allergi: Kan aggregater af peptider fra nedbrudte mælkeproteiner medføre en udvikling af mælkeallergi**

**General information**
State: Published
Organisations: Division of Toxicology and Risk Assessment, National Food Institute, Enzyme and Protein Chemistry, Department of Systems Biology
Authors: Bøgh, K. L. (Intern), Madsen, C. B. (Intern), Barkholt, V. (Intern)
Pages: 252-254
Publication date: 2008
Main Research Area: Technical/natural sciences

**Publication information**
Journal: Mælkeritidende
Volume: 10
ISSN (Print): 0024-9645
Ratings:
ISI indexed (2013): ISI indexed no
ISI indexed (2012): ISI indexed no
ISI indexed (2011): ISI indexed no
Original language: Danish
Source: orbit
Source-ID: 233477
Publication: Communication › Journal article – Annual report year: 2008

**Sensitisation capacity of intact and digested 2S albumin from Brazil nut in a Brown Norway rat model**

**General information**
State: Published
Organisations: Division of Toxicology and Risk Assessment, National Food Institute
Authors: Kroghsbo, S. (Intern), Rigby, N. M. (Ekstern), Bøgh, K. L. (Intern), Mills, E. N. C. (Ekstern), Madsen, C. B. (Intern)
Publication date: 2008
Event: Abstract from Nordic Research Symposium in Allergy, Sønderborg, Denmark, .
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 234822
Publication: Research › Conference abstract for conference – Annual report year: 2008

**Degraded food allergens may retain their sensitising capacity**

**General information**
State: Published
Organisations: National Food Institute, Division of Toxicology and Risk Assessment, Technical University of Denmark, Institute of Food Research
**Epitope mapping of intact and digested Ara h 1**

**General information**
State: Published
Organisations: Division of Toxicology and Risk Assessment, National Food Institute
Publication date: 2006
Event: Abstract from XXV Congress of the European Academy of Allergology and Clinical Immunology, Vienna, Austria.
Main Research Area: Technical/natural sciences
Electronic versions: Abstract1.pdf
Source: orbit
Source-ID: 237787
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2006

**Projects:**

**Allergenicity of camel milk**
National Food Institute
Period: 01/05/2018 → 30/04/2021
Number of participants: 4
PhD Student: Maryniak, Natalia Zofia (Intern)
Supervisor: Hansen, Egon Bech (Intern)
Sancho Vega, Ana Isabel (Intern)
Main Supervisor: Bøgh, Katrine Lindholm (Intern)

**Financing sources**
Source: Internal funding (public)
Name of research programme: Samfinansierede - Virksomhed
Project: PhD

**Health related effects of quinoa- impact on intestinal permeability and immune responses**
National Food Institute
Period: 01/12/2017 → 30/11/2020
Number of participants: 4
PhD Student: Ballegaard, Anne-Sofie Ravn (Intern)
Supervisor: Pilegaard, Kirsten (Intern)
Rasmussen, Peter Have (Intern)
Main Supervisor:
ALLEVIATE - A novel strategy for food allergy prevention and treatment

Food allergy is an adverse effect to otherwise harmless proteins in the food, whereas oral tolerance is the default result from ingestion of food proteins. Food allergy is a major health problem of growing concern, affecting ~5-8% of young children and 2-4% of adults. No reliable strategy exists for prevention and treatment of food allergy, and strict avoidance of the offending food is presently the only viable management option. Living with food avoidance has a huge impact on the quality of life of food allergic patients, with daily fear of serious or even fatal reactions. The need for efficient methods for prevention and treatment is therefore evident and urgent.

The purpose of the project is to develop methods to prevent and treat food allergy using a novel strategy, recently invented. Our vision is to overcome limitations in current strategies for food allergy prevention and treatment; being efficient without inducing allergic reactions.

The specific goals of the project are:
1) To develop protein ingredients for a new generation of hypoallergenic (HA) infant formulas (IF) for cow’s milk allergy (CMA) prevention
2) To develop a drug candidate for use in immunotherapy (IT) for peanut allergy (PA) treatment

These products would have the capacity to enhance the quality of life for millions of patients in risk of developing CMA and of patients with an already established PA. The market potential is great for both product categories. In addition, the newly developed strategy may form the basis for prevention, treatment and diagnostic products targeting other food allergies.

National Food Institute
Research Group for Gut Microbiology and Immunology
Department of Chemistry
Organic Chemistry
Research Group for Microbial Biotechnology and Biorefining
Office for Innovation & Sector Services
Medical University of Vienna
University of Toronto
University of Leeds
Arla Foods Ingredients Group P/S
Period: 01/01/2017 → 31/12/2020
Number of participants: 9
Food Allergy, Immunotherapy, Infant formula, Allergy, Milk allergy, Peanut allergy
Acronym: ALLEVIATE
Project participant:
Madsen, Charlotte Bernhard (Intern)
Kryger, Karsten (Intern)
Qvortrup, Katrine (Intern)
Jensen, Peter Ruhdal (Intern)
Bang-Berthelsen, Claus Heiner (Intern)
Ottesen, Peter Conrad (Intern)
Sancho Vega, Ana Isabel (Intern)
Project Manager, organisational:
Bang-Berthelsen, Iben (Intern)
Project Manager, academic:
Bøgh, Katrine Lindholm (Intern)
Project

Microbiota and cow’s milk tolerance
Cow’s milk allergy is a health problem of growing concern for which reason efficient strategies for the prevention is urgently needed. In recent years it has been demonstrated that the gut microbiota composition influences the development of allergy. However, our knowledge about how the microbiota composition influences the sensitising or tolerance inducing capacities of the food is only scarcely described. The objectives of this project are: (1) to increase our knowledge about
the interplay between food proteins and the gut microbiota, and how this interplay impact on induction of cow’s milk allergy versus tolerance, and (2) in a broader perspective to gain knowledge about mechanisms influenced by microbiota, which drives the immune system towards allergy or tolerance. Intact whey, which is one fraction of cow’s milk often used for infant formula, and enzymatic hydrolysed products hereof, used for hypoallergenic infant formulas, will used as model protein ingredients. The interplay between whey-based ingredients and the gut microbiota will be investigated in in vitro fermentation studies based on faecal samples from food allergic and healthy infants, as well as in animal studies in which the gut microbiota is manipulated by antibiotics treatment. Microbial composition will be analysed by 16S rRNA gene sequencing in combination with quantitative real-time PCR. The allergy or tolerance inducing capacity of the different whey-based ingredients and the influence of the gut microbiota composition will be analysed by evaluating different serological and cell based end-points. Appropriate functional in vitro, in vivo and ex vivo assays will be applied to investigate the mechanism by which the gut microbiota and metabolites hereof impact on directing the immune system towards allergy or tolerance.

National Food Institute
Research Group for Gut Microbiology and Immunology
Arla Foods Ingredients Group P/S
Period: 01/01/2016 → 31/08/2019
Number of participants: 4
Milk allergy, tolerance, infant formulas, gut microbiota
Number of related Ph.D. students: 1
Project participant:
Graversen, Katrine (Intern)
Licht, Tine Rask (Intern)
Bahl, Martin Iain (Intern)
Project Manager, academic:
Bøgh, Katrine Lindholm (Intern)

Microbiota and cow's milk tolerance
National Food Institute
Period: 15/12/2015 → 29/07/2019
Number of participants: 4
PhD Student:
Graversen, Katrine (Intern)
Supervisor:
Bahl, Martin Iain (Intern)
Licht, Tine Rask (Intern)
Main Supervisor:
Bøgh, Katrine Lindholm (Intern)

Financing sources
Source: Internal funding (public)
Name of research programme: Samfinansieret - Andet
Project: PhD

Food allergy skin sensitisation
Allergic sensitisation to foods may occur in infancy without prior oral exposure to the offending food. This has led to the assumption that food allergy sensitisation may occur through alternative routes, such as via the skin. Recently, concern has been raised regarding the safety of use of cosmetic and personal care products containing food proteins and derivatives hereof, especially hydrolysed wheat proteins. However, little is known about the conditions necessary for proteins and their derivatives to sensitise via the skin. In this project we will develop an animal model for IgE mediated protein induced skin sensitisation. This will allow us to study the influences of: 1) protein/peptide sizes, 2) protein/peptide aggregation tendency, 3) matrices in which the proteins/peptides are present and 4) skin conditions, on the skin sensitising capacity of protein products. Intact wheat and different enzyme and acid hydrolysed wheat products, used in cosmetic and personal care products will be used as model proteins and applied on intact, damaged as well as inflamed skin, in order for examination of: 1) specific IgG1 and IgE antibody responses, according to: antibody levels, antibody avidity and cross reactivity by means of different ELISAs, 2) IgE functionality by means of in vivo skin test, 3) protein/peptide reactivity and cross-reactivity by means of immunoblotting, 4) proliferative responses of lymphocytes from the regional lymph nodes after stimulation with different wheat products, 5) cytokine responses of lymphocytes from regional lymph nodes after stimulation with different wheat products, and 6) histopathology of skin. With this project we anticipate to contribute with substantial knowledge to our understanding on how and why food proteins sensitise through the skin. This is important for the potential prevention of new cases of food allergy.
National Food Institute
Research Group for Gut Microbiology and Immunology
Period: 01/10/2015 → 30/09/2018
Number of participants: 1
Project participant:
Bøgh, Katrine Lindholm (Intern)

Financing sources
Source: Private funding (private)
Name of research programme: The Lundbeck Foundation
Amount: 2,100,000.00 Danish Kroner
Year of approval: 2015

A novel strategy for hypoallergenic infant formulas
PoC project
National Food Institute
Research Group for Gut Microbiology and Immunology
Period: 01/05/2015 → 30/06/2016
Number of participants: 2
Project participant:
Kryger, Karsten (Intern)
Project Manager, academic:
Bøgh, Katrine Lindholm (Intern)

Improving Allergy Risk Assessment Strategy for new food proteins
The main objective of the Action is to build an interdisciplinary European network of scientists with a broad range of expertise to discuss new ideas for more and innovative predictive models and approaches to improve the current allergenicity risk assessment strategy of proteins from novel or modified foods. This should lead to the transfer of scientific advances to European food companies to develop safe products, advise food safety authorities on better risk assessment and influence public opinion on the safety of novel sustainable food.

National Food Institute
Division of Toxicology and Risk Assessment
TNO, Netherlands
Vienna University of Technology
Novozymes A/S
National Institute for Agronomic Research
Paul-Ehrlich-Institut
University of Athens
Unilever
Period: 01/01/2014 → 31/12/2017
Number of participants: 3
Acronym: ImpARAS
Project participant:
Bøgh, Katrine Lindholm (Intern)
Madsen, Charlotte Bernhard (Intern)
Project Manager, organisational:
Verhoeckx, Kitty (Ekstern)

Allergic versus tolerogenic characteristics of cow's milk hydrolysates
Cow’s milk allergy is a growing problem in the Western world, where it affects up to 2.5% of all infants. Currently, the only accepted and safe management of food allergy is exclusion of all offending foods from the diet. However for infants with cow’s milk allergy or infants with an increased risk for development of cow’s milk allergy, special infant formulas based on
hydrolysed cow’s milk proteins are available. Extensively hydrolysed infant formulas are used primarily for children with an already diagnosed cow’s milk allergy (secondary prevention), whereas partially hydrolysed infant formulas are used primarily for infants predisposed for developing cow’s milk allergy (primary prevention). However, our knowledge about which characteristics of cow’s milk proteins that contributes to the development of allergy and which contributes to the prevention of allergy are very scarce. In order to establish knowledge-based strategies for production of new and improved hypo-allergenic infant formulas, we therefore need thorough studies investigating which properties of milk proteins that direct the immune system towards allergy and which that direct the immune system towards tolerance (primary or secondary prevention). Such studies must be conducted in animal models of food allergy.

The main objective of this project is to investigate and characterise the properties of cow’s milk based hydrolysates contributing to sensitisation (allergy induction) and the properties that prevents allergy by the induction of tolerance. The project aims to establish two new animal models based on our own colony of Brown Norway rats to study: (1) induction of tolerance in non-allergic subjects (primary prevention) and (2) induction of tolerance in already sensitised subjects (secondary prevention). These models will together with our well-established model for examination of sensitising (allergy inducing) capacity of food proteins and their breakdown products form the basis for studying the properties of cow’s milk based hydrolysates contributing to allergy versus tolerance induction. A total of four extensively and four partially hydrolysed cow’s milk protein products will be tested in the three animal models. These hydrolysates will differ from each other in: (1) degree of hydrolysis, (2) peptide composition, (3) complex formation, (4) residual intact proteins and (5) starting material. Collectively this will allow us to provide knowledge for establishment of new and improved infant formulas for allergy prevention.

Project year 1 will focus on and end up with establishment of the two new animal models for testing of tolerance and project year 2 will focus on and end up with a panel of tests for ability of hydrolysates to induce allergy, primary prevention or secondary prevention. Results from this project will at first be presented at international conferences and at the latest in 2016 be published in Danish as well as in internationally peer-reviewed journals.
National Food Institute
Division of Toxicology and Risk Assessment
Period: 01/01/2011 → 31/12/2015
Number of participants: 3
Protein, Digestion
Acronym: INFOGEST
Project participant:
Madsen, Charlotte Bernhard (Intern)
Bøgh, Katrine Lindholm (Intern)

Project Manager, organisational:
Dupont, Didier (Ekstern)

Allergenicity of Peptides from Food Allergens - a Food Allergy Sensitisation Study
National Food Institute
Period: 01/01/2007 → 27/06/2012
Number of participants: 6
Phd Student:
Bøgh, Katrine Lindholm (Intern)
Supervisor:
Barkholt, Vibeke (Intern)
Main Supervisor:
Madsen, Charlotte Bernhard (Intern)
Examiner:
Jessen, Flemming (Intern)
Knippels, Léon M. J. (Ekstern)
Skov, Per Stahl (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: 1/3 DTU-stip, 2/3 FUR/andet
Project: PhD

Activities:

3rd ImpARAS Conference
Period: 10 Oct 2017 → 12 Oct 2017
Charlotte Bernhard Madsen (Organizer)
Katrine Lindholm Bøgh (Organizer)

National Food Institute
Research Group for Gut Microbiology and Immunology

Description
Improving Allergy Risk Assessment Strategy for new food proteins (ImpARAS)
Degree of recognition: International

Related event

3rd ImpARAS Conference
10/10/2017 → 12/10/2017
Elsinore, Denmark
Activity: Attending an event › Participating in or organising a conference

Sensitisation capacity of intact and digested 2S albumin from Brazil nut in a Brown Norway rat model
Period: 1 Jan 2008 → …
Katrine Lindholm Bøgh (Speaker)
Digested Ara h 1 retains its sensitising capacity in Brown Norway rats

Period: 1 Jan 2007 → …
Katrine Lindholm Bøgh (Speaker)
National Food Institute
Division of Toxicology and Risk Assessment

Description
Place: 8th Nordic Symposium on Allergy, Sønderborg

Unknown external organisation
Activity: Talks and presentations › Conference presentations

Epitope mapping of intact and digested Ara h 1

Period: 1 Jan 2006 → …
Katrine Lindholm Bøgh (Speaker)
National Food Institute
Division of Toxicology and Risk Assessment

Description
Place: Vienna, Austria

Press clippings:

Forkningsprojektet ALLEVIATE
Katrine Lindholm Bøgh
13/06/2017
National Food Institute, Research Group for Gut Microbiology and Immunology

Media coverage (1)

Uddybning af og status på forskningsprojektet Alleviate
13/06/2017
Allergia.se, Denmark, Web
Susanne Rosén
Katrine Lindholm Bøgh
National Food Institute, Research Group for Gut Microbiology and Immunology
Press / Media

Innovationsfondsparkfonden ALLEVIATE
Katrine Lindholm Bøgh
19/01/2017
National Food Institute, Research Group for Gut Microbiology and Immunology

**Media contribution (1)**

**Innovationsfondsprojektet ALLEVIATE**
19/01/2017
Astma-Allergi Danmarks hjemmeside og medlemsblad, Print
Henriette Baun Gautier
Katrine Lindholm Bøgh
National Food Institute, Research Group for Gut Microbiology and Immunology
Press / Media

**Produktudvikling til modermælkserstatninger**
Katrine Lindholm Bøgh
12/01/2017
National Food Institute, Research Group for Gut Microbiology and Immunology

**Media contribution (1)**

**Produktudvikling til modermælkserstatninger**
12/01/2017
Food Supply, Web
Morten Vittrup Lund
Katrine Lindholm Bøgh
National Food Institute, Research Group for Gut Microbiology and Immunology
Press / Media

**Alleviate forskningsprojekt - udvikling af produkter til forebyggelse og behandling af fødevareallergier**
Katrine Lindholm Bøgh
20/12/2016
National Food Institute, Research Group for Gut Microbiology and Immunology

**Media contribution (1)**

**Alleviate forskningsprojekt - udvikling af produkter til forebyggelse og behandling af fødevareallergier**
20/12/2016
Ritzau, Print
Sabrina Melina Andersen
Katrine Lindholm Bøgh
National Food Institute, Research Group for Gut Microbiology and Immunology
Press / Media