A Maternal Gluten-Free Diet Reduces Inflammation and Diabetes Incidence in the Offspring of NOD Mice

Early-life interventions in the intestinal environment have previously been shown to influence diabetes incidence. We therefore hypothesized that a gluten-free (GF) diet, known to decrease the incidence of type 1 diabetes, would protect against the development of diabetes when fed only during the pregnancy and lactation period. Pregnant nonobese diabetic (NOD) mice were fed a GF or standard diet until all pups were weaned to a standard diet. The early-life GF environment dramatically decreased the incidence of diabetes and insulitis. Gut microbiota analysis by 16S rRNA gene sequencing revealed a pronounced difference between both mothers and their offspring on different diets, characterized by increased numbers of Akkermansia, Proteobacteria, and TM7 in the GF diet group. In addition, pancreatic forkhead box P3 regulatory T cells were increased in GF-fed offspring, as were M2 macrophage gene markers and tight junction-related genes in the gut, while intestinal gene expression of proinflammatory cytokines was reduced. An increased proportion of T cells in the pancreas expressing the mucosal integrin alpha 4 beta 7 suggests that the mechanism involves increased trafficking of gut-primed immune cells to the pancreas. In conclusion, a GF diet during fetal and early postnatal life reduces the incidence of diabetes. The mechanism may involve changes in gut microbiota and shifts to a less proinflammatory immunological milieu in the gut and pancreas.
Postnatal amniotic fluid intake reduces gut inflammatory responses and necrotizing enterocolitis in preterm neonates

Preterm neonates are susceptible to gastrointestinal disorders such as necrotizing enterocolitis (NEC). Maternal milk and colostrum protect against NEC via growth promoting, immunomodulatory, and antimicrobial factors. The fetal enteral diet amniotic fluid (AF), contains similar components, and we hypothesized that postnatal AF administration reduces inflammatory responses and NEC in preterm neonates. Preterm pigs (92% gestation) were delivered by caesarean section and fed parental nutrition (2 days) followed by enteral (2 days) porcine colostrum (COLOS, n = 7), infant formula (FORM, n = 13), or AF supplied before and after introduction of formula (AF, n = 10) in experiment 1, and supplied only during the enteral feeding period in experiment 2 (FORM, n = 16; AF, n = 14). The NEC score was reduced in both AF and COLOS pigs, relative to FORM, when AF was provided prior to full enteral feeding (9.9 and 7.7 compared with 17.3, P <0.05). There was no effect of AF when provided only during enteral feeding. AF pigs showed decreased bacterial abundance in colon and intestinal inflammation-related genes (e.g., TNF-α, IL-1α, IL-6, NOS) were downregulated, relative to FORM pigs with NEC. Anti-inflammatory properties of AF were supported by delayed maturation and decreased TNF-α production in murine dendritic cells, as well as increased proliferation and migration, and downregulation of IL-6 expression in intestinal cells (IEC-6, IPEC-J2). Like colostrum, AF may reduce NEC development in preterm neonates by suppressing the proinflammatory responses to enteral formula feeding and gut colonization when provided before the onset of NEC.

General information
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Comparative analysis of a large panel of non-starch polysaccharides reveals structures with selective regulatory properties in dendritic cells

Scope: Structural-based recognition of foreign molecules is essential for activation of dendritic cells (DCs) that play a key role in regulation of gut mucosal immunity. Orally ingested non-starch polysaccharides (NSP) are ascribed many health-promoting properties, but currently we lack insight into the impact of structure and size for their capacity to affect immune responses. Methods and results: This study addresses the importance of chemical structure, size, origin and presence of contaminants for the capacity of both dietary and non-food NSP to modulate DC. Of 28 NSP products, β-glucans of microbial and plant origin and the galactomannan guar gum were found to modulate the DC cytokine pattern induced by the Toll-like receptor 4-ligand LPS giving rise to reduced IL-12p70 and increased IL-10 levels, whereas IL-6 production was unaffected. A large proportion of the tested NSP were able to down-regulate LPS-induced IL-12p70 production. The most potent NSP induced up-regulation of CD86 on DC independently of LPS stimulation. Cereal-based β-glucans showed less potency than β-glucans of microbial origin, but proper molecular weight composition and preparation may improve effectiveness. Conclusions: Collectively, this comparative study revealed that some plant-derived NSP besides those of microbial origin exert modulation of the DC phenotype, with the exact structure being important for the activity.
The complexity of the murine microbiota influences the important recruitment of immune cells in early life

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Milk Bioactives to Prevent Gut Inflammation

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Bifidobacterium bifidum Actively Changes the Gene Expression Profile Induced by Lactobacillus acidophilus in Murine Dendritic Cells

Dendritic cells (DC) play a pivotal regulatory role in activation of both the innate as well as the adaptive immune system by responding to environmental microorganisms. We have previously shown that Lactobacillus acidophilus induces a strong production of the pro-inflammatory and Th1 polarizing cytokine IL-12 in DC, whereas bifidobacteria do not induce IL-12 but inhibit the IL-12 production induced by lactobacilli. In the present study, genome-wide microarrays were used to investigate the gene expression pattern of murine DC stimulated with Lactobacillus acidophilus NCFM and Bifidobacterium bifidum Z9. L. acidophilus NCFM strongly induced expression of interferon (IFN)-beta, other virus defence genes, and cytokine and chemokine genes related to the innate and the adaptive immune response. By contrast, B. bifidum Z9 up-regulated genes encoding cytokines and chemokines related to the innate immune response. Moreover, B. bifidum Z9 inhibited the expression of the Th1-promoting genes induced by L. acidophilus NCFM and had an additive effect on genes of the innate immune response and Th2 skewing genes. The gene encoding Jun dimerization protein 2 (JDP2), a transcription factor regulating the activation of JNK, was one of the few genes only induced by B. bifidum Z9. Neutralization of IFN-beta abrogated L. acidophilus NCFM-induced expression of Th1-skewing genes, and blocking of the JNK pathway completely inhibited the expression of IFN-beta. Our results indicate that B. bifidum Z9 actively inhibits the expression of genes related to the adaptive immune system in murine dendritic cells and that JPD2 via blocking of IFN-beta plays a central role in this regulatory mechanism.

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CD4+ T-cell activation is differentially modulated by bacteria-primed dendritic cells, but is generally down-regulated by n-3 polyunsaturated fatty acids

Appropriate activation of CD4+ T cells is fundamental for efficient initiation and progression of acquired immune responses. Here, we showed that CD4+ T-cell activation is dependent on changes in membrane n-3 polyunsaturated fatty acids (PUFAs) and is dynamically regulated by the type of signals provided by dendritic cells (DCs). Upon interaction with DCs primed by different concentrations and species of gut bacteria, CD4+ T cells were activated according to the type of DC stimulus. The levels of CD80 were found to correlate to the levels of expression of CD28 and to the proliferation of CD4+ T cells, while the presence of CD40 and CD86 on DCs inversely affected inducible costimulator (ICOS) and cytotoxic T-lymphocyte antigen-4 (CTLA-4) levels in CD4+ T cells. For all DC stimuli, cells high in n-3 PUFAs showed reduced ability to respond to CD28 stimulation, to proliferate, and to express ICOS and CTLA-4. Diminished T-cell receptor (TCR) and CD28 signalling was found to be responsible for n-3 PUFA effects. Thus, the dietary fatty acid composition influences the overall level of CD4+ T-cell activation induced by DCs, while the priming effect of the DC stimuli modulates CD80, CD86 and CD40 levels, thereby affecting and shaping activation of acquired immunity by differential regulation of proliferation and costimulatory molecule expression in CD4+ T cells.
Dietary fibers as immunoregulatory compounds in health and disease

Many nonstarch polysaccharides (NSPs) classified as dietary fibers have been reported to possess immunoregulatory properties. The fibers reported to activate or by other means modulate immune responses originate from both plant, fungal, and microbial sources and constitute highly distinct structures. In order to enhance our understanding of factors important for the immunoregulatory activities, this article addresses the importance of chemical structure, origin, and purity of fibers for their capacity to interact with key regulatory immune cells. Furthermore, we assess bioavailability, and discuss possible mechanisms involved. The binding of some NSPs to carbohydrate receptors on immune cells is well established and this event leads to activation or other changes. Especially, certain beta-glucans and some mannans have demonstrated immunomodulatory capacity with the specific structure being important for the activity. Within beta-glucans the activity varies according to structure, molecular weight, and solubility. As many of the preparations tested constitute crude extracts or partly purified NSPs, the risk of contaminants holding immunoregulatory activities should not be ignored. To what extent NSPs enter systemic circulation has been difficult to assess, partly due to lack of sensitive analytical methods. The presence of NSPs in blood and Peyer's patches in the gut has been demonstrated, supporting encounter between NSPs and immune cells, but bioavailability studies still constitute a major challenge. Studies demonstrating in vivo effects of beta-glucans on microbial infections and cancer treatment strongly indicate an immunoregulatory mechanism behind the effects. However, the potential of NSPs as immunoregulatory food ingredients is still far from fully explored.
Lactobacillus acidophilus induces a slow but more sustained chemokine and cytokine response in naïve foetal enterocytes compared to commensal Escherichia coli

The first exposure to microorganisms at mucosal surfaces is critical for immune maturation and gut health. Facultative anaerobic bacteria are the first to colonise the infant gut, and the impact of these bacteria on intestinal epithelial cells (IEC) may be determinant for how the immune system subsequently tolerates gut bacteria. RESULTS: To mirror the influence of the very first bacterial stimuli on infant IEC, we isolated IEC from mouse foetuses at gestational day 19 and from germ-free neonates. IEC were stimulated with gut-derived bacteria, Gram-negative Escherichia coli Nissle and Gram-positive Lactobacillus acidophilus NCFM, and expression of genes important for immune regulation was measured together with cytokine production. E. coli Nissle and L. acidophilus NCFM strongly induced chemokines and cytokines, but with different kinetics, and only E. coli Nissle induced down-regulation of Toll-like receptor 4 and up-regulation of Toll-like receptor 2. The sensitivity to stimulation was similar before and after birth in germ-free IEC, although Toll-like receptor 2 expression was higher before birth than immediately after. CONCLUSIONS: In conclusion, IEC isolated before gut colonisation occurs at birth, are highly responsive to stimulation with gut commensals, with L. acidophilus NCFM inducing a slower, but more sustained response than E. coli Nissle. E. coli may induce intestinal tolerance through very rapid up-regulation of chemokine and cytokine genes and down-regulation of Toll-like receptor 2, while regulating also responsiveness to Gram-positive bacteria.

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Lactobacillus acidophilus induces virus immune defence genes in murine dendritic cells by a Toll-like receptor-2-dependent mechanism

Lactobacilli are probiotics that, among other health-promoting effects, have been ascribed immunostimulating and virus-preventive properties. Certain Lactobacillus spp. have been shown to possess strong interleukin-12 (IL-12) -inducing properties. As IL-12 production depends on the up-regulation of type I interferons (IFNs), we hypothesized that the strong...
IL-12-inducing capacity of Lactobacillus acidophilus NCFM in murine bone-marrow-derived dendritic cells (DCs) is caused by an up-regulation of IFN-beta, which subsequently induces IL-12 and the double-stranded RNA binding Toll-like receptor-3 (TLR-3). The expression of the genes encoding IFN-beta, TLR-3, IL-12 and IL-10 in DCs upon stimulation with L. acidophilus NCFM was determined. Lactobacillus acidophilus NCFM induced a much stronger expression of Ifn-beta, Il-12 and Il-10 compared with the synthetic double-stranded RNA ligand Poly I:C, whereas the levels of expressed Tlr-3 were similar. Whole genome microarray gene expression analysis revealed that other genes related to viral defence were significantly up-regulated and among the strongest induced genes in DCs stimulated with L. acidophilus NCFM. The ability to induce IFN-beta was also detected in another L. acidophilus strain (X37), but was not a property of other probiotic strains tested, i.e. Bifidobacterium bifidum Z9 and Escherichia coli Nissle 1917. The IFN-beta expression was markedly reduced in TLR-2(-/-) DCs, dependent on endocytosis, and the major cause of the induction of Il-12 and Tlr-3 in DCs stimulated with L. acidophilus NCFM. Collectively, our results reveal that certain lactobacilli trigger the expression of viral defence genes in DCs in a TLR-2 manner dependent on IFN-beta.
Pseudomonas aeruginosa quorum-sensing signal molecules interfere with dendritic cell-induced T-cell proliferation

Pseudomonas aeruginosa releases a wide array of toxins and tissue-degrading enzymes. Production of these malicious virulence factors is controlled by interbacterial communication in a process known as quorum sensing. An increasing body of evidence reveals that the bacterial signal molecule N-(3-oxododecanoyl)-l-homoserine lactone (OdDHL) exhibits both quorum-sensing signalling and immune-modulating properties. Recently, yet another quorum-sensing signal molecule, the Pseudomonas quinolone signal (PQS), has been shown to affect cytokine release by mitogen-stimulated human T cells. In
the present article we demonstrate that both OdDHL and PQS decrease the production of interleukin-12 (IL-12) by Escherichia coli lipopolysaccharide-stimulated bone marrow-derived dendritic cells (BM-DCs) without altering their IL-10 release. Moreover, BM-DCs exposed to PQS and OdDHL during antigen stimulation exhibit a decreased ability to induce T-cell proliferation in vitro. Collectively, this suggests that OdDHL and PQS change the maturation pattern of stimulated DCs away from a proinflammatory T-helper type I directing response, thereby decreasing the antibacterial activity of the adaptive immune defence. OdDHL and PQS thus seem to possess dual activities in the infection process: as inducers of virulence factors as well as immune-modulators facilitating the infective properties of this pathogen.
Reduced ex Vivo Interleukin-6 Production by Dietary Fish Oil Is Not Modified by Linoleic Acid Intake In Healthy Men

Fish oil (FO) is considered antiinflammatory, but evidence regarding its effect on human cytokine production is conflicting. High linoleic acid (LA) intake may impair any effects of FO. The aim of this study was to investigate how FO combined with high or low LA intake affected ex vivo cytokine production from cultures of whole blood, peripheral blood mononuclear cells (PBMC), and monocytes in healthy men. The study was a double-blinded, controlled, 2 X 2 factorial 8-wk intervention. Sixty-four healthy men were randomized to 5 mL/d FO or olive oil (O0) provided in capsules and to spreads and oils with high or low LA content, resulting in LA intakes of 7 +/- 2% and 4 +/- 1% energy, respectively. We measured eicosapentaenoic acid (EPA) in PBMC and stimulated cytokine production in whole blood and PBMC 24-h cultures before and immediately after intervention and after an 8-wk wash-out period, and in monocyte cultures immediately after intervention. PBMC-EPA was markedly increased by FO (P <0.001). LA intake did not modify the incorporation of FO and tended to have only a slight effect on PBMC-EPA by itself (P = 0.06). Lipopolysaccharide (LPS)-stimulated whole-blood interleukin (IL)-6 production immediately after intervention was lower with FO than O0 (P = 0.02) but did not correlate with PBMC-EPA in the FO groups (r = -0.12; P = 0.53; n = 31). The LA intake did not modify IL-6 production or the effect of FO. Neither FO nor LA intake affected the production of tumor necrosis factor-alpha, IL-10, or interferon-gamma in any of the cultures. In conclusion, FO intake reduced IL-6 production from LPS-stimulated whole blood in healthy men compared with 00, but the effect was not modified by the LA intake. J. Nutr. 139: 1410-1414, 2009.
Whole-blood culture is a valid low-cost method to measure monocytic cytokines - A comparison of cytokine production in cultures of human whole-blood, mononuclear cells and monocytes

Whole-blood and peripheral blood mononuclear cell (PBMC) cultures are used as non-validated surrogate measures of monocytic cytokine production. The aim of this investigation was to compare ex vivo cytokine production from human whole-blood and PBMC with that from isolated monocytes. We also assessed the intra- and inter-individual variation in cytokine production. In 64 healthy men (age 19-40 years) IL-6, TNF and IL-10 were measured by enzyme-linked immunosorbent assay in supernatants from whole-blood, PBMC and monocytes cultured 24 h with lipopolysaccharide (LPS) or UV-killed L acidophilus. Cytokines produced from whole-blood was found to be more strongly correlated with monocytic cytokines than cytokines from PBMC, particularly after LPS-stimulation: $r=0.57$, $P= 50\%$ smaller than the inter-individual variation ($P$).
Dendritic Cells from Peyer's Patches and Mesenteric Lymph Nodes Differ from Spleen Dendritic Cells in their Response to Commensal Gut Bacteria

Commensal gut bacteria have potent effects on the immune system, which are partially mediated by intestinal dendritic cells (DC). Distinct commensals confer different properties to in vitro-generated DC. The aim of the present study was to reveal strain-dependent maturation patterns in primary DC. To this end, we compared the response of mouse Peyer's patch (PP) DC, mesenteric lymph node (MLN) DC and spleen DC to the commensal bacteria, Bifidobacterium longum Q46, Lactobacillus acidophilus X37 and Escherichia coli Nissle 1917. Bacterial maturation of DC occurred independently of tissue origin. Expression of CCR7 and CD103 on the surface of MLN DC, necessary for the induction of gut-homing regulatory T cells, increased with stimulation by Gram-positive commensals. Bacteria-dependent cytokine production (IL-6, IL-10 and TNF-alpha) was similar in spleen and MLN DC, and contaminant cells in these DC preparations produced IFN-gamma in response to L. acidophilus. In contrast, PP DC produced IL-6 only in response to E. coli, little IL-10 and no TNF-alpha, and this low cytokine production was not due to inhibition by IL-10 or TGF-beta. Bifidobacteria downregulate IL-6, TNF-alpha and IL-12 production induced in in vitro-generated DC by L. acidophilus. Similar inhibition was observed in splenic DC, but not in MLN DC. MLN cells responded to bacterial stimulation with higher IFN-gamma production than spleen cells, possibly due to the presence of more responsive natural killer cells. Commensal bacteria therefore play specific roles in the gut immune system distinguishable from the effect they would have if recognized by the systemic immune system.

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Scopus rating (2001): SJR 0.746 SNIP 0.63
Scopus rating (2000): SJR 0.876 SNIP 0.608
Dietary soya saponins increase gut permeability and play a key role in the onset of soyabean-induced enteritis in Atlantic salmon (Salmo salar L.)

are naturally occurring amphiphilic molecules and have been associated with many biological activities. The aim of the present study was to investigate whether soya saponins trigger the onset of soyabean-induced enteritis in Atlantic salmon (Salmo salar L.), and to examine if dietary soya saponins increase the epithelial permeability of the distal intestine in Atlantic salmon. Seven experimental diets containing different levels of soya saponins were fed to seawater-adapted Atlantic salmon for 53 d. The diets included a fishmeal-based control diet, two fishmeal-based diets with different levels of added soya saponins, one diet containing 25 % lupin kernel meal, two diets based on 25 % lupin kernel meal with different levels of added soya saponins, and one diet containing 25 % defatted soyabean meal. The effect on intestinal morphology, intestinal epithelial permeability and faecal DM content was examined. Fish fed 25 % defatted soyabean meal displayed severe enteritis, whereas fish fed 25 % lupin kernel meal had normal intestinal morphology. The combination of soya saponins and fishmeal did not induce morphological changes but fish fed soya saponins in combination with lupin kernel meal displayed significant enteritis. Increased epithelial permeability was observed in fish fed 25 % defatted soyabean meal and in fish fed soya saponin concentrate independent of the protein source in the feed. The study demonstrates that soya saponins, in combination with one or several unidentified components present in legumes, induce an inflammatory reaction in the distal intestine of Atlantic salmon. Soya saponins increase the intestinal epithelial permeability but do not, per se, induce enteritis.
Effect on dendritic cells of aloe vera and pomme granate products from Forever Living Products

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Fish oil in combination with high or low intakes of linoleic acid lowers plasma triacylglycerols but does not affect other cardiovascular risk markers in healthy men

Both (n-3) long-chain PUFA (LCPUFA) and linoleic acid [LA, 18:2(n-6)] improve cardiovascular disease (CVD) risk factors, but a high-LA intake may weaken the effect of (n-3) LCPUFA. In a controlled, double-blind, 2 x 2-factorial 8-wk intervention, we investigated whether fish oil combined with a high- or low-LA intake affects overall CVD risk profile. Healthy men (n = 64) were randomized to 5 mL/d fish oil capsules (FO) [mean intake 3.1 g/d (n-3) LCPUFA] or olive oil capsules (control) and to oils and spreads with either a high (S/B) or a low (R/K) LA content, resulting in a 7.3 g/d higher LA intake in the S/B groups than in the R/K groups. Diet, (n-3) LCPUFA in peripheral blood mononuclear cells, blood pressure (BP), heart rate (HR), and plasma CVD risk markers were measured before and after the intervention. FO lowered fasting plasma triacylglycerol (TAG) (P <0.001) by 51% and 19% in the FO+R/K-group and FO+S/B-group, respectively, which was also reflected in postprandial TAG measured after the intervention (P <0.01). Although a fat x FO interaction was found for monocyte chemoattractant protein-1, neither the FO nor fat intervention affected fasting plasma cholesterol, glucose, insulin, fibrinogen, C-reactive protein, interleukin-6, vascular cell adhesion molecule-1, P-selectin, oxidized LDL, cluster of differentiation antigen 40 ligand (CD40L), adiponectin, or fasting or postprandial BP or HR after adjustment for body weight changes. In conclusion, neither fish oil supplementation nor the LA intake had immediate pronounced effects on the overall CVD risk profile in healthy men, but fish oil lowered plasma TAG in healthy subjects with initially low concentrations.
Tarmfloras betydning for immunforsvaret kortlægges

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The effects of fish oil and high or low linoleic acid intake on fatty acid composition of human peripheral blood mononuclear cells

Dietary intake of 18:2n-6 and 18:3n-3 may affect endogenous production and incorporation of n-3 long-chain PUFA (LCPUFA) from fish oils (170). This double-blinded controlled 2 x 2-factorial 8-week intervention investigates the effects of high and low 18:2n-6 intake in combination with FO-supplementation on tissue fatty acid composition. Healthy young men (n = 64) were randomized to capsules with FO or olive oil (control) (4-4 (2-0-5-6) ml/d) and to either sunflower oil and margarine (S/B) or rapeseed oil and a butter spread (R/K) to provide a high or a low 18:2n-6 intake. Diet was measured by 4-d weighed dietary records at baseline, during and 8 weeks after the intervention and tissue incorporation as fatty acid composition of peripheral blood mononuclear cells (PBMC). The fat intervention gave a mean difference in the 18:2n-6 intake of 7.3 g/d (95 % CI 4.6, 10.0) and a similar 18:3n-3 intake in the groups. The R/K groups had a 0.2 % fatty acid (FA%) (95 % CI 0.0, 0.4, P=0.02) higher content of 22:5n-3 in the PBMC, a tendency of slightly higher 20:5n-3 (P=0.06), but no more 22:6n-3 (P=0.83) than the SIB groups. FO effectively raised the PBMC content of all n-3 LCPUFA (P
Toll-like receptor 2 and nucleotide-binding oligomerization domain-2 play divergent roles in the recognition of gut-derived lactobacilli and bifidobacteria in dendritic cells

Summary: The gut microbiota is vital in the maintenance of homeostasis in the gut immune system. Its diversity and composition play major roles in relation to allergies and inflammatory bowel diseases, and administration of lactic acid bacteria (LAB), such as lactobacilli and bifidobacteria, has positive effects on these pathologies. However, the mechanisms behind the beneficial effects are largely unknown. Here we reveal divergent roles played by Toll-like receptor-2 (TLR2) and nucleotide-binding oligomerization domain-2 (NOD2) in dendritic cell (DC) recognition of LAB. Murine bone-marrow-derived DC lacking NOD2 produce higher levels of interleukin-10 (IL-10) and reduced levels of IL-12 and tumour necrosis factor-α (TNF-α) in response to LAB. This indicates that peptidoglycan is partly responsible for the T helper type 1 skewing effect of certain LAB. Dendritic cells that are TLR2-/- produce less IL-12 and TNF-α and more IL-10 in response to some strains of lactobacilli, while they produce more IL-12 and less IL-10 in response to bifidobacteria. The same tendency was found in human monocyte-derived DC. We have previously reported that the weak IL-12-inducing and TNF-α-induced bifidobacteria inhibit the T helper type 1 skewing effect induced by strong immunostimulatory lactobacilli. Here we show that this immunoinhibitory effect of bifidobacteria is dependent on TLR2 and independent of NOD2. Moreover, independently of the cytokine pattern induced by intact LAB, cell wall fractions of all LAB, as well as synthetic lipoproteins possess immunoinhibitory capacities in both human and murine DC. These novel findings suggest that LAB act as immunoregulators through interaction of lipoprotein with TLR2 and as immunostimulators through interaction of peptidoglycan with NOD2.

General information
Immunomodulatory properties of probiotic bacteria: Effects on dendritic cells and their interactions with NK cells and T cells

Certain lactic acid bacteria (LAB) are part of the commensal intestinal flora and considered beneficial for health, as they compete with pathogens for adhesion sites in the intestine and ferment otherwise indigestible compounds. Another important property of these so-called probiotic bacteria is the ability to modulate the immune response. This thesis describes the immunomodulatory properties of gut-derived bacterial strains on different antigen-presenting cells, and the effector cell responses elicited by bacterially stimulated antigen-presenting cells in natural killer (NK) cells and T cells. Autologous NK cells and mature dendritic cells (DC) mutually activate each other and this interaction is believed to be important for NK cytotoxic activity against cancer cells and for T cell polarisation. The first study included in this thesis establishes that LAB, as potent stimulators of monocyte-derived DC, are capable of directing NK cell responses. All tested strains increased NK cell proliferation and cytotoxic activity via maturation of DC, whereas only IL-12-inducing LAB induced IFN-gamma production in NK cells. Specific LAB, capable of inhibiting IL-12 production in DC also inhibited IFN-gamma production in NK cells. Secondly, it was investigated whether the strain-dependent induction of IL-12 by LAB and E. coli strains observed in monocyte-derived DC also occurred in freshly isolated blood myeloid DC and monocytes. Both types of blood antigen-presenting cells produced cytokines when stimulated with bacteria, and the cytokine pattern induced by specific bacteria resembled the pattern induced in MoDC, except for TNF-alpha and IL-6, which were induced in response to different bacteria in blood DC/monocytes and monocyte-derived DC. Autologous NK cells produced IFN-gamma when cultured with blood DC, monocytes and monocyte-derived DC and IL-12-inducing bacteria, whereas only DC induced IFN-gamma production in allogeneic T cells. In vitro-generated DC is a commonly used model of tissue DC, but they differ in certain aspects from intestinal DC, which are in direct contact with the intestinal microbiota. In the last study, we isolated DC from Peyer’s patches, mesenteric lymph nodes, and spleens of mice, and stimulated these cells with strains of LAB and E. coli. Spleen and mesenteric lymph node DC responded to stimulation with cytokine production comparable to in vitro-generated DC. Peyer’s patch DC produced only IL-6. Cells from spleen and mesenteric lymph nodes enriched in DC rapidly produced IFN-gamma when stimulated with the bacteria that induce IFN-gamma production in NK and T cells via in vitro-generated DC. Especially mesenteric lymph node cells produced large amounts of IFN-gamma, which may indicate that mesenteric lymph node NK cells have a strong potential for cytokine-production in response to commensal bacteria.
Monoclonal antibody-based Surface Plasmon Resonance sensors for pathogen detection

A biosensor is an analytical device, which incorporates a biological sensing element integrated within a physicochemical transducer. The aim of a biosensor is to produce an electronic signal, which is proportional to the interaction of analytes with the sensing element. This means that the sensor essentially transforms molecular interactions into a digital signal, thereby making detection of analytes label-free. Biosensors are used for detection of analytes ranging from small drug molecules to food- and waterborne microorganisms as well as biowarfare pathogens. In future farming, plant production will be concentrated at few and very large farms. In order to reduce the pesticide use, it is necessary for the farm manager to have detailed knowledge of the distribution of weeds, diseases and pests within the fields. However, field-monitoring by manual inspection is time consuming and expensive. Biosensors, that can detect and quantify specific plant pathogens and map these to defined positions within the field, would enable the farm manager to perform a precise and targeted application of pesticides and thereby reduce and optimise the use of agrochemicals. The ideal scenario for precision agriculture is to have real-time, robust and low-cost sensors, for both soil and air, which can be operated by personnel with limited or no training in plant pathology. In the present thesis focus is put on the development of immunological sensors for detection of two model plant pathogens, Puccinia striiformis f.sp. tritici, the cause of wheat yellow rust and Phytophthora infestans, the cause of late blight disease in potato. As no antibody existed against urediniospores from P. striiformis, mouse monoclonal antibodies (mAbs) were produced and characterised. IgM-isotype mAbs from nine hybridoma cell lines were screened for cross-reactivity against representatives from common genera. Two specific mAbs were chosen for further characterisation and used to develop a competitive ELISA (using mAb4) and a subtractive inhibition ELISA (using mAb8). The subtractive inhibition ELISA was found to be more sensitive with a detection limit of 1.5 \times 10^5 urediniospores/ml. The assay setup consists of incubation of urediniospores with mAb8, removal of urediniospore-bound mAb8 by centrifugation and quantification of the remaining unbound mAb8 by rabbit anti-mouse IgM antibody. The remaining free mAb8 is thereby related to the initial cell concentration. Assay performance was investigated by cross-reactivity studies against other rust fungi. Cross-reactivity was found with Puccinia recondita and Puccinia hordet, suggesting that the ~39 kDa mAb8-antigen might be a conserved structural component in the surface of Puccinia species. The subtractive inhibition assay was further developed for label-free detection using a Surface Plasmon Resonance sensor. The polyclonal anti-mouse IgM was immobilised on a sensor surface and used for capture and quantification of mAb8. Optimal regeneration conditions were identified and 20 mM HCl effectively regenerated the surface. The assay had a similar sensitivity as the ELISA with a detection limit of 3.1 \times 10^5 urediniospores/ml. P. striiformis was furthermore detected in a mixture with the rust species Melampsora euphorbia, which underlined the specificity of the sensor. A Surface Plasmon Resonance sensor was further developed for detection of P. infestans sporangia. An existing Phytophthora genera mAb (phyt/G1470) was found to be highly specific when tested for cross-reactivity against spores from ascomycetes, deuteromycetes and basidiomycetes in a subtractive inhibition ELISA. The subtractive inhibition assay was incorporated in a Surface Plasmon Resonance sensor and optimal assay and regeneration conditions were identified. Calibration curves were generated and a detection limit of 2.22 \times 10^6 sporangia/ml was achieved. The assay analysis time of 75 minutes is superior to existing immuno- and nucleotide-based assays for P. infestans detection. In conclusion, the results presented in this thesis describe the first use of Surface Plasmon Resonance immunosensors for plant pathogen detection and represent a first step towards the implementation of plant pathogen immunosensors on-site.

General information
State: Published
Organisations: Enzyme and Protein Chemistry, Department of Systems Biology, Risø National Laboratory for Sustainable Energy
Authors: Skottrup, P. D. (Intern), Nicolaisen, M. (Intern), Frøkiær, H. (Intern), Justesen, A. F. (Intern)
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Bakteriefloren i tarmen afbalancerer immunsystemet: Den rigtige bakterieflora i tarmen kan modvirke allergi og inflammatoriske sygdomme

General information
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Organisations: Center for Biological Sequence Analysis, Department of Systems Biology
Authors: Fink, L. N. (Intern), Zeuthen, L. (Intern), Frøkiær, H. (Intern)
Detection of Fungal Spores Using a Generic Surface Plasmon Resonance Immunoassay

This paper describes a biosensor-based method for detection of fungal spores using Surface Plasmon Resonance (SPR). The approach involves the use of a mouse monoclonal antibody (Pst mAb8) and a SPR sensor for label-free detection of urediniospores from the model organism Puccinia striiformis f.sp. tritici (Pst). In the subtractive inhibition assay, urediniospores and Pst mAb8 were mixed, urediniospore-bound Pst mAb8 removed by centrifugation and the remaining Pst mAb8 quantified using the SPR sensor. Assay conditions were optimised and a detection limit of $3.1 \times 10^5$ urediniospores/ml was achieved. Spiked Pst samples were further examined in a background of a related spore and it was found that Pst quantification was possible in this mixture. This study represents the first use of SPR technology for fungal spore detection as well as the first report of a successful biosensor-based detection strategy for Pst.

General information

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Organisations: Enzyme and Protein Chemistry, Department of Systems Biology, Dublin City University, Danish Institute of Agricultural Sciences
Authors: Skottrup, P. (Intern), Hearty, S. (Ekstern), Frøkiær, H. (Intern), Leonard, P. (Ekstern), Hejgaard, J. (Intern), O'Kennedy, R. (Ekstern), Nicolaisen, M. (Ekstern), Fejer Justesen, A. (Ekstern)
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Web of Science (2015): Indexed yes
Dietary fibres differentially modulate the bacterially induced maturation of dendritic cells

**General information**

State: Published
Organisations: Center for Biological Sequence Analysis, Department of Systems Biology
Authors: Wismar, R. (Intern), Pedersen, S. B. (Intern), Laerke, H. (Ekstern), Frøkiær, H. (Intern)
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Publication date: 2007
Distinct gut-derived lactic acid bacteria elicit divergent dendritic cell-mediated NK cell responses

Lactic acid bacteria (LAB) are abundant in the gastrointestinal tract where they continuously regulate the immune system. NK cells are potently activated by dendritic cells (DCs) matured by inflammatory stimuli, and NK cells are present in the gut epithelium and in mesenteric lymph nodes, but it is not known how NK-DC interactions are affected by the predominantly non-pathogenic LAB. We demonstrate that human DCs exposed to different strains of gut-derived LAB consistently induce proliferation, cytotoxicity and activation markers in autologous NK cells. On the contrary, strains of LAB differ greatly in their ability to induce DC-dependent IFN-gamma production by NK cells. This suggests that DCs stimulated by gut LAB may expand the pool of NK cells and increase their cytotoxic potential. Specific LAB, inducing high levels of IL-12 in DCs, may promote amplification of a type-1 response via potent stimulation of IFN-gamma production in NK cells. Combining IFN-gamma-inducing and non-inducing LAB completely abrogates DC-mediated IFN-gamma production by NK cells, and therefore LAB modulating IFN-gamma production in NK cells may be important regulators of the immune response.
Epithelial cells prime the immune response to an array of gut-derived commensals towards a tolerogenic phenotype through distinct actions of thymic stromal lymphopoietin and transforming growth factor-beta

Humans and other mammals coexist with a diverse array of microbes colonizing the intestine, termed the microflora. The relationship is symbiotic, with the microbes benefiting from a stable environment and nutrient supply, and the host gaining competitive exclusion of pathogens and continuously maintenance of the gut immune homeostasis. Here we report novel crosstalk mechanisms between the human enterocyte cell line, Caco2, and underlying human monocyte-derived DC in a transwell model where Gram-positive (G+) commensals prevent Toll-like receptor-4 (TLR4)-dependent Escherichia coli-induced semimaturiation in a TLR2-dependent fashion. These findings add to our understanding of the hypo-responsiveness of the gut epithelium towards the microflora. Gut DC posses a more tolerogenic phenotype than conventional DC. Here we show that Caco2 spent medium (SM) induces tolerogenic DC with lower expression of maturation markers, interleukin (IL)-12p70, and tumour necrosis factor-alpha when matured with G+ and Gram-negative (G-) commensals, while IL-10 production is enhanced in DC upon encountering G+ commensals and reduced upon encountering G- bacteria. The Caco2 SM-induced tolerogenic phenotype is also seen in DC priming of naive T cells with elevated levels of transforming growth factor-beta (TGF-beta) and markedly reduced levels of bacteria-induced interferon-
gamma production. Caco2 cell production of IL-8, thymic stromal lymphopoietin (TSLP) and TGF-beta increases upon microbial stimulation in a strain dependent manner. TSLP and TGF-beta co-operate in inducing the tolerogenic DC phenotype but other mediators might be involved.
Epithelial cells prime the immune response to an array of gut-derived commensals towards a tolerogenic phenotype through the distinct action of thymic stromal lymphopoietin and transforming growth factor beta

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Authors: Zeuthen, L. (Intern), Fink, L. N. (Intern), Frøkiær, H. (Intern)
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Web of Science (2016): Impact factor 2.424
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Scopus rating (2015): SJR 1.074 SNIP 1.016 CiteScore 2.55
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Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
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Web of Science (2014): Impact factor 2.618
BFI (2013): BFI-level 1
Fish oil supplementation modulates immune function in healthy infants

(n-3) PUFA influence immune function in adults and may also affect immune maturation during development. This randomized trial is, to our knowledge, the first to investigate whether fish oil supplementation in late infancy modifies immune responses. The study was a 2 x 2 intervention in 64 healthy Danish infants, who received cow’s milk or infant formula alone or with fish oil (FO) (3.4 ± 1.1 mL/d) from 9 to 12 mo of age. Before and after the intervention, fatty acid composition of erythrocyte membranes, plasma IgE, C-reactive protein, and soluble IL-2 receptor concentrations were measured. TNF-alpha, INF-gamma, and IL-10 concentrations in whole-blood cultures, stimulated for 22 h with LPS+phytohema-glutinin (PHA) or Lactobacillus paracasei, were also determined. IgA was measured in feces when infants were 10 mo of age. FO supplementation effectively raised erythrocyte (n-3) PUFA (P <0.001), increased L. paracasei induced INF-gamma (P= 0.05) and tended to reduce LPS+PHA-induced IL-10 (P = 0.08). The FO intervention did not affect any of the other analyzed immune variables. The erythrocyte content of eicosapentanoic acid was negatively associated with LPS+PHA-induced IL-10 (r = -0.38, P = 0.02). Feeding milk rather than formula did not affect cytokine production, but plasma soluble IL-2 receptor concentration was greater in the formula group than in the cow's milk group (P = 0.03). Since the capacity to produce INF-gamma has been proposed as a maturation marker for the immune system in early life, this study suggests a faster immune maturation with FO supplementation with no apparent reduction in immune activation. The implications for later health need further investigation.

General information
State: Published
Human antigen-presenting cells respond differently to gut-derived probiotic bacteria but mediate similar strain-dependent NK and T cell activation

The intestinal microbiota is essential for homeostasis of the local and systemic immune system, and particularly strains of lactic acid bacteria and Escherichia coli have been shown to have balancing effects on inflammatory conditions such as allergy and inflammatory bowel disease. However, in vitro assessment of the immunomodulatory effects of distinct strains may depend strongly on the cell type used as a model. To select the most appropriate model for screening of beneficial bacteria in human cells, the response to strains of intestinal bacteria of three types of antigen-presenting cells (APC) was compared; blood myeloid dendritic cells (DC), monocyte-derived DC and monocytes, and the effector response of natural killer cells and naïve T cells was characterized. Maturation induced by gut-derived bacteria differed between APC, with blood DC and monocytes responding with the production of IL-6 and tumour necrosis factor-alpha to bacteria, which elicited mainly IL-10 in monocyte-derived DC. In contrast, comparable IFN-gamma production patterns were found in both natural killer cells and naïve T cells induced by all bacteria-matured APC. An inhibitory effect of certain strains on this IFN-gamma production was also mediated by all types of APC. The most potent responses were induced by monocyte-derived DC, which thus constitute a sensitive screening model.
Influence of gut microbiota on immunological maturation in infancy

General information
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Organisations: Department of Systems Biology
Authors: Sørensen, R. B. (Intern), Pedersen, S. B. (Intern), Boye, M. (Intern), Frøkiær, H. (Intern)
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Influence of gut microbiota on immunological maturation in infancy

General information
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Organisations: Department of Systems Biology

Influence of gut microbiota on immunological maturation in infancy

General information
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Organisations: Department of Systems Biology
Influence of gut microbiota on immunological maturation in infancy

General information
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Organisations: Department of Systems Biology, Division of Veterinary Diagnostics and Research, National Veterinary Institute
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Maturation and function of the immune system is highly influenced by the establishment of the microbiota in the gut, which in turn, particularly in infancy, is influenced by factors such as maternal microbiota and the environment, including diet. Studies have shown that although lymph nodes are able to elicit mixed Th1/Th2 responses, Th2 responses dominate in the spleen in the neonatal mouse. In this study, we compared phenotypic markers present on mesenteric lymph nodes (mLNs) and spleens from 3 weeks old mice, to levels found in adult mice. We found that mLNs displayed levels of CD4+ and CD8+ T-cells as well as NK-cells similar to those found in adult mice, while splenocytes expressed severely reduced levels of these markers and were impaired in their ability to proliferate in response to anti-CD3/anti-CD28. To further
characterize the development of immunological maturation in spleens from young mice, female mice were administered different probiotics during pregnancy and lactation and their offspring sacrificed at the age of 3 weeks. Interestingly, intake of Bb. longum Q46 or E. coli Nissle 1917 resulted in reduced levels of CD4, CD8 and CD49b on the cell surface of splenocytes as well as impaired ex vivo proliferative abilities of T lymphocytes as measured by 3H-TdR incorporation. Furthermore, Bb. longum Q46 and E. coli Nissle 1917 promoted a non-Th2 cytokine profile in splenocytes from offspring, and reduced cellular activation during ex vivo polyclonal stimulation. These results show that, although the maturation status of spleens, as representatives for the systemic immune system in mice aged 3 weeks, is quite low compared to mLNs, the maturation status and effector-function of spleens can be altered by administering probiotics during pregnancy.

**General information**
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Authors: Sørensen, R. B. (Intern), Pedersen, S. B. (Intern), Frøkiær, H. (Intern)
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**Kan kosten påvirke vores risiko for at udvikle alærgi?**

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**Monoclonal antibodies for the detection of Puccinia striiformis urediniospores**

The fungal pathogen Pst causes yellow rust disease in wheat plants leading to crop losses. The organism spreads by releasing wind-dispersed urediniospores from infected plants. In this study a library of novel monoclonal antibodies (mAbs) was developed against Pst urediniospores. Nine mAb-producing cell lines were cloned and their cross-reactivities characterised against a panel of airborne fungal spores representing genera commonly found in the same environment as Pst. Two specific mAbs were used to develop a competitive ELISA (Pst mAb4) and a subtractive inhibition ELISA (Pst mAb8). Standard curves for both assays had good intra- and interday reproducibility. The subtractive inhibition ELISA had greater sensitivity with a detection limit of 1.5 105 spores ml1. Cross-reactivity studies of Pst mAb8 in the subtractive inhibition ELISA, showed reaction with other Puccinia spores only, suggesting that common epitopes exist within this genus. The biosensor-compatible Pst mAb8 assay principle developed in this study has the potential to be implemented in future ‘label-free’ in-the-field systems for Pst detection.

**General information**
State: Published
Organisations: Department of Systems Biology, Enzyme and Protein Chemistry, Danish Institute of Agricultural Sciences, Dublin City University
Authors: Skottrup, P. (Intern), Frøkiær, H. (Intern), Hearty, S. (Ekstern), O'Kennedy, R. (Ekstern), Hejgaard, J. (Intern), Nicolaisen, M. (Ekstern), Justesen, A. F. (Ekstern)
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**Publication information**
Probiotic bacteria interact differently with dendritic cells from gut and spleen

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Main Research Area: Technical/natural sciences

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Scopus rating (2014): SJR 1.294 SNIP 1.096 CiteScore 2.64
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BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.957 SNIP 1.036 CiteScore 2.46
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ISI indexed (2013): ISI indexed yes
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BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.867 SNIP 0.89 CiteScore 2.35
Web of Science (2012): Impact factor 1.661
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BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.889 SNIP 0.95 CiteScore 2.38
Production of recombinant peanut allergen Ara h 2 using Lactococcus lactis

Background: Natural allergen sources can supply large quantities of authentic allergen mixtures for use as immunotherapeutics. However, such extracts are complex, difficult to define, vary from batch to batch, which may lead to unpredictable efficacy and/or unacceptable levels of side effects. The use of recombinant expression systems for allergen production can alleviate some of these issues. Several allergens have been tested in high-level expression systems and in most cases show immunoreactivity comparable to their natural counterparts. The gram positive lactic acid bacterium Lactococcus lactis is an attractive microorganism for use in the production of protein therapeutics. L. lactis is considered food grade, free of endotoxins, and is able to secrete the heterologous product together with few other native proteins. Hypersensitivity to peanut represents a serious allergic problem. Some of the major allergens in peanut have been described. However, for therapeutic usage more information about the individual allergenic components is needed. In this paper we report recombinant production of the Ara h 2 peanut allergen using L. lactis. Results: A synthetic ara h2 gene was cloned into an L. lactis expression plasmid containing the P170 promoter and the SP310mut2 signal sequence. Flask cultures grown overnight showed secretion of the 17 kDa Ara h 2 protein. A batch fermentation resulted in 40 mg/L recombinant Ara h 2. Purification of Ara h 2 from the culture supernatant was done by hydrophobic exclusion and size separation. Mass spectrometry and N-terminal analysis showed a recombinant Ara h 2 of full length and correctly processed by the signal peptidase. The immunological activity of recombinant Ara h 2 was analysed by ELISA using antibodies specific for native Ara h 2. The recombinant Ara h 2 showed comparable immunoreactivity to that of native Ara h 2. Conclusion: Recombinant production of Ara h 2 using L. lactis can offer high yields of secreted, full length and immunologically active allergen. The L. lactis expression system can support recombinant allergen material for immunotherapy and component resolved allergen diagnostics.

General information
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Proteome-analysis of gut bacteria-matured dendritic cells

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Organisations: Department of Systems Biology
Authors: Pedersen, S. B. (Intern), Kragh, M. (Ekstern), Søndergaard, J. N. (Ekstern), Bjørkan, L. (Ekstern), Jacobsen, S. (Intern), Frøkiær, H. (Intern)
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Proteome-analysis of gut bacteria-matured dendritic cells

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Scopus rating (2015): SJR 1.074 SNIP 1.016 CiteScore 2.55
Web of Science (2015): Impact factor 2.461
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.294 SNIP 1.096 CiteScore 2.64
Web of Science (2014): Impact factor 2.618
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.957 SNIP 1.036 CiteScore 2.46
Web of Science (2013): Impact factor 2.747
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Proteome-analysis of gut bacteria-matured dendritic cells

General information
State: Published
Organisations: Department of Systems Biology, Center for Biological Sequence Analysis, Enzyme and Protein Chemistry, Technical University of Denmark
Authors: Pedersen, S. B. (Intern), Kragh, M. (Intern), Søndergaard, J. N. (Intern), Bjerkan, L. (Ekstern), Jacobsen, S. (Intern), Frøkiær, H. (Intern)
Publication date: 2007
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 199066
Publication: Research - peer-review › Poster – Annual report year: 2007

Saponin-containing subfractions of soybean molasses induce enteritis in the distal intestine of Atlantic salmon

The current work aimed at tracing the causative components for soybean-induced enteritis in Atlantic salmon (Salmo salar L.). Soybean molasses was subjected to phase separation using n-butanol. Three subfractions were obtained as follows: butanol phase, precipitate, and water phase. The biochemical composition of soybean molasses and the obtained subfractions were analyzed in detail: Protein, fat, and ash were quantified according to standard methods. Sucrose, raffinose, and stachyose were quantified using high-performance anion-exchange chromatography. Soyasaponins were quantified using reverse-phase high-performance liquid chromatography. Finally, sodium dodecyl sulfate-polyacrylamide gel electrophoresis was used to evaluate the size distribution of the proteins present in each fraction. Molasses and the different subfractions were thereafter fed to Atlantic salmon in two successive fish trials. The level of intestinal inflammation was evaluated by light microscopy using a semiquantitative scoring system. Histological assessments revealed that Atlantic salmon fed a combination of butanol phase and precipitate displayed significant enteritis. Atlantic
salmon fed the water phase displayed normal intestinal morphology. The causative components for soybean-induced enteritis withstand butanol treatment and prolonged heating at 70 degrees C. Sucrose, raffinose, stachyose, nor soybean proteins larger than 10 kDa induce enteritis alone. Soyasaponins, or components that follow the same solubility pattern, trigger the inflammatory reaction. We therefore suggest that soybean-induced enteritis in Atlantic salmon is induced by soyasaponins alone or by soyasaponins in combination with other factors, e.g., antigenic soybean proteins or the intestinal microflora.

**General information**

State: Published  
Organisations: Center for BioProcess Engineering, Department of Chemical and Biochemical Engineering, Department of Systems Biology  
Authors: Knudsen, D. (Ekstern), Uran, P. (Ekstern), Arnous, A. (Intern), Koppe, W. (Ekstern), Frøkiær, H. (Intern)  
Pages: 2261-2267  
Publication date: 2007  
Main Research Area: Technical/natural sciences

**Publication information**

Journal: Journal of Agricultural and Food Chemistry  
Volume: 55  
Issue number: 6  
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  
Scopus rating (2017): CiteScore 3.64 SJR 1.269 SNIP 1.343  
Web of Science (2017): Impact factor 3.412  
BFI (2016): BFI-level 2  
Web of Science (2016): Indexed yes  
Scopus rating (2016): CiteScore 3.45 SJR 1.305 SNIP 1.343  
Web of Science (2016): Impact factor 3.154  
Web of Science (2016): Indexed yes  
BFI (2015): BFI-level 2  
Scopus rating (2015): SJR 1.224 SNIP 1.245 CiteScore 3.23  
Web of Science (2015): Impact factor 2.857  
Web of Science (2015): Indexed yes  
BFI (2014): BFI-level 2  
Scopus rating (2014): SJR 1.267 SNIP 1.413 CiteScore 3.25  
Web of Science (2014): Impact factor 2.912  
Web of Science (2014): Indexed yes  
BFI (2013): BFI-level 2  
Scopus rating (2013): SJR 1.43 SNIP 1.47 CiteScore 3.44  
Web of Science (2013): Impact factor 3.107  
ISI indexed (2013): ISI indexed yes  
Web of Science (2013): Indexed yes  
BFI (2012): BFI-level 2  
Scopus rating (2012): SJR 1.408 SNIP 1.464 CiteScore 3.2  
Web of Science (2012): Impact factor 2.906  
ISI indexed (2012): ISI indexed yes  
Web of Science (2012): Indexed yes  
BFI (2011): BFI-level 2  
Scopus rating (2011): SJR 1.389 SNIP 1.441 CiteScore 3.1  
Web of Science (2011): Impact factor 2.823  
ISI indexed (2011): ISI indexed yes  
Web of Science (2011): Indexed yes  
BFI (2010): BFI-level 2  
Scopus rating (2010): SJR 1.42 SNIP 1.391
The effects of fish oil combined with high and low PUFA intake on tissue fatty acid composition and cardiovascular risk markers in healthy men

General information
State: Published
Organisations: Department of Systems Biology
Authors: Damsgaard, C. (Ekstern), Frøkiær, H. (Intern), Lauritzen, L. (Ekstern)
Pages: 281-281
Publication date: 2007
Main Research Area: Technical/natural sciences

Publication information
Journal: Annals of Nutrition and Metabolism
Volume: 51
ISSN (Print): 0250-6807
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 1.057 SJR 1.317 CiteScore 2.78
Web of Science (2017): Impact factor 3.051
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 1.215 SNIP 1.003 CiteScore 2.69
The potential of gut bacteria-matured DCs to activate CD4+ T cells highly depends on the lipid composition of the T cell membrane

General information
State: Published
Organisations: Center for Biological Sequence Analysis, Department of Systems Biology
Authors: Pedersen, S. B. (Intern), Lund, P. (Intern), Kjær, T. (Intern), Straarup, E. M. (Intern), Hellgren, L. (Intern), Frøkiær, H. (Intern)
The potential of gut bacteria-matured DCs to activate CD4+ T cells highly depends on the lipid composition of the T cell membrane

General information
State: Published
Organisations: Department of Systems Biology, Center for Biological Sequence Analysis
Authors: Pedersen, S. B. (Intern), Lund, P. (Intern), Kjær, T. (Intern), Straarup, E. M. (Intern), Hellgren, L. (Intern), Frøkiær, H. (Intern)
Pages: 65-65
Publication date: 2007
Main Research Area: Technical/natural sciences

Publication information
Journal: Annals of Nutrition and Metabolism
Volume: 51
Issue number: Suppl. 1
ISSN (Print): 0250-6807
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 1.057 SJR 1.317 CiteScore 2.78
Web of Science (2017): Impact factor 3.051
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 1.215 SNIP 1.003 CiteScore 2.69
Web of Science (2016): Impact factor 2.424
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.074 SNIP 1.016 CiteScore 2.55
Web of Science (2015): Impact factor 2.461
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.294 SNIP 1.096 CiteScore 2.64
Web of Science (2014): Impact factor 2.618
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.957 SNIP 1.036 CiteScore 2.46
Web of Science (2013): Impact factor 2.747
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.867 SNIP 0.89 CiteScore 2.35
Web of Science (2012): Impact factor 1.661
ISI indexed (2012): ISI indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.889 SNIP 0.95 CiteScore 2.38
Web of Science (2011): Impact factor 2.257
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
Assessment of Lupin Allergenicity in the Cholera Toxin Model: Induction of IgE Response Depends on the Intrinsic Properties of the Conglutins and Matrix Effects

General information
State: Published
Organisations: Department of Systems Biology, Università degli Studi di Milano
Authors: Foss, F. N. (Intern), Duranti, M. (Ekstern), Magni, C. (Ekstern), Frøkiær, H. (Intern)
Pages: 141-150
Publication date: 2006
Main Research Area: Technical/natural sciences

Publication information
Journal: International Archives of Allergy and Immunology
Volume: 141
Issue number: 2
ISSN (Print): 1018-2438
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 0.883 SJR 0.989 CiteScore 2.52
Web of Science (2017): Impact factor 2.437
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 1.055 SNIP 1.068 CiteScore 2.61
Web of Science (2016): Impact factor 2.72

Bibliographical note
10th European Nutrition Conference July 10-13, 2007, Paris, France
Source: orbit
Source-ID: 213750
Publication: Research - peer-review › Conference abstract in journal – Annual report year: 2007
A Surface Plasmon Resonance Immunosensor for Detection of Phytophthora infestans

In this study we focused on the development of a Surface Plasmon Resonance (SPR) immunosensor for Phytophthora infestans detection. The fungus-like organism is the cause of potato late blight and is a major problem in potato growing regions of the world. Efficient control is dependent on early detection of P. infestans sporangia. The wind-dispersed sporangia are large, with a diameter range of 12-23 µm, meaning that direct sporangia capture on antibody surfaces would have a limited sensitivity in SPR assays. Here we have developed an alternative SPR immunosensor based on a subtractive inhibition assay format.
A Surface Plasmon Resonance Immunosensor for Detection of urediniospores from Puccinia striiformis f. sp. tritici

Different kinetic in incorporation and depletion of n-3 fatty acids in erythrocytes and leukocytes of mice

Different kinetic in incorporation and depletion of n-3 fatty acids in erythrocytes and leukocytes of mice

Different kinetic in incorporation and depletion of n-3 fatty acids in erythrocytes and leukocytes of mice

Different kinetic in incorporation and depletion of n-3 fatty acids in erythrocytes and leukocytes of mice

Different kinetic in incorporation and depletion of n-3 fatty acids in erythrocytes and leukocytes of mice
Distinct Gut-Derived Bacteria Differentially Affect Three Types of Antigen-Presenting Cells and Impact on NK- and T-Cell Responses

Objectives Gut bacteria are assumed essential for development and maintenance of a balanced immune system. Specifically, stimulation of antigen-presenting cells (APCs) by gut bacteria is important for polarisation of the immune response. This experiment was designed to reveal similarities and differences between the reaction patterns of three types of human APCs when stimulated with intestinal bacteria. Furthermore, the effect of these APCs on NK-cells and T-cells
was examined. Methodology The APCs used in this study were blood monocytes, blood dendritic cells, and dendritic cells differentiated from monocytes. Monocyte-derived dendritic cells constitute a commonly used model of dendritic cell function. The APCs were cultured for 18 h with four different gut bacteria: Lactobacillus acidophilus X37, Lactobacillus reuteri DSM 12246, E. coli Nissle 1917 or Bifidobacterium longum Q46. Results & Discussion To examine the polarising effect of gut bacteria on APCs, surface markers and cytokines were measured. The co-stimulatory molecules CD40 and CD86 were induced to a different extent together with CD83. Interleukin-12 (a Th1 cytokine) was only induced by Lactobacillus acidophilus. Interleukin-10, which promotes the development of regulatory T-cells, was mainly induced by the other bacteria. Interleukin-6 and tumour necrosis factor are pro-inflammatory cytokines, often induced by pathogens, but also by some gut bacteria. The effect of the four gut bacteria on monocyte-derived dendritic cells has previously been examined, but this study revealed that their effect on other kinds of APCs is markedly different. When APCs matured by different bacteria were added to either NK-cells or T-cells, different APCs combined with distinct strains of bacteria caused the production of varying amounts of cytokines. Conclusions Distinct gut bacteria possess individual properties leading to different effects on APCs, NK-cells and T-cells. Because NK-cells play a major role in T-cell polarisation, and because the APCs affect T-cells directly, gut bacteria may be very important in maintaining a balanced immune response through these mechanisms. The bacteria examined can potentially be used in tailored probiotic foods exploring their immunomodulatory properties.

**General information**

State: Published
Organisations: Enzyme and Protein Chemistry, Department of Systems Biology
Authors: Fink, L. N. (Intern), Hansen, A. M. V. (Intern), Frøkiær, H. (Intern)
Number of pages: 53
Publication date: 2006
Event: Poster session presented at Nutrigenomics and Health: LMC International Food Congress, Copenhagen.
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 189393
Publication: Research - peer-review » Poster – Annual report year: 2006

**Early nutrition and immunity - progress and perspectives**

The immune system exists to protect the host against pathogenic organisms and highly complex pathways of recognition, response, elimination and memory have evolved in order to fulfil this role. The immune system also acts to ensure tolerance to ‘self’, to food and other environmental components, and to commensal bacteria. A breakdown in the tolerogenic pathways can also lead to inflammatory diseases. The prevalence of inflammatory diseases, including atopic disorders, has increased over the last 60 years. The development of tolerance is the result of active immune mechanisms and both development and maintenance of tolerance are lifelong processes which start very early in life, even prenatally. Profound immunologic changes occur during pregnancy, involving a polarization of T helper (Th) cells towards a dominance of Th2 and regulatory T cell effector responses in both mother and fetus. This situation is important to maintain pregnancy through avoidance of the rejection of the immunologically incompatible fetus. During the third trimester of human pregnancy, fetal T cells are able to mount antigen-specific responses to environmental and food-derived antigens and antigen-specific T cells are detectable in cord blood in virtually all newborns indicating in utero sensitization. If the neonatal immune system is not able to down-regulate the pre-existing Th2 dominance effectively then an allergic phenotype may develop. Changes occur at, and soon after, birth in order that the immune system of the neonate becomes competent and functional and that the gut becomes colonized with bacteria. Exposure to bacteria during birth and from the mother's skin and the provision of immunologic factors in breast milk are amongst the key events that promote maturation of the infant's gut and gut-associated and systemic immune systems. The introduction of formula and of solid foods exposes the infant to novel food antigens and also affects the gut flora. Nutrition may be the source of antigens to which the immune system must become tolerant, provide factors, including nutrients, that themselves might modulate immune maturation and responses, and provide factors that influence intestinal flora, which in turn will affect antigen exposure, immune maturation and immune responses. Through these mechanisms it is possible that nutrition early in life might affect later immune competence, the ability to mount an appropriate immune response upon infection, the ability to develop a tolerogenic response to ‘self’ and to benign environmental antigens, and the development of immunologic disorders. A Workshop held in February 2006 considered recent findings in the areas of oral tolerance, routes of sensitization to allergens and factors affecting the development of atopic disease; factors influencing the maturation of dendritic cells and the development of regulatory T cells; the influence of gut microflora on immunity, allergic sensitization and infectious disease; the role of nutrition in preventing necrotizing enterocolitis in an animal model of preterm birth; and the role of PUFA of different classes in influencing immune responses and in shaping the development of atopic disease. This report summarizes the content of the lectures and the subsequent discussions.

**General information**

State: Published
Organisations: Department of Systems Biology
Effects of dietary fatty acids on T-cell responses induced by dendritic cells

General information
State: Published
Organisations: Department of Systems Biology
Authors: Pedersen, S. B. (Intern), Kjær, T. (Intern), Lund, P. (Intern), Straarup, E. M. (Intern), Hellgren, L. (Intern), Frøkiær, H. (Intern)
Publication date: 2006
Event: Poster session presented at LMC International Food Congress 2006, Copenhagen, Denmark.
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 193846
Publication: Research - peer-review › Journal article – Annual report year: 2006

Fish oil affects immune function in 9 to 12 month old infants
Background - n-3 Polyunsaturated fatty acids (PUFA) are thought to affect immune function and may affect immune maturation in early life. Objective - To examine if fish oil supplementation in late infancy could modify immune function. Design - A 2×2 intervention with fish oil (3.4 ± 1.1 ml/day) or no fish oil and cow’s milk or infant formula from 9 to 12 month of age in 64 healthy Danish infants. Before and after the intervention we measured the fatty acid composition of erythrocyte (RBC) membranes, plasma IgE levels, C-reactive protein and soluble IL-2 receptors (sIL-2R) as well as cytokine production in whole-blood cultures stimulated with lipopolysaccharide (LPS)/phytohaemaglutinin (PHA) or Lactobacillus paracasei for 22 h. IgA was measured in feces at 10 months of age. Results - Fish oil supplementation effectively raised RBC n-3 PUFA (p

General information
State: Published
Organisations: Department of Systems Biology, University of Copenhagen
Authors: Damsgaard, C. T. (Ekstern), Lauritzen, L. (Ekstern), Kjær, T. (Intern), Frøkiær, H. (Intern)
Publication date: 2006
Event: Abstract from Novel Aspects of Fatty Acids, Ystad, Sweden, .
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 189371
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2006

Immunogenicity of κ-Casein and Glycomacropeptide

General information
Immunomodulating potential of supplementation with probiotics: a dose-response study in healthy young adults

Certain probiotic microorganisms have been found beneficial in the treatment of immune-related diseases and may also affect immune function in healthy people. Intervention studies of probiotics in healthy humans are urgently required. Here, the immunomodulating potential of Bifidobacterium animalis ssp. lactis (BB-12) and Lactobacillus paracasei ssp. paracasei (CRL-431) was studied in a double-blind placebo-controlled parallel dose-response trial (n=71) based on five randomly assigned groups of young healthy adults supplemented for 3 weeks with 0, 10(8), 10(9), 10(10) and 10(11) CFU day(-1), respectively, of a mixture of BB-12 and CRL-431. No statistically significant dose-dependent effect was found for phagocytic activity in blood leukocytes, fecal immunoglobulin A (IgA) concentrations or production of interferon-gamma and interleukin-10 in blood cells. When evaluating data according to the amount of viable BB-12 recovered from faeces, the interferon-gamma production in blood cells was significantly reduced. In conclusion, no solid effect on the immune function of young healthy adults supplemented with even high doses of B. animalis ssp. lactis BB-12 and L. paracasei ssp. paracasei CRL-431 was demonstrated in this study.

General information
State: Published
Organisations: Department of Systems Biology, Enzyme and Protein Chemistry
Authors: Christensen, H. R. (Intern), Larsen, C. (Ekstern), Kæstel, P. (Ekstern), Rosholm, L. B. (Ekstern), Sternberg, C. (Intern), Michaelsen, K. (Ekstern), Frøkiær, H. (Intern)
Pages: 380-390
Publication date: 2006
Main Research Area: Technical/natural sciences

Publication information
Journal: F E M S Immunology and Medical Microbiology
Volume: 47
ISSN (Print): 0928-8244
Ratings:
Web of Science (2018): Indexed yes
Scopus rating (2017): CiteScore 2.52
Web of Science (2017): Impact factor 2.337
Web of Science (2017): Indexed yes
Scopus rating (2016): CiteScore 2.23
Web of Science (2016): Impact factor 2.335
Scopus rating (2015): SJR 1.306 SNIP 0.739 CiteScore 2.12
Web of Science (2015): Impact factor 2.483
Scopus rating (2014): SJR 1.284 SNIP 0.903 CiteScore 2.32
Web of Science (2014): Impact factor 2.403
Web of Science (2014): Indexed yes
Scopus rating (2013): SJR 1.222 SNIP 0.784
Lactic Acid Bacteria Inducing a Weak Interleukin-12 and Tumor Necrosis Alpha Response in Human Dendritic Cells Inhibit Strongly Stimulating Lactic Acid Bacteria but Act Synergistically with Gram-Negative Bacteria

The development and maintenance of immune homeostasis indispensably depend on signals from the gut flora. Lactic acid bacteria (LAB), which are gram-positive (G+) organisms, are plausible significant players and have received much attention. Gram-negative (G-) commensals, such as members of the family Enterobacteriaceae, may, however, be immunomodulators that are as important as G+ organisms but tend to be overlooked. Dendritic cells (DCs) are crucial immune regulators, and therefore, the present study aimed at investigating differences among human gut flora-derived LAB and G- bacteria in their patterns of DC polarization. Human monocyte-derived DCs were exposed to UV-killed bacteria, and cytokine secretion and surface marker expression were analyzed. Profound differences in the DC polarization patterns were found among the strains. While strains of LAB varied greatly in their capacity to induce interleukin-12 (IL-12) and tumor necrosis factor alpha (TNF-α), G- strains were consistently weak IL-12 and TNF-α inducers. All strains induced significant amounts of IL-10, but G- bacteria were far more potent IL-10 inducers than LAB. Interestingly, we found that when weakly IL-12- and TNF-α-inducing LAB and strong IL-12- and TNF-α-inducing LAB were mixed, the weakly IL-12- and TNF-α-inducing LAB efficiently inhibited otherwise strong IL-12- and TNF-α-inducing LAB, yet when weakly IL-12- and TNF-α-inducing LAB were mixed with G- bacteria, they synergistically induced IL-12 and TNF-α. Furthermore, strong IL-12- and TNF-α-inducing LAB efficiently up-regulated surface markers (CD40, CD83, CD86, and HLA-DR), which were inhibited by weakly IL-12- and TNF-α-inducing LAB. All G- bacteria potently up-regulated surface
markers; however, these markers were not inhibited by weakly IL-12- and TNF-α-inducing LAB. These much divergent DC stimulation patterns among intestinal bacteria, which encompass both antagonistic and synergistic relationships, support the growing evidence that the composition of the gut flora affects immune regulation and that compositional imbalances may be involved in disease etiology.

**General information**

State: Published
Organisations: Enzyme and Protein Chemistry, Department of Systems Biology
Authors: Zeuthen, L. H. (Intern), Christensen, H. R. (Ekstern), Frøkiær, H. (Intern)
Pages: 365-375
Publication date: 2006
Main Research Area: Technical/natural sciences

**Publication information**

Journal: Clinical and Vaccine Immunology
Volume: 13
Issue number: 3
ISSN (Print): 1556-6811
Ratings:
- BFI (2018): BFI-level 1
- Web of Science (2018): Indexed yes
- BFI (2017): BFI-level 1
- Scopus rating (2017): CiteScore 2.63
- Web of Science (2017): Impact factor 2.872
- Web of Science (2017): Indexed yes
- BFI (2016): BFI-level 1
- Scopus rating (2016): CiteScore 2.35
- Web of Science (2016): Impact factor 2.425
- BFI (2015): BFI-level 1
- Scopus rating (2015): CiteScore 2.38
- Web of Science (2015): Impact factor 2.277
- BFI (2014): BFI-level 1
- Scopus rating (2014): CiteScore 2.66
- Web of Science (2014): Impact factor 2.47
- BFI (2013): BFI-level 1
- Scopus rating (2013): CiteScore 2.69
- Web of Science (2013): Impact factor 2.37
- ISI indexed (2013): ISI indexed yes
- BFI (2012): BFI-level 1
- Scopus rating (2012): CiteScore 2.7
- Web of Science (2012): Impact factor 2.598
- ISI indexed (2012): ISI indexed yes
- BFI (2011): BFI-level 1
- Scopus rating (2011): CiteScore 2.77
- Web of Science (2011): Impact factor 2.546
- ISI indexed (2011): ISI indexed yes
- Web of Science (2011): Indexed yes
- BFI (2010): BFI-level 1
- Web of Science (2010): Impact factor 2.471
- BFI (2009): BFI-level 1
- BFI (2008): BFI-level 1
- Web of Science (2006): Indexed yes
- Web of Science (2004): Indexed yes
- Web of Science (2002): Indexed yes
Original language: English
Source: orbit
Source-ID: 189388
Publication: Research - peer-review › Journal article – Annual report year: 2006
Soyasaponins resist extrusion cooking and are not degraded during gut passage in Atlantic salmon (Salmo salar L.)

The stability of soyasaponins in fish feed formulations was investigated. The level of soyasaponin Ab, Bb, Bc, Ba-2,3-dihydro-2,5-dihydroxy-6-methyl-4H-pyran-4-one (Ba-DDMP), Bb-DDMP, and BcDDMP was quantified in 15 samples of defatted soybean meal, two full fat soybean meals, and two soybean protein concentrates by reverse phase high-performance liquid chromatography. The total level of saponins in the 15 samples of commercial defatted soybean meal ranged from 4.8-6.8 µmol/g (5.1-7.0 g/kg). The two full fat meals contained 4.4 and 4.7 µmol/g whereas no saponins could be detected in the alcohol-extracted soybean protein concentrates. Fifteen batches of fish feed containing 20% defatted soybean meal were produced by twin-screw extrusion from the 15 different samples of defatted soybean meal. Extrusion did not reduce the total level of group B saponins, but the ratio between DDMP-conjugated group B saponins and non-DDMP-conjugated group B saponins was slightly reduced. A soybean-containing diet was fed to seawater adapted Atlantic salmon for 9 weeks. Yttrium oxide was included in the feed as an inert marker in order to estimate the disappearance of saponins during gut passage. High levels of intact non-DDMP-conjugated group B soyasaponins were found in feces whereas only low levels of DDMP-conjugated saponins could be detected. The overall disappearance of saponins was close to zero, and the concentration of intact saponins in dry feces reached levels several fold higher than dietary levels. The present work demonstrates that non-DDMP-conjugated group B soyasaponins resist extrusion cooking and remain intact during gut passage in Atlantic salmon. The latter is contrary to earlier findings in endothermic animals.
A Generic Method for Fungal Spore Detection: The use of a monoclonal antibody and surface plasmon resonance

General information
State: Published
Organisations: Enzyme and Protein Chemistry, Department of Systems Biology, Dublin City University, Danish Institute of Agricultural Sciences
Authors: Skottrup, P. (Intern), Hearty, S. (Ekstern), Frøkiær, H. (Intern), Leonard, P. (Ekstern), Hejgaard, J. (Intern), O’Kennedy, R. (Ekstern), Nicolaisen, M. (Ekstern), Justesen, A. F. (Ekstern)
Publication date: 2005
Event: Poster session presented at 3rd annual iNANO meeting, Ebeltoft, Denmark, .
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 195318
Publication: Research › peer-review › Journal article – Annual report year: 2006

Characterization of a large panel of lactic acid bacteria derived from the human gut for their capacity to polarize dendritic cells

General information
State: Published
Organisations: Department of Systems Biology
Authors: Christensen, H. R. (Intern), Frøkiær, H. (Intern)
Pages: S142-S142
Publication date: 2005
Main Research Area: Technical/natural sciences

Publication information
Journal: Journal of Biotechnology
Volume: 118
ISSN (Print): 0168-1656
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 2.64 SJR 0.929 SNIP 0.86
Web of Science (2017): Impact factor 2.533
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 2.88 SJR 1.004 SNIP 0.929
Web of Science (2016): Impact factor 2.599
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.068 SNIP 0.988 CiteScore 2.87
Web of Science (2015): Impact factor 2.667
Web of Science (2015): Indexed yes
Combinatorial effects of dietary fatty acids and probiotics on T-cell responses induced by dendritic cells

General information
State: Published
Dietary lectins and the immune response.

General information
State: Published
Organisations: Department of Systems Biology, Enzyme and Protein Chemistry
Authors: Kjær, T. (Intern), Frøkiær, H. (Intern)
Pages: 271-295
Publication date: 2005

Host publication information
Title of host publication: Reviews in food and nutrition toxicity
Volume: 2
Place of publication: London
Publisher: CRC Press
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 185029
Publication: Research - peer-review › Book chapter – Annual report year: 2006

Dietary oil emulsions enhance the absorption of active food allergens without effecting oral tolerance induction unless lipopolysaccharide is present

General information
State: Published
Organisations: Department of Systems Biology
Authors: Pedersen, S. B. (Intern), Lindved, B. I. K. (Intern), Christensen, H. R. (Intern), Kjær, T. (Intern), Frøkiær, H. (Intern)
Publication date: 2005

Publication information
Original language: English
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 199056
Publication: Research › Sound/Visual production (digital) – Annual report year: 2005

Effect of maternal dietary cow’s milk on the immune response to beta-lactoglobulin in the offspring: A four generation study in mice

Evaluation of immune responses to food proteins in animal models requires that the animals are not already sensitized or orally tolerized against the proteins in question. Since maternal transfer of specific immune responses has been observed, breeding of animals on an antigen-free diet for several generations may be necessary to obtain immunologically naive animals. METHODS: To determine the most appropriate breeding conditions of mice to be used in immunological studies on food proteins, we examined immune responses towards beta-lactoglobulin (BLG) in mice bred on a milk-containing diet (F0) and then for three generations (F1-F3) on a commercially available milk-free diet. The specific antibody and cell-proliferative response to BLG was compared in non-immunized and immunized BALB/c mice, and in mice orally tolerized to BLG prior to immunization. RESULTS: The immune response to BLG in the F1 generation deviated from the response observed in the F0 and F2/F3 generations. Importantly, trace amounts of BLG detected in the commercial milk-free diet did not induce oral tolerance. CONCLUSIONS: The study showed that breeding mice on an antigen-free diet for at least two generations is required to attain animals appropriate for immunological studies of food proteins. Although the small quantity of BLG in the milk-free diet did not induce detectable oral tolerance in the present study, it is strongly recommended that the potential effect of contaminating dietary antigen is considered in future studies on food proteins.

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Publication information
Journal: International Archives of Allergy and Immunology
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Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 0.883 SJR 0.989 CiteScore 2.52
Web of Science (2017): Impact factor 2.437
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 1.055 SNIP 1.068 CiteScore 2.61
Web of Science (2016): Impact factor 2.72
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.217 SNIP 1.056 CiteScore 2.48
Web of Science (2015): Impact factor 2.677
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.982 SNIP 1.056 CiteScore 2.57
Web of Science (2014): Impact factor 2.673
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.872 SNIP 1.09 CiteScore 2.36
Web of Science (2013): Impact factor 2.433
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.854 SNIP 0.917 CiteScore 2.28
Web of Science (2012): Impact factor 2.248
ISI indexed (2012): ISI indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.995 SNIP 1.016 CiteScore 2.47
Web of Science (2011): Impact factor 2.403
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 0.859 SNIP 0.964
Web of Science (2010): Impact factor 2.235
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 0.878 SNIP 0.958
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 0.903 SNIP 0.938
Scopus rating (2007): SJR 0.936 SNIP 0.957
Scopus rating (2006): SJR 0.991 SNIP 1.028
Web of Science (2006): Indexed yes
Scopus rating (2005): SJR 0.915 SNIP 1.01
Web of Science (2005): Indexed yes
Scopus rating (2004): SJR 0.879 SNIP 0.743
Web of Science (2004): Indexed yes
Effect of prior dietary exposure to cow's milk protein on antigen-specific and nonspecific cellular proliferation in mice

General information
State: Published
Organisations: Enzyme and Protein Chemistry, Department of Systems Biology
Authors: Pedersen, S. B. (Intern), Magyar, O. H. (Ekstern), Barkholt, V. (Intern), Frøkiær, H. (Intern)
Pages: 217-225
Publication date: 2005
Main Research Area: Technical/natural sciences

Publication information
Journal: Journal of Dairy Research
Volume: 72
ISSN (Print): 0022-0299
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 0.759 SJR 0.573 CiteScore 1.33
Web of Science (2017): Impact factor 1.17
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 0.648 SNIP 0.883 CiteScore 1.66
Web of Science (2016): Impact factor 1.409
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.694 SNIP 0.888 CiteScore 1.54
Web of Science (2015): Impact factor 1.5
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.732 SNIP 0.954 CiteScore 1.79
Web of Science (2014): Impact factor 1.598
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.625 SNIP 0.828 CiteScore 1.49
Web of Science (2013): Impact factor 1.394
ISI indexed (2013): ISI indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.67 SNIP 0.937 CiteScore 1.54
Web of Science (2012): Impact factor 1.373
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.775 SNIP 1.016 CiteScore 1.61
Effects of lactic acid bacteria

General information
State: Published
Organisations: Department of Systems Biology, Enzyme and Protein Chemistry
Authors: Christensen, H. R. (Intern), Frøkiær, H. (Intern)
Pages: 1167-1204
Publication date: 2005

Host publication information
Title of host publication: Food Biotechnology: second edition, Revised and Expanded
Place of publication: New York
Publisher: Marcel Dekker
Edition: 2
Main Research Area: Technical/natural sciences
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Source-ID: 184968
Publication: Research - peer-review › Journal article – Annual report year: 2005

Fish oil supplementation of lactating mothers affects cytokine production in 2½-year-old children

General information
State: Published
Organisations: Department of Systems Biology, Enzyme and Protein Chemistry, University of Copenhagen
Authors: Lauritzen, L. (Ekstern), Kjær, T. (Intern), Fruekilde, M. (Intern), Michaelsen, K. F. (Ekstern), Frøkiær, H. (Intern)
Pages: 669-679
Publication date: 2005
Main Research Area: Technical/natural sciences

Publication information
Journal: Lipids
Volume: 40
Original language: English
Source: orbit
Lupin allergenicity explored in the cholera toxin model of food allergy

General information
State: Published
Organisations: Department of Systems Biology
Authors: Foss, F. N. (Intern), Frøkiær, H. (Intern)
Pages: 185-194
Publication date: 2005

Host publication information
Title of host publication: Optimised processes for preparing healthy and added value food ingredients from lupin kernels, the european protein-rich grain legume : Proceedings of the final conference of the european project
ISBN (Print): 88-548-0267-0
Main Research Area: Technical/natural sciences
Conference: Healthy ProFood : 09.11.2005 - 10.11.2005, Milano, Italien, 01/01/2005
Source: orbit
Source-ID: 185181
Publication: Research › Article in proceedings – Annual report year: 2005

Maternal transfer of oral tolerance to ingested soy proteins

General information
State: Published
Organisations: Department of Systems Biology
Authors: Christensen, H. R. (Intern), Brix, S. (Ekstern), Frøkiær, H. (Intern)
Pages: 61-61
Publication date: 2005
Main Research Area: Technical/natural sciences

Publication information
Journal: Immunology
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Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 3.72 SJR 1.69 SNIP 0.938
Web of Science (2017): Impact factor 3.358
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 3.74 SJR 1.964 SNIP 0.965
Web of Science (2016): Impact factor 3.701
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 2.075 SNIP 0.965 CiteScore 3.83
Web of Science (2015): Impact factor 4.078
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 2.048 SNIP 1.043 CiteScore 3.61
Web of Science (2014): Impact factor 3.795
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 2.086 SNIP 1.084 CiteScore 3.97
Web of Science (2013): Impact factor 3.735
ISI indexed (2013): ISI indexed yes
Milk-derived GM3 and GD3 differentially inhibit dendritic cell maturation and effector functionalities

Gangliosides are complex glycosphingolipids, which exert immune-modulating effects on various cell types. Ganglioside GD(3) and GM(3) are the predominant gangliosides of human breast milk but during the early phase of lactation, the content of GD(3) decreases while GM(3) increases. The biological value of gangliosides in breast milk has yet to be elucidated but when milk is ingested, dietary gangliosides might conceptually affect immune cells, such as dendritic cells (DCs). In this study, we address the in vitro effect of GD(3) and GM(3) on DC effector functionalities. Treatment of bone marrow-derived DCs with GD(3) before lipopolysaccharide-induced maturation decreased the production of interleukin-6 (IL-6), IL-10, IL-12 and tumor necrosis factor-alpha as well as reduced the alloreactivity in mixed leucocyte reaction (MLR). In contrast, only IL-10 and IL-12 productions were significantly inhibited by GM(3) and the potency of DCs to activate CD4(+) cells in MLR was unaffected by GM(3). However, both gangliosides suppressed expression of CD40, CD80, CD86 and major histocompatibility complex class II on DCs. Because GD(3) overall inhibits DC functionalities more than GM(3), the immune modulating effect of the ganglioside fraction of breast milk might be more prominent in the commencement of lactation during which the milk contains the most GD(3).

General information
State: Published
Organisations: Center for Biological Sequence Analysis, Department of Systems Biology
Authors: Brønnum, H. (Ekstern), Seested, T. (Ekstern), Hellgren, L. (Intern), Pedersen, S. B. (Intern), Frøkiær, H. (Intern)
Publication date: 2005
Natural Killer Cells are Activated by Lactic Acid Bacteria-Matured Dendritic Cells

General information
State: Published
Organisations: Enzyme and Protein Chemistry, Department of Systems Biology
Authors: Fink, L. N. (Intern), Christensen, H. R. (Intern), Zeuthen, L. H. (Intern), Frøkiær, H. (Intern)
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Event: Poster session presented at 2nd International Workshop on Probiotics in Gastric and Intestinal Disorders, Copenhagen, Denmark.
Main Research Area: Technical/natural sciences
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Post-weaning maintenance of oral tolerance to β-lactoglobulin: the importance of antigen presence in the diet

General information
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Organisations: Department of Systems Biology
Authors: Pedersen, S. B. (Intern), Christensen, H. R. (Intern), Barkholt, V. (Intern), Frøkiær, H. (Intern)
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Sialic acid-containing milk proteins show differential immunomodulatory activities independently of sialic acid

General information
State: Published
Organisations: Department of Systems Biology, Enzyme and Protein Chemistry, Aarhus University
Authors: Mikkelsen, T. L. (Intern), Bakmann, S. (Ekstern), Barkholt, V. (Intern), Sørensen, E. S. (Ekstern), Frøkiær, H. (Intern)
Pages: 7673-7680
Publication date: 2005
Main Research Area: Technical/natural sciences
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Journal: Journal of Agricultural Food Chemistry
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Original language: English
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Publication: Research - peer-review › Journal article – Annual report year: 2005
The degree and nature of glycomacropeptide association is dependent on whether the peptide is free or restricted in casein.

General information
State: Published
Organisations: Department of Systems Biology, Enzyme and Protein Chemistry, University of Milan, University of Campania "Luigi Vanvitelli"
Authors: Mikkelsen, T. L. (Intern), Frøkiær, H. (Intern), Topp, C. (Ekstern), Bonomi, F. (Ekstern), Iametty, S. (Ekstern), Picariello, G. (Ekstern), Ferranti, P. (Ekstern), Barkholt, V. (Intern)
Pages: 4228-4238
Publication date: 2005
Main Research Area: Technical/natural sciences

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BFI (2017): BFI-level 2
Scopus rating (2017): CiteScore 2.84 SJR 1.35 SNIP 1.491
Web of Science (2017): Impact factor 2.749
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 2.66 SJR 1.331 SNIP 1.484
Web of Science (2016): Impact factor 2.474
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 1.479 SNIP 1.488 CiteScore 2.63
Web of Science (2015): Impact factor 2.408
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 1.434 SNIP 1.504 CiteScore 2.78
Web of Science (2014): Impact factor 2.573
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 1.411 SNIP 1.589 CiteScore 2.82
Web of Science (2013): Impact factor 2.55
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 1.443 SNIP 1.717 CiteScore 2.79
Web of Science (2012): Impact factor 2.566
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 1.413 SNIP 1.582 CiteScore 2.59
Web of Science (2011): Impact factor 2.564
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 1.354 SNIP 1.518
Web of Science (2010): Impact factor 2.497
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 2
Scopus rating (2009): SJR 1.329 SNIP 1.724
What about the possible allergenicity of lupin?

General information
State: Published
Organisations: Unknown
Authors: Frøkiær, H. (Intern)
Pages: 18
Publication date: 2005
Main Research Area: Technical/natural sciences

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Volume: 45
Original language: English
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Source-ID: 185001
Publication: Research - peer-review › Journal article – Annual report year: 2005

Det vi spiser påvirker vores immunforsvar – men hvordan?

General information
State: Published
Organisations: Enzyme and Protein Chemistry, Department of Systems Biology
Authors: Christensen, H. R. (Intern), Kjær, T. (Ekstern), Pedersen, S. B. (Intern), Frøkiær, H. (Intern)
Pages: 26-27
Publication date: 2004
Main Research Area: Technical/natural sciences

Publication information
Journal: Dansk Kemi
Volume: 84
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Ratings:
ISI indexed (2013): ISI indexed no
Dietary oil emulsions enhance the absorption of native food allergens without affecting oral tolerance induction unless lipopolysaccharide is present

General information
State: Published
Organisations: Department of Systems Biology
Authors: Pedersen, S. B. (Intern), Lindved, B. I. K. (Intern), Christensen, H. R. (Intern), Kjær, T. (Intern), Frøkiær, H. (Intern)
Publication date: 2004
Event: Poster session presented at 9th International symposium on immunological, chemical and clinical problems of food allergy, Budapest, Hungary.
Main Research Area: Technical/natural sciences

Health promoting compounds in vegetables and fruits: A systematic approach for identifying plant components with impact on human health

Vegetables contain unknown compounds with important health promoting effect. The described project defined and tested a two-step screening procedure for identification of such compounds. Step 1 is initial screening according to three criteria: 1.1, chemically reactive functional groups; 1.2, toxicity at high concentrations or other bioactivity; and 1.3, presence in healthy foods. Step 2 is testing for minimum criteria defining health-promoting compounds: 2.1, positive or biphasic ("hormesis") responses in bioassay; 2.2, human tissue concentrations corresponding to beneficial effects in bioassay; and 2.3, possibility to control content in food. Falcarinol from carrots fulfilled all 6 criteria and subsequently showed anticancer effect in rats.

General information
State: Published
Organisations: Enzyme and Protein Chemistry, Department of Systems Biology
Authors: Brandt, K. (Ekstern), Christensen, L. (Ekstern), Hansen-Møller, J. (Ekstern), Hansen, S. (Ekstern), Haraldsdottir, J. (Ekstern), Jespersen, L. (Ekstern), Purup, S. (Ekstern), Karazmi, A. (Ekstern), Barkholt, V. (Intern), Frøkiær, H. (Intern), Købæk-Larsen, M. (Ekstern)
Pages: 384-393
Publication date: 2004
Main Research Area: Technical/natural sciences
Immune response in mice to ingested soya protein: antibody production, oral tolerance and maternal transfer

While allergic reactions to soya are increasingly investigated, the normal immune response to ingested soya is scarcely described. In the present study, we wanted to characterise the soya-specific immune response in healthy mice ingesting soya protein. Mice fed a soya-containing diet (F0) and mice of the first (F1) and second (F2) offspring generation bred on
a soya protein-free diet were used either directly or were transferred between the soya-containing and soya protein-free diet during pregnancy or neonatal life. The mice were compared as to levels of naturally occurring specific antibodies analysed by ELISA, and to the presence of oral tolerance detected as a suppressed antibody and cell-proliferation response upon immunisation with soya protein. F0 mice generated soya-specific antibodies, while oral tolerance to the same soya proteins was also clearly induced. When F0 dams were transferred to soya protein-free feed before mating, the F1 and F2 offspring generations showed no significantly different response, indicating that soya-specific immune components were not maternally transmitted. However, the ingestion of dietary soya protein by F1 mice during late pregnancy and lactation caused a lasting antibody response in the offspring, but in this case in the absence of oral tolerance. This indicates that, under certain conditions, factors involved in spontaneous antibody production can be transmitted from mother to offspring. Understanding the immune response to soya protein ingested under healthy conditions is important in the assessment of adverse effects of soya protein and in the use of animal allergy models. The present results add to this understanding.

General information
State: Published
Organisations: Enzyme and Protein Chemistry, Department of Systems Biology
Authors: Christensen, H. R. (Intern), Pedersen, S. B. (Intern), Frøkiær, H. (Intern)
Pages: 725-732
Publication date: 2004
Main Research Area: Technical/natural sciences

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Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 3.65 SJR 1.756 SNIP 1.555
Web of Science (2017): Impact factor 4.586
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 3.46 SJR 2.055 SNIP 1.535
Web of Science (2016): Impact factor 4.844
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.583 SNIP 1.442 CiteScore 3.52
Web of Science (2015): Impact factor 4.051
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.532 SNIP 1.273 CiteScore 3.18
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 2.746 SNIP 2.479 CiteScore 3.61
Web of Science (2013): Impact factor 3.861
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 2.308 SNIP 2.427 CiteScore 3.12
Web of Science (2012): Impact factor 5.5
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 2.085 SNIP 1.649 CiteScore 3.13
Web of Science (2011): Impact factor 4.842
ISI indexed (2011): ISI indexed yes
Background: Natural killer (NK) cells are lymphocytes of the non-specific immune system recognizing cancerous cells and cells altered by viral infection. Recently, it was proposed that a non-cytolytic subset of NK cells serves a regulatory role by secreting cytokines, possibly affecting both antigen presenting cells and T-cells. Bacteria translocating across the gastrointestinal mucosa are presumed to gain access to NK cell compartments, as consumption of certain strains of lactic acid bacteria has been shown to increase in vivo NK cytotoxic activity. On-going research in our lab aims at describing strain-dependent effects of lactic acid bacteria on regulatory functions of NK-cells. Here, we have investigated how human gut flora-derived non-pathogenic lactic acid bacteria affect NK cells in vitro, by measuring proliferation and IFN-gamma production of human peripheral blood NK cells upon bacterial stimulation.

Methods: CD3-CD56+ NK cells were isolated from buffy coats by negative isolation using a lineage specific antibody cocktail and magnetic beads binding the labelling antibodies on non-NK cells. NK cells were incubated either with 10 microg/ml UV-inactivated lactic acid bacteria or 10 microg/ml phytohemagglutinin (PHA) as a proliferation control. Proliferation was assessed by incorporation of radioactive thymidine into NK cell DNA. Cytokine concentrations were determined by ELISA.

Results: Co-incubation of NK cells and a Lactobacillus acidophilus strain for four days caused increased proliferation of the NK cells and induced IFN-gamma production, both to levels comparable to PHA stimulation. The proliferative response was further enhanced when autologous monocytes were present, probably because cytokines secreted by monocytes having engulfed bacteria stimulated the growth of the NK cells. In contrast, a Lactobacillus paracasei strain caused the NK cells to proliferate only in the presence of monocytes. Conclusion: In this study we have demonstrated that various strains of gut flora-derived lactic acid bacteria have the capacity to activate NK cells in vitro, in a monocyte dependent or independent way. Our results indicate that if NK cells encounter lactic acid bacteria or components hereof in the gut mucosa, this affects NK cell activation by inducing proliferation and cytokine production. Such activation of NK cells may potentially skew an on-going or subsequent immune response towards a Th1 response.
Lactobacilli Differentially Activate Natural Killer Cells

Bacteria translocating across the gastrointestinal mucosa are presumed to gain access to NK cell compartments, as consumption of certain lactic acid bacteria has been shown to increase in vivo NK cytotoxicity. On-going research in our lab aims at describing strain-dependent effects of lactic acid bacteria on regulatory functions of NK-cells. Here, we have investigated how human gut flora-derived non-pathogenic lactobacilli affect NK cells in vitro, by measuring proliferation and IFN-gamma production of human peripheral blood NK cells upon bacterial stimulation. CD3-CD56+ NK cells were incubated with 10 microg/ml UV-inactivated bacteria for four days. Proliferation was assessed by incorporation of radioactive thymidine into NK cell DNA and cytokine concentrations were determined by ELISA. Co-incubation of NK cells and a Lactobacillus acidophilus strain caused increased proliferation of the NK cells and induced IFN-gamma production. The proliferative response was further enhanced in the presence of autologous monocytes, probably because cytokines, secreted by monocytes having engulfed bacteria, stimulated the growth of the NK cells. In contrast, a Lactobacillus paracasei strain caused the NK cells to proliferate only in the presence of monocytes. These results demonstrate that various lactobacilli have the capacity to activate NK cells in vitro, in a monocyte dependent or independent way. Such activation of NK cells may potentially skew an on-going or subsequent immune response towards a Th1 response.

Lactobacilli Modulate Natural Killer Cell Responses In Vitro

Natural killer (NK) cells are cells of the non-specific immune system lysing altered self-cells. A non-cytolytic subset of NK cells may serve a regulatory role by secreting cytokines. Bacteria translocating across the gastrointestinal mucosa are presumed to gain access to NK cells, as consumption of certain lactic acid bacteria has been shown to increase in vivo NK cytotoxicity. Here, we investigated how human gut flora-derived lactobacilli affect NK cells in vitro, by measuring proliferation and IFN-gamma production of human NK cells upon bacterial stimulation. CD3-CD56+ NK cells were incubated with 10 microg/ml UV-inactivated bacteria or 10 microg/ml phytohemagglutinin (PHA) for four days. Proliferation was assessed by incorporation of radioactive thymidine into NK cell DNA. The IFN-gamma concentration was measured by ELISA. Incubation of NK cells with a Lactobacillus acidophilus strain increased the proliferation of the NK cells and induced IFN-gamma production, both to levels comparable to PHA stimulation. The proliferative response was further enhanced with autologous monocytes present, probably because cytokines, secreted by monocytes having engulfed bacteria, stimulated the NK cells. In contrast, a Lactobacillus paracasei strain caused the NK cells to proliferate only in the presence of monocytes. These results demonstrate that various strains of lactobacilli have the capacity to activate NK cells in vitro, in a monocyte dependent or independent way. Hence, the encounter of NK cells with lactic acid bacteria will affect NK cell activation. Such activation of NK cells may potentially skew an on-going or subsequent immune response towards a Th1 response.
Lipopolysaccharide contamination of beta-lactoglobulin affects the immune response against intraperitoneally and orally administered antigen

Microbial components in the environment are potent activators of the immune system with capacity to shift the active immune response towards priming of Th1 and/or Th2 cells. Lipopolysaccharide (LPS), a cell-wall component of Gram-negative bacteria, is extensively present in food products like cow's milk. It is not well established, however, how this presence of LPS affects oral tolerance induction. Methods: We studied the effect of LPS contamination in a commercial preparation of the cow milk protein beta-lactoglobulin (beta-LG) on antigen-specific immune responses. IgG1/IgG2a production upon intraperitoneal immunization without adjuvant was measured, and oral tolerance induction against beta-LG after administration of either an aqueous solution or water-in-oil (w/o) emulsion of beta-LG was evaluated. Results: LPS contamination of beta-LG provoked a beta-LG-specific IgG2a response, as well as an enhanced beta-LG-specific IgG1 response upon intraperitoneal immunization. Oral tolerance induction to beta-LG was induced by aqueous solutions of beta-LG with and without LPS administration. Conversely, oral administration of w/o-emulsified beta-LG prevented oral tolerance to beta-LG only when the beta-LG was contaminated with LPS. Conclusions: LPS contamination of an aqueous protein solution does not affect oral tolerance induction, whereas LPS present in emulsion prevents oral tolerance induction towards the food protein.
Natural Killer Cells Are Activated by Lactic Acid Bacteria-Matured Dendritic Cells

Natural killer (NK) cells are cells of the non-specific immune system lysing altered self-cells. A non-cytolytic subset of NK cells may serve a regulatory role by secreting cytokines. Bacteria translocating across the gastrointestinal mucosa are presumed to gain access to NK cells, as consumption of certain lactic acid bacteria has been shown to increase in vivo NK cytotoxicity. Here, we investigated how human gut flora-derived lactobacilli affect NK cells in vitro, by measuring proliferation and IFN-γ production of human NK cells upon bacterial stimulation. Human peripheral blood NK cells were incubated with 10 microg/ml UV-inactivated bacteria or 10 microg/ml phytohemagglutinin (PHA) for four days. Proliferation was assessed by incorporation of radioactive thymidine into NK cell DNA. The IFN-γ concentration was measured by ELISA. Incubation of NK cells with a Lactobacillus acidophilus strain increased the proliferation of the NK cells and induced IFN-γ production, both to levels comparable to PHA stimulation. The proliferative response was further enhanced with autologous monocytes present, probably because cytokines, secreted by monocytes having engulfed bacteria, stimulated the NK cells. In contrast, a Lactobacillus paracasei strain caused the NK cells to proliferate only in the presence of monocytes. These results demonstrate that various strains of lactobacilli have the capacity to activate NK cells in vitro, in a monocyte dependent or independent way. Hence, the encounter of NK cells with lactic acid bacteria will affect NK cell activation. Such activation of NK cells may potentially skew an on-going or subsequent immune response towards a Th1 response.

Antigenic specificity of serum antibodies in mice fed soy protein

Background: Soybean protein is used in a number of food products but unfortunately is also a common cause of food allergy. Upon ingestion of soy protein, healthy mice like other animals and humans generate a soy-specific antibody response in the absence of signs of illness. Not much is known about the relationship between the immunogenic proteins
involved in this nonleterious antibody response and the pathological response associated with food allergy. The objective of the present study was to characterize the antigenic specificity of the soy protein-specific antibody response generated in healthy mice ingesting soy protein. Methods: Blood from mice fed a soy-containing diet was analyzed using ELISA and immunoblot for antibody reactivity towards various soy protein fractions and pure soy proteins/subunits. Mice bred on a soy-free diet were used as controls. Results: The detectable antigenic specificity of the serum antibodies of soy-consuming mice comprised glycinin and beta-conglycinin. Immunoblots with soy protein extract demonstrated antibody reactivity towards both the basic and the acidic chains of glycinin and the beta-conglycinin subunits with an individual response pattern among mice. Moreover, antibody reactivity was found towards the native quaternary structure of glycinin. Conclusions: Mice ingesting soy protein generate an antibody response with reactivity towards glycinin and beta-conglycinin. Antibody reactivity found towards the native quaternary structure of glycinin indicates an oral immunogenicity of the highly processing-resistant oligomerized glycinin.

**General information**
State: Published
Organisations: Enzyme and Protein Chemistry, Department of Systems Biology
Authors: Christensen, H. R. (Intern), Bruun, S. (Ekstern), Frøkiær, H. (Intern)
Pages: 58-67
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**Publication information**
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Issue number: 1
ISSN (Print): 1018-2438
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Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
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Web of Science (2017): Impact factor 2.437
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 1.055 SNIP 1.068 CiteScore 2.61
Web of Science (2016): Impact factor 2.72
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.217 SNIP 1.056 CiteScore 2.48
Web of Science (2015): Impact factor 2.677
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.982 SNIP 1.056 CiteScore 2.57
Web of Science (2014): Impact factor 2.673
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.872 SNIP 1.09 CiteScore 2.36
Web of Science (2013): Impact factor 2.433
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.854 SNIP 0.917 CiteScore 2.28
Web of Science (2012): Impact factor 2.248
ISI indexed (2012): ISI indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.995 SNIP 1.016 CiteScore 2.47
Web of Science (2011): Impact factor 2.403
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 0.859 SNIP 0.964
Web of Science (2010): Impact factor 2.235
Experimental parameters differentially affect the humoral response of the cholera-toxin-based murine model of food allergy

Background: Recent studies have developed a murine model of IgE-mediated food allergy based on oral co-administration of antigen and cholera toxin (CT) to establish a maximal response for studying immunopathogenic mechanisms and immunotherapeutic strategies. However, for studying subtle immunomodulating factors or factors effective during response initiation, this maximal response-based model is less suitable due to a lack of sensitivity. Therefore, in attempts to identify essential parameters to fine-tune the immune response towards a submaximal level, potentially more sensitive, we were interested in characterizing the individual effects of the parameters in the CT-based model: CT dose, antigen type and dose, and number of immunizations. Methods: BALB/c mice were orally sensitized weekly for 3 or 7 weeks with graded doses of CT and various food antigens (soy-trypsin inhibitor, ovalbumin or ovomucoid). Antigen-specific IgG1, IgG2a, IgA and IgE were monitored by ELISA. Results: The CT dose exerted a clear dose-dependent effect on the antigen-specific antibody response whereas the antigen dose tended to affect the kinetics of the developing response. Both the intensity and kinetics of the antibody response depended on the type of antigen and number of immunizations. Conclusions: The critical parameters of the CT-based murine allergy model differentially control the intensity and kinetics of the developing immune response. Adjustment of these parameters could be a key tool for tailoring the response to submaximal levels rendering the model potentially more sensitive for evaluating the effect of subtle immunomodulating factors that would be lost in the maximal response-based model.

General information
State: Published
Organisations: Enzyme and Protein Chemistry, Department of Systems Biology
Authors: Kroghsbo, S. (Ekstern), Christensen, H. R. (Intern), Frøkiær, H. (Intern)
Pages: 256-263
Publication date: 2003
Main Research Area: Technical/natural sciences

Publication information
Journal: International Archives of Allergy and Immunology
Volume: 131
Issue number: 4
ISSN (Print): 1018-2438
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 0.883 SJR 0.989 CiteScore 2.52
Web of Science (2017): Impact factor 2.437
Immunomodulatory effects induced by endotoxin present in some commercial β-lactoglobulin preparations

General information
State: Published
Immunostimulatory Potential of β-Lactoglobulin Preparations: Effects Caused by Endotoxin Contamination

Background: The immunomodulating potential residing in cow’s milk proteins is currently receiving increasing attention because of growing interest in functional foods and the complex problem of cow’s milk allergy. One of the major cow’s milk allergens, whey protein beta-lactoglobulin, has previously been shown to mediate cellular activation in both human and murine immune cells.

Objective: We examined the response to different beta-lactoglobulin preparations in naive immune cells.

Methods: Splenocytes and cells from mesenteric lymph nodes derived from BALB/c mice bred and maintained on a milk-free diet were cultured in vitro with different beta-lactoglobulin preparations. Cell proliferation, cytokine production, and increases in intracellular glutathione were used as cellular activation markers. Moreover, the effect of beta-lactoglobulin on cytokine production in murine bone-marrow-derived dendritic cells was examined.

Results: We observed that some commercial beta-lactoglobulin preparations induced pronounced proliferation of both spleen cells and cells from mesenteric lymph nodes; production of TNF-alpha, IL-6, IL-1beta, and IL-10; and an increased level of intracellular glutathione in spleen cell cultures. Furthermore, TNF-alpha, IL-6, IL-1beta, and IL-10 production was induced in murine bone-marrow-derived dendritic cells. Purification of beta-lactoglobulin from raw milk using nondenaturating conditions, however, revealed that the beta-lactoglobulin per se did not possess the immunomodulatory activity. Eventually, the immunostimulatory effect was found to be caused by endotoxin contamination.

Conclusion: These results identify endotoxin as the main immunostimulatory component present in some commercial beta-lactoglobulin preparations. Moreover, the present study makes it evident that immunomodulatory effects attributed to beta-lactoglobulin need to be reassessed.

General information
State: Published
Organisations: Department of Systems Biology, Enzyme and Protein Chemistry, Nestle
Authors: Pedersen, S. B. (Intern), Bovetto, L. (Ekstern), Fritsche, R. (Ekstern), Barkholt, V. (Intern), Frøkiær, H. (Intern)
Pages: 1216-1222
Publication date: 2003
Main Research Area: Technical/natural sciences

Publication information
Journal: Journal of Allergy and Clinical Immunology
Volume: 112
Issue number: 6
ISSN (Print): 0091-6749
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): CiteScore 6.94 SJR 5.049 SNIP 2.6
Web of Science (2017): Impact factor 13.258
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 6.87 SJR 5.618 SNIP 2.901
Web of Science (2016): Impact factor 13.081
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 5.739 SNIP 2.849 CiteScore 6.62
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 4.969 SNIP 2.935 CiteScore 6.61
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Low-dose oral tolerance due to antigen in the diet suppresses differentially the cholera toxin-adjuvantized IgE, IgA and IgG response

Background: Cholera toxin (CT) is used as a mucosal adjuvant amongst other applications for studying food allergy because oral administration of antigen with CT induces an antigen-specific type 2 response, including IgE and IgA production. Priorly established oral tolerance due to antigen in the diet may radically impact on the CT-adjuvantized immune response. The present study served to evaluate the effect of priorly established low-dose oral tolerance on the CT-adjuvantized immune response towards a food antigen. Methods: Mice fed a diet containing microgram levels of the soy protein Kunitz soy-trypsin inhibitor (KSTI) (F0 mice) and mice fed a soy-free diet (F2 mice) were orally immunized with KSTI and CT. KSTI-specific serum IgG1, IgG2a, IgA and IgE and fecal IgA were monitored. KSTI-stimulated cell proliferation and interleukin (IL)-6 production were determined. Results: The anti-KSTI IgE and IgA responses in the F0 mice were substantially suppressed, while the IgG1 and IgG2a responses were not suppressed after five oral immunizations. The response suppression tended to decline with increasing numbers of immunizations suggesting that the suppression could be overcome by multiple immunizations. However, cell proliferation and IL-6 production were clearly suppressed even after five immunizations. Conclusions: Priorly established low-dose oral tolerance considerably suppressed the CT-adjuvantized KSTI-specific IgE, IgA and cellular immune response but only weakly and transiently the IgG response. The results revealed that low-dose oral tolerance includes the mucosal IgA response and that CT, albeit mediating an antigen-specific response, does not fully abrogate priorly established oral tolerance.
Reduction of immunoreactivity of bovine beta-lactoglobulin upon combined physical and proteolytic treatment

Bovine beta-lactoglobulin was hydrolyzed with trypsin or chymotrypsin before, during and after treatment at 600 MPa and pH 6.8 for 10 min at 30, 37 and 44°C. The extent of beta-lactoglobulin hydrolysis under pressure was noticeably higher than at atmospheric pressure, particularly when chymotrypsin was used. Addition of proteases at ambient pressure to previously pressure-treated beta-lactoglobulin gave only a modest increase in proteolysis with respect to the untreated protein. Products of enzyme hydrolysis under pressure were separated by reverse-phase HPLC, and were found to be different from those obtained at atmospheric pressure when chymotrypsin was used. The residual immunological reactivity of the products of combined pressure-enzyme treatment was assessed on the unresolved hydrolysates by ELISA tests using polyclonal and monoclonal antibodies, and on individual hydrolytic fractions by Western Blotting using sera of paediatric patients allergic to whey proteins in cow milk. The immunoreactivity of the whole hydrolysates was related to their content of residual intact beta-lactoglobulin, and no immunological reactivity was found for all the products of chymotrypsin hydrolysis under pressure. The results indicate that chymotrypsin effectively hydrolysed hydrophobic regions of beta-lactoglobulin that were transiently exposed during the pressure treatments and that were not accessible in the native protein or in the protein that had been previously pressure treated.

General information

State: Published
Organisations: Department of Systems Biology
Authors: Bonomi, F. (Ekstern), Fiocchi, A. (Ekstern), Frøkjær, H. (Intern), Gaiaschi, A. (Ekstern), Iametti, S. (Ekstern), Poiesi, C. (Ekstern), Rasmussen, P. (Ekstern), Restani, P. (Ekstern), Rovere, P. (Ekstern)
Pages: 51-59
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Main Research Area: Technical/natural sciences

Publication information

Journal: Journal of dairy research
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ISSN (Print): 0022-0299
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 0.759 SJR 0.573 CiteScore 1.33
Web of Science (2017): Impact factor 1.17
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 0.648 SNIP 0.883 CiteScore 1.66
Web of Science (2016): Impact factor 1.409
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.694 SNIP 0.888 CiteScore 1.54
Web of Science (2015): Impact factor 1.5
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.732 SNIP 0.954 CiteScore 1.79
Web of Science (2014): Impact factor 1.598
BFI (2013): BFI-level 1
The oral immunogenicity of BioProtein, a bacterial single-cell protein, is affected by its particulate nature

The bacterial single-cell protein BioProtein (BP: Norferm Danmark, Odense, Denmark), produced by fermentation of natural gas with methanotrophic bacteria, is a potential protein source for man and animals. For human consumption, removal of the nucleic acid is necessary. Preliminary studies have shown that ingested BP induces a specific immune response. The objective of the present study was to characterize the type of response, its development over time and product-related causative factors. Mice were fed with diets containing 60 g nucleic acid-reduced BP/kg, 240 g nucleic acid-reduced BP/kg, 240 g untreated BP (basic BP)/kg or 240 g casein/kg (control). In another study, mice were fed 240 g basic BP/kg, whole cell-free BP-culture homogenate or control diet. The immune response was monitored using an ELISA for BP-specific immunoglobulin in blood and BP-specific immunoglobulin A in blood and saliva. Ingested BP induced a steady specific mucosal and systemic immune response, characterized by a dose-dependent production of immunoglobulin and immunoglobulin A in blood and immunoglobulin A in saliva. Basic BP and nucleic acid-reduced BP induced identical responses. However, feeding mice BP-culture homogenate induced immunoglobulin A in saliva but there was no systemic response. The antibodies from BP-fed mice cross-reacted with BP-culture homogenate revealing the presence of the same antigenic components in the two products despite the different oral immunogenicity. Thus, ingestion of BP induces a persistent mucosal and systemic immune response of which the systemic response can be avoided by ingesting a BP preparation free of whole cells. This indicates the importance of the non-particulate constitution of single-cell protein products intended for human or animal consumption.

General information
State: Published
Organisations: Department of Systems Biology
Authors: Christensen, H. R. (Intern), Larsen, L. (Ekstern), Frøkiær, H. (Intern)
Induction of oral tolerance with micro-doses of ovomucoid depends on the length of the feeding period

Oral administration of antigen induces antigen-specific immunologic tolerance, which is known to be dose-dependent. We studied the influence of continuous oral administration of nanogram and microgram doses of antigen on oral tolerance induction. Mice were continuously exposed to varying doses (1 ng-1 mg/day) of ovomucoid (OM) for a minimum of 30 days and a maximum of 100 days. It was possible to induce oral tolerance measured as reduced proliferation and antibody production (immunoglobulin (Ig)G1, IgG2a, and total Igs) when mice were fed 1 mg of OM/day for 40 or 50 days. It was not possible to induce oral tolerance with daily doses of antigen of 10 mug or less. Feeding of 100 mug OM/day for 40 and 50 days and 1 mg OM/day for 30 days generated tolerization of Th2-dependent responses, but retained an intact response of Th1-dependent antibodies, whereas feeding of 1 mg OM/day for 40 and 50 days resulted in tolerization of both Th1- and Th2-antibody responses. The results presented here suggest that there is a threshold of microgram-doses below which oral tolerance cannot be induced, and that selective suppression of Th2 responses can be achieved by continuous microdose feeding, while an extension of the feeding dose or feeding period tolerizes both Th1- and Th2-dependent responses.

General information
State: Published
Organisations: Enzyme and Protein Chemistry, Department of Systems Biology
Authors: Kjær, T. (Intern), Frøkiær, H. (Intern)
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Ratings:
BFI (2018): BFI-level 1
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BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 0.621 SJR 0.891 CiteScore 2.11
Web of Science (2017): Impact factor 2.314
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 2.03 SJR 0.979 SNIP 0.644
Web of Science (2016): Impact factor 2.256
Lactobacilli differentially modulate expression of cytokines and maturation surface markers in murine dendritic cells

Dendritic cells (DC) play a pivotal immunoregulatory role in the Th1, Th2, and Th3 cell balance and are present throughout the gastrointestinal tract. Thus, DC may be targets for modulation by gut microbes, including ingested probiotics. In the present study, we tested the hypothesis that species of Lactobacillus, important members of the gut flora, differentially activate DC. Bone marrow-derived murine DC were exposed to various lethally irradiated Lactobacillus spp. and resultant
culture supernatants were analyzed for IL-6, IL-10, IL-12, and TNF-alpha. Substantial differences were found among strains in the capacity to induce IL-12 and TNF-a production in the DC. Similar but less pronounced differences were observed among lactobacilli in the induction of IL-6 and IL-10. Although all strains up-regulated surface MHC class II and B7-2 (CD86), which is indicative of DC maturation, those lactobacilli with greatest capacity to induce IL-12 were most effective. Remarkably, Lactobacillus reuteri DSM12246, a poor IL-12 inducer, inhibited IL-12, IL-6, and TNF-alpha induction by the otherwise strong cytokine inducer L. casei CHCC3139, while IL-10 production remained unaltered. In analogous fashion, L. reuteri reduced L casei-induced up-regulation of B7-2. These results suggest that different species of Lactobacillus exert very different DC activation patterns and, furthermore, at least one species may be capable of inhibiting activities of other species in the genus. Thus, the potential exists for Th1/Th2/Th3-driving capacities of the gut DC to be modulated according to composition of gut microflora, including ingested probiotics.
Modulation of ovomucoid-specific oral tolerance in mice fed plant extracts containing lectins

We investigated the effect of feeding extracts of four different legumes (red kidney bean (Phaseolus vulgaris), peanut (Arachis hypogaea), soyabean (Glycine max) and pea (Pisum sativum) on the specific immune response against a food protein. Mice were fed ovomucoid and the specific immune response was evaluated. Ovomucoid fed alone resulted in oral tolerance induction measured as both a reduced ovomucoid-specific spleen cell proliferation and antibody response. Feeding kidney-bean extract prevented induction of oral tolerance to ovomucoid measured as spleen cell proliferation in vitro. Pure kidney-bean lectin also prevented oral tolerance induction, suggesting that lectin in the kidney-bean extract caused inhibition of oral tolerance. Parenteral administration (intravenous and intraperitoneal) of pure kidney-bean lectin had no significant influence on oral tolerance induction. Soyabean extract also influenced the immune response against ovomucoid; however, this was not as pronounced as for kidney bean and was only significant (P<0.001) for the antibody response. No effect was observed when pea extract was fed and peanut extract had a non-significant effect on induction of oral tolerance and on the general immune response. Plasma antibodies against kidney-bean lectin, but not against the three other legume lectins, were detected. Our current findings show that other dietary components can influence the specific immune response against food proteins. Various dietary components may thus contribute to the onset of adverse immunological responses.
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<td>SJR 1.532 SNIP 1.273 CiteScore 3.18</td>
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<td>2012</td>
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<td>SJR 2.308 SNIP 2.427 CiteScore 3.12</td>
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<td>2011</td>
<td>BFI-level 1</td>
<td>SJR 2.085 SNIP 1.649 CiteScore 3.13</td>
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<td>2010</td>
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<td>2009</td>
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<td>2008</td>
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<td>2007</td>
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<td>2006</td>
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<td>SJR 0.715 SNIP 0.925</td>
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<td>2005</td>
<td>Indexed yes</td>
<td>SJR 0.519 SNIP 1.139</td>
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<td>2004</td>
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<td>SJR 0.626 SNIP 1.088</td>
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<td>2003</td>
<td>Indexed yes</td>
<td>SJR 0.727 SNIP 1.509</td>
<td>Indexed yes</td>
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Proteolysis of bovine beta-lactoglobulin during thermal treatment in subdenaturing conditions highlights some structural features of the temperature-modified protein and yields fragments with low immunoreactivity

Bovine beta-lactoglobulin was hydrolyzed with trypsin or chymotrypsin in the course of heat treatment at 55, 60 and 65°C at neutral pH. At these temperatures beta-lactoglobulin undergoes significant but reversible structural changes. In the conditions used in the present study, beta-lactoglobulin was virtually insensitive to proteolysis by either enzyme at room temperature, but underwent extensive proteolysis when either protease was present during the heat treatment. High-temperature proteolysis occurs in a progressive manner. Mass spectrometry analysis of some large-sized breakdown intermediates formed in the early steps of hydrolysis indicated that both enzymes effectively hydrolyzed some regions of beta-lactoglobulin that were transiently exposed during the physical treatments and that were not accessible in the native protein. The immunochemical properties of the products of beta-lactoglobulin hydrolysis were assessed by using various beta-lactoglobulin-specific antibodies, and most epitopic sites were no longer present after attack of the partially unfolded protein by the two proteases.

General information
State: Published
Organisations: Department of Systems Biology
Authors: Iametti, S. (Ekstern), Rasmussen, P. (Ekstern), Frøkiær, H. (Intern), Ferranti, P. (Ekstern), Addeo, F. (Ekstern), Bonomi, F. (Ekstern)
Pages: 1362-1372
Publication date: 2002
Main Research Area: Technical/natural sciences

Publication information
Journal: European journal of biochemistry
Volume: 269
Issue number: 5
ISSN (Print): 0014-2956
Ratings:
BFI (2018): BFI-level 1
BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 3.86
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 4.06
BFI (2015): BFI-level 1
Scopus rating (2015): CiteScore 3.92
BFI (2014): BFI-level 1
Scopus rating (2014): CiteScore 3.94
BFI (2013): BFI-level 1
Scopus rating (2013): CiteScore 4.02
ISI indexed (2013): ISI indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): CiteScore 3.84
ISI indexed (2012): ISI indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): CiteScore 3.36
Sialin-syreholdige mælkeproteiner – Har strukturen betydning for den biologiske aktivitet?

General information
State: Published
Organisations: Unknown
Authors: Mikkelsen, T. L. (Ekstern), Frøkiær, H. (Intern), Barkholt, V. (Ekstern)
Pages: 422-424
Publication date: 2002
Main Research Area: Technical/natural sciences

Publication information
Journal: Mejeritidende
Volume: 18
Original language: Danish
Publication: Research › Journal article – Annual report year: 2002

Abolishment of maternally induced oral tolerance to β-lactoglobulin in adult mice by feeding a milk-free diet from weaning

General information
State: Published
Organisations: Department of Systems Biology
Authors: Johansen, S. (Intern), Christensen, H. R. (Intern), Barkholt, V. (Intern), Frøkiær, H. (Intern)
Publication date: 2001

Publication information
Original language: English
Main Research Area: Technical/natural sciences
Source-ID: 199060
Publication: Research › Sound/Visual production (digital) – Annual report year: 2001

Influence of the diet on the specific immune response against soy proteins in mice

General information
State: Published
Organisations: Department of Systems Biology
Authors: Christensen, H. R. (Intern), Johansen, S. (Intern), Frøkiær, H. (Intern)
Publication date: 2001
Event: Poster session presented at 8th International Symposium on Immunological, Chemical and Clinical Problems of Food Allergy, Venezia, Italy.
Main Research Area: Technical/natural sciences
Source-ID: 199062
Publication: Research - peer-review › Poster – Annual report year: 2001

Processing: impacts on seed nutrition value: scientific, technological, and economical aspects
Transfer of tolerance to β-lactoglobulin from mothers to offspring: A four generation study in mice

Analysis of immuno-modulating capacity of peptides from bovine β-casein

Kvantitering af proteiner

Comparison of influence from soybean and pea prtoenase inhibitors on the in vivo and in vitro digestibility of a casein based diet
Influence of industrial processing of peas on the content of antinutritional factors and the in vitro digestibility

The effect of fermentation on components of potential significance for the allergenicity of pea was analyzed. Pea flour was fermented with three lactic acid bacteria, Pediococcus pentosaceus, Lactococcus raffinolactis, and Lactobacillus plantarum, and two fungi, Rhizopus microsporus, var. oligosporus and Geotrichum candidum. Residual antigenicity against antipea antibodies was reduced to 10% by the three lactic acid bacteria and R. microsporus. Reactions to anti-pea profilin and anti-Bet v I were still detectable after fermentation. The contents of lectin and pea protease inhibitor were not reduced by the microorganisms. (C) Munksgaard 1998.

Protein modification by fermentation: Effect of fermentation on the potential allergenicity of pea

The effect of fermentation on components of potential significance for the allergenicity of pea was analyzed. Pea flour was fermented with three lactic acid bacteria, Pediococcus pentosaceus, Lactococcus raffinolactis, and Lactobacillus plantarum, and two fungi, Rhizopus microsporus, var. oligosporus and Geotrichum candidum. Residual antigenicity against antipea antibodies was reduced to 10% by the three lactic acid bacteria and R. microsporus. Reactions to anti-pea profilin and anti-Bet v I were still detectable after fermentation. The contents of lectin and pea protease inhibitor were not reduced by the microorganisms. (C) Munksgaard 1998.
The influence of plant lectins on immune response

General information
State: Published
Organisations: Department of Biochemistry and Nutrition, Technical University of Denmark, University of Copenhagen
Authors: Kjær, T. M. R. (Intern), Mikkelsen, T. (Ekstern), Tonsgaard, M. C. (Ekstern), Rossen, M. (Ekstern), Sørensen, S. (Ekstern), Frøkiær, H. (Intern)
Pages: 198-202
Publication date: 1998

Host publication information
Title of host publication: Plant Proteins from European Crops. Food and non-Food Applications
Place of publication: Berlin
Publisher: Springer
Main Research Area: Technical/natural sciences
Conference: Plant Proteins from European Crops, Nantes, 01/01/1997
Source-ID: 171819
Publication: Research - peer-review › Article in proceedings – Annual report year: 1998

Development of a monoclonal antibody to urinary degradation products from the C-terminal telopeptide alpha 1 chain of type I collagen. Application in an enzyme Immunoassay and comparison to CrossLaps(TM) ELISA.

A monoclonal antibody MAbA7 was raised against a synthetic peptide having a sequence (EKAHDGGR) specific for a part of the C-telopeptide alpha 1 chain of type I collagen. MAbA7 was labelled with horseradish peroxide and used in a competitive one-step enzyme-linked immunosorbent assay (ELISA) for measurement of urinary type I collagen degradation products. The assay was technically evaluated and preliminary clinical data are presented. The measuring range was 200-7000 µg l(-1) with a detection limit of 25 µg l(-1). Within-run and total CVs were 5.5 and 8.0%, respectively. Analytical recovery averaged 96.6%±5.3 (mean±1SD). Values obtained in the ELISA were highly correlated (r=0.93) to values obtained by a commercially available assay (CrossLaps(TM) ELISA) known to measure urinary degradation products derived from the C-telopeptide of type I collagen reflecting the rate of bone resorption. Investigation of the urinary fragments responsible for the immunological response in the two assays revealed, however, that they are not identical. Values obtained in urine samples from postmenopausal women (n=108) and patients with Paget's disease (n=6) increased 43% (p<0.01) and 28-fold (p<0.001), respectively, when compared to a premenopausal level (n=50). A decrease in the urinary concentrations of 67% (p<0.01) was seen after 6 months in urine samples from postmenopausal women (n=13) receiving hormone replacement therapy (HRT) compared to a group receiving placebo (n=9). Likewise, the urinary concentrations decreased 88% (p<0.001) in early postmenopausal women receiving bisphosphonate therapy (n=11) for a period of 9 months compared to a group receiving placebo (n=12). These results suggest that the monoclonal antibody and the new assay may be useful for further investigations of the physiological and clinical importance of type I collagen degradation.

General information
State: Published
Organisations: Department of Biochemistry and Nutrition, Osteometer Biotech A/S
Pages: 73-83
Publication date: 1997
Main Research Area: Technical/natural sciences

Publication information
Journal: Scandinavian Journal of Clinical & Laboratory Investigation
Volume: 57
Issue number: 1
ISSN (Print): 0036-5513
Ratings:
BFI (2018): BFI-level 1
Controversial aspects in the pathophysiology of duodenal ulcer. Response. (Correspondence)

General information
State: Published
Organisations: Department of Biochemistry and Nutrition, Copenhagen University Hospital
Pages: 831-832
Publication date: 1996
Main Research Area: Technical/natural sciences

Publication information
Journal: Scandinavian Journal of Gastroenterology
Volume: 31
Issue number: 8
ISSN (Print): 0036-5521
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 2.35 SJR 1.226 SNIP 0.91
Web of Science (2017): Impact factor 2.629
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 2.38 SJR 1.108 SNIP 0.918
Web of Science (2016): Impact factor 2.526
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.947 SNIP 0.764 CiteScore 2.19
Web of Science (2015): Impact factor 2.199
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.072 SNIP 0.999 CiteScore 2.44
Web of Science (2014): Impact factor 2.361
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.122 SNIP 0.987 CiteScore 2.33
Web of Science (2013): Impact factor 2.329
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.111 SNIP 1.023 CiteScore 2.23
Web of Science (2012): Impact factor 2.156
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.107 SNIP 0.916 CiteScore 1.97
Web of Science (2011): Impact factor 2.019
ISI indexed (2011): ISI indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 0.107 SNIP 0.824
Web of Science (2010): Impact factor 1.966
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 0.171 SNIP 0.823
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 0.232 SNIP 0.882
Scopus rating (2007): SJR 0.304 SNIP 1.248
Scopus rating (2006): SJR 0.692 SNIP 1.429
Gastric bicarbonate secretion and release of prostaglandin E2 are increased in duodenal ulcer patients, but not in Helicobacter pylori positive healthy subjects.

Background: Duodenal ulcer (DU) patients have impaired proximal duodenal mucosal bicarbonate secretion at rest and in response to luminal acid with higher acid-stimulated mucosal release of prostaglandin (PG) E(2) than healthy subjects. Our purpose was to determine whether this abnormality was present also in the stomach of DU patients. Methods: Simultaneous determinations of gastric and duodenal bicarbonate secretion and luminal release of PGE(2) were performed in 16 healthy volunteers (5 Helicobacter pylori-positive) and 8 inactive DU patients (all H. pylori-positive).

Results: In healthy volunteers the rates of gastroduodenal bicarbonate secretion and the release of PGE(2), were not influenced by H. pylori status. In inactive DU patients the rates of basal (704 +/- 84 versus 356 +/- 40 mu mol/h: mean +/- SEM) and vagally stimulated (modified sham feeding) (1724 +/- 376 versus 592 +/- 52 mu mol/h) gastric bicarbonate secretion were higher (p < 0.05) than in the health, whereas the corresponding rates (339 +/- 42 versus 591 +/- 51 mu mol/h and 543 +/- 99 versus 778 +/- 69 mu mol/h) in duodenal bicarbonate secretion were lower (p < 0.05). In addition, inactive DU patients had higher basal (148 +/- 32 versus 53 +/- 5 ng/h) and stimulated (291 +/- 84 versus 131 +/- 25 ng/h) gastric release of PGE(2), but only the basal release of PGE(2) into the duodenum was significantly increased (20 +/- 3 versus 5 +/- 1 ng/h; p < 0.05). Conclusion: Increased mucosal production of PGE(2) may be responsible for the abnormally high gastric secretion of bicarbonate in inactive DU patients. Th; defective duodenal secretion of bicarbonate observed in these patients may be a consequence of previous ulceration rather than the mere presence of H. pylori infection.

General information
State: Published
Organisations: Department of Biochemistry and Nutrition, Copenhagen University Hospital
Authors: A, M. (Ekstern), Hillingsø, J. (Ekstern), Frøkiær, H. (Intern), Bukhave, K. (Intern), Rask-Madsen, J. (Ekstern)
Pages: 38-41
Publication date: 1996
Main Research Area: Technical/natural sciences

Publication information
Journal: Scandinavian Journal of Gastroenterology
Volume: 31
Issue number: 1
ISSN (Print): 0036-5521
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 2.35 SJR 1.226 SNIP 0.91
Web of Science (2017): Impact factor 2.629
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 2.38 SJR 1.108 SNIP 0.918
Web of Science (2016): Impact factor 2.526
BFI (2015): BFI-level 1
Heat inactivation kinetics of the two Trypsin inhibitors during high-temperature-short-time processing of soymilk

**General information**

State: Published
Organisations: Department of Biotechnology, Department of Biochemistry and Nutrition
Authors: Rouhana, A. (Ekstern), Adler-Nissen, J. (Intern), Cogan, U. (Ekstern), Frøkiær, H. (Intern)
Pages: 265-269
Publication date: 1996
Main Research Area: Technical/natural sciences
Identification of IgE-binding egg white proteins: Comparisons of results obtained by different methods

General information
State: Published
Organisations: Department of Biochemistry and Nutrition
Authors: Aabin, B. (Ekstern), Poulsen, L. (Ekstern), Ebbehøj, K. (Ekstern), Nørgaard, L. (Ekstern), Frøkiær, H. (Intern), Bindslev-Jensen, C. (Ekstern), Barkholt, H. V. (Intern)
Pages: 50-57
Publication date: 1996
Main Research Area: Technical/natural sciences

Publication information
Journal: International Archives of Allergy and Immunology
Volume: 109
ISSN (Print): 1018-2438
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 0.883 SJR 0.989 CiteScore 2.52
Web of Science (2017): Impact factor 2.437
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 1.055 SNIP 1.068 CiteScore 2.61
Web of Science (2016): Impact factor 2.72
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.217 SNIP 1.056 CiteScore 2.48
Web of Science (2015): Impact factor 2.677
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.982 SNIP 1.056 CiteScore 2.57
Web of Science (2014): Impact factor 2.673
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.872 SNIP 1.09 CiteScore 2.36
Web of Science (2013): Impact factor 2.433
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.854 SNIP 0.917 CiteScore 2.28
Web of Science (2012): Impact factor 2.248
ISI indexed (2012): ISI indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.995 SNIP 1.016 CiteScore 2.47
Web of Science (2011): Impact factor 2.403
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
Modelling affinity maturation in germinal centers.

**General information**

State: Published
Organisations: Department of Biochemistry and Nutrition
Authors: Kesmir, C. (Intern), Søndergaard, I. (Intern), Frøkiær, H. (Intern)
Pages: 738
Publication date: 1996
Main Research Area: Technical/natural sciences

**Publication information**

Journal: Scandinavian Journal of Immunology
Volume: 43
ISSN (Print): 0300-9475
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 0.621 SJR 0.891 CiteScore 2.11
Web of Science (2017): Impact factor 2.314
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 2.03 SJR 0.979 SNIP 0.644
Web of Science (2016): Impact factor 2.256
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.933 SNIP 0.679 CiteScore 1.97
Web of Science (2015): Impact factor 2.27
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.901 SNIP 0.665 CiteScore 1.91
Projects:

Regulation of Host Metabolism by the Gut Microbiota

Department of Systems Biology
Period: 01/10/2012 → 26/04/2017
Number of participants: 6
Phd Student:
Andersen, Daniel (Intern)
Supervisor:
Pedersen, Susanne Brix (Intern)
Main Supervisor:

Hellgren, Lars (Intern)

Examiner:

Lahl, Katharina (Intern)
Frøkiær, Hanne (Intern)
Zeyda, Maximilian (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: Forskningsrådsfinansiering

Relations
Publications:
Interactions between host metabolism, immune regulation, and the gut microbiota in diet-associated obesity and metabolic dysfunction
Project: PhD

Colostrum for gut protection and recovery
National Veterinary Institute
Period: 01/12/2008 → 27/03/2013
Number of participants: 6
Phd Student:
Støy, Ann Cathrine Findal (Intern)
Supervisor:
Sangild, Per (Ekstern)
Main Supervisor:
Heegaard, Peter Mikael Helweg (Intern)
Examiner:
Schou, Kirstine Klitgaard (Intern)
Frøkiær, Hanne (Intern)
Weström, Björn Ragnar (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: Institut stipendie (DTU) Samf.
Project: PhD

Impact of Colonization on Immune System Development
National Food Institute
Period: 01/11/2007 → 02/07/2014
Number of participants: 6
Phd Student:
Kristensen, Matilde Bylov (Intern)
Supervisor:
Frekær, Hanne (Intern)
Main Supervisor:
Licht, Tine Rask (Intern)
Examiner:
Hellgren, Lars (Intern)
Pedersen, Anders Elm (Ekstern)
Sanz, Yolanda (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: Globaliseringsmidler
Project: PhD


**Milk Bioactives to Prevent Gut Inflammation**

Department of Systems Biology  
Period: 01/02/2007 → 22/09/2010  
Number of participants: 7  
Phd Student:  
Møller, Hanne Kristine (Intern)  
Supervisor:  
Frøkiær, Hanne (Intern)  
Sangild, Per (Ekstern)  
Main Supervisor:  
Hellgren, Lars (Intern)  
Examiner:  
Heegaard, Peter Mikael Helweg (Intern)  
Chatterton, Dereck E. W. (Ekstern)  
Eaton, Simon James (Ekstern)

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

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**Nutritional Immunology**

National Food Institute  
Department of Systems Biology  
National Institute of Aquatic Resources  
Period: 04/01/2007 → 31/12/2011  
Number of participants: 10  
Project participant:  
Wilcks, Andrea (Intern)  
Bergström, Anders (Intern)  
Andersen, Jens Bo (Intern)  
Metzdorff, Stine Broeng (Intern)  
Fink, Lisbeth Nielsen (Intern)  
Nielsen, Nina Skall (Intern)  
Project Manager, organisational:  
Licht, Tine Rask (Intern)  
Frøkiær, Hanne (Intern)  
Hellgren, Lars (Intern)  
Jacobsen, Charlotte (Intern)

**Financing sources**  
Source: [Ordinær drift UK 10]  
Name of research programme: [Ordinær drift UK 10]  
Amount: 3,250,000.00 Danish Kroner  
Project

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**Effects of bacterial colonization on immune maturation**

The Gut Ecology group at the National Food Institute, Technical University of Denmark investigates effects of bacterial colonization on the maturation of the immune system in early life.

We do this by use of germ-free and monoclonized mouse models.

The project is closely related to other projects in the Gut Ecology research group, where we analyze the intestinal microbiota in infants.

**Project financing:**  
Globalization funds (through FoodDTU)
National Food Institute
Division of Food Microbiology
Communications and Management Secretariat
Period: 01/01/2007 → 01/01/2012
Number of participants: 7
Number of related Ph.D. students: 1
Project participant:
Bergström, Anders (Intern)
Nellemann, Christine (Intern)
Frøkiær, Hanne (Intern)
Metzdorff, Stine Broeng (Intern)
Fink, Lisbeth Nielsen (Intern)
Project Manager, organisational:
Licht, Tine Rask (Intern)
Phd Student:
Kristensen, Matilde Bylov (Intern)

Prebiotics for Prevention of Gastrointestinal Infections
National Food Institute
Department of Systems Biology
Period: 01/01/2007 → 01/09/2011
Number of participants: 7
Acronym: PreGI
Project participant:
Wilcks, Andrea (Intern)
Bergström, Anders (Intern)
Andersen, Jens Bo (Intern)
Poulsen, Morten (Intern)
Project Manager, organisational:
Licht, Tine Rask (Intern)
Frøkiær, Hanne (Intern)
Pedersen, Susanne Brix (Intern)

Financing sources
Source: Forskningsrådene - Andre
Name of research programme: Forskningsrådene - Andre
Amount: 8,500,000.00 Danish Kroner

Creation of a database of dangerous organisms
Department of Systems Biology
Number of participants: 6
Phd Student:
Pletscher-Frankild, Sune (Intern)
Supervisor:
Lundegaard, Claus (Intern)
Main Supervisor:
Lund, Ole (Intern)
Examiner:
Pedersen, Anders Gorm (Intern)
Borghans, José A.M. (Ekstern)
Frøkiær, Hanne (Intern)

Financing sources
Source: Internal funding (public)
Name of research programme: Eksternt finansieret virksomhed

Relations
Publications:
Degenerate Peptide Specificity of MHC Molecules and T cell Receptors in Immunodominance and Tolerance
Project: PhD

Structure Based Antigen Prediction
Department of Systems Biology
Number of participants: 5
Phd Student:
Andersen, Pernille (Intern)
Main Supervisor:
Lund, Ole (Intern)
Examiner:
Frøkiær, Hanne (Intern)
Arnot, David (Ekstern)
Regenmortel, Marc H. V. Van (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: Eksternt finansieret virksomhed
Project: PhD

Utilization of Soy Products as a Protein Source for Rainbow Trout and Atlantic Salmon
Department of Systems Biology
Period: 01/02/2004 → 28/09/2007
Number of participants: 6
Phd Student:
Knudsen, Sven David Lausten (Intern)
Supervisor:
Koppe, Wolfgang (Ekstern)
Main Supervisor:
Frøkiær, Hanne (Intern)
Examiner:
Barkholt, Vibeke (Intern)
Gruppen, Harry (Ekstern)
Waagbo, Rune (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: Ansat eksternt
Project: PhD

Anvendelse af Mælkesyrebakterier til Vaccinefremstilling
Department of Systems Biology
Period: 01/12/2003 → 07/11/2007
Number of participants: 5
Phd Student:
Glenting, Jacob (Ekstern)
Supervisor:
Israelsen, Hans (Intern)
Main Supervisor:
Frøkiær, Hanne (Intern)
Examiner:
Søndergaard, Ib (Intern)
**Sørensen, Kim (Intern)**

**Financing sources**  
*Source: Internal funding (public)*  
*Name of research programme: Ansat eksternt*  
*Project: PhD*

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**Allergy and infant nutrition**  
Enzyme and Protein Chemistry  
Department of Systems Biology  
**Period:** 30/10/2003 → 31/12/2005  
**Number of participants:** 1  
**Project Manager, organisational:**  
Frøkiær, Hanne (Intern)  

**Financing sources**  
*Source: Forskningsrådene - Andre*  
*Name of research programme: Forskningsrådene - Andre*  
*Amount: 1,994,400.00 Danish Kroner*  
*Project*

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**Immunomodulating Properties of Probiotic Bacteria**  
Department of Systems Biology  
**Period:** 01/09/2003 → 29/10/2007  
**Number of participants:** 6  
**PhD Student:**  
Fink, Lisbeth Nielsen (Intern)  
**Supervisor:**  
Christensen, Hanne Risager (Intern)  
**Main Supervisor:**  
Frøkiær, Hanne (Intern)  
**Examiner:**  
Lund, Ole (Intern)  
De Jong, Esther C. (Ekstern)  
Hokland, Marianne (Ekstern)

**Financing sources**  
*Source: Internal funding (public)*  
*Name of research programme: DTU-lønnet stipendie*  
*Project: PhD*

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**Udvikling af biosensor til detektion af svampesporer**  
Department of Systems Biology  
**Period:** 01/09/2003 → 16/03/2007  
**Number of participants:** 7  
**PhD Student:**  
Skottrup, Peter Durand (Intern)  
**Supervisor:**  
Justesen, Annemarie Fejer (Intern)  
**Nicolaisen, Mogens (Intern)**  
**Main Supervisor:**  
Frøkiær, Hanne (Intern)  
**Examiner:**  
Søndergaard, Ib (Intern)  
Lübeck, Mette (Intern)  
Stjernesjö, Åse (Ekstern)

**Financing sources**
Prediction of technological and sensory quality of trout

Manufacturing food of high and uniform quality requires good knowledge of the characteristics of the raw material, and knowledge of how these characteristics vary between different raw materials. It is also necessary to know how suitable a given raw material is for different types of product, and how the interaction between raw materials and production technology affects the sensory quality of the final product.

The most important differences between fish raw materials will be reflected in the pheno type of the fish, irrespective of whether the cause of this is genetic or environmental. Characterization of pheno type will thus we appropriate to identifying the characteristics of the raw material (protein markers) that will be included in a model to predict the technological and sensory quality of the final product.

The project will produce a number of frozen and smoked products from different raw materials. Characterisation of pheno types will take place through proteom analyses, where image analysis of 2DE gels will reveal protein markers that can potentially relate the quality of the final product to the characteristics of the original raw material. These proteins will be identified using mass spectroscopy and antibodies against them will be raised. The antibodies will be used to develop rapid immune chemical methods. The quality of both the different varieties of raw materials and the

National Food Institute
Division of Industrial Food Research
Department of Systems Biology
Enzyme and Protein Chemistry
Period: 01/08/2003 → 30/04/2009
Number of participants: 6
Project participant:
Kjærgård, Inger Vibeke Holst (Intern)
Godiksen, Helene (Intern)
Hylland, Grethe (Intern)
Barkholt, Vibeke (Intern)
Frøkiær, Hanne (Intern)

Project

Anti-nutritional factors in soy products and their effect on Atlantic salmon performance

Enzyme and Protein Chemistry
Department of Systems Biology
Period: 09/05/2003 → 30/11/2003
Number of participants: 1
Project Manager, organisational:
Frøkiær, Hanne (Intern)

Financing sources
Source: Sam.arb.aftaler - Udenlandske offentlige og private
Name of research programme: Sam.arb.aftaler - Udenlandske offentlige og private
Amount: 313,335.00 Danish Kroner
Project

Probiotiske bakterier : belysning af interaktioner med det cellulære immunsystem, stimulering af tarmepitelets forsvarsmekanismer og gavnlig indvirkning på spædbørns immunstatus, tarmulumhinde og dermed sundhed

Enzyme and Protein Chemistry
Department of Systems Biology
**Probio Tec BCV cap**

Enzyme and Protein Chemistry  
**Department of Systems Biology**  
**Period:** 03/04/2003 → 01/06/2004  
**Number of participants:** 1  
**Project Manager, organisational:** Frøkiær, Hanne (Intern)  
**Financing sources**  
Source: Sam.arb.aftaler, Private danske - Andre virksomheder  
Name of research programme: Sam.arb.aftaler, Private danske - Andre virksomheder  
Amount: 250,000.00 Danish Kroner  
**Project**

**Optimised processes for preparing healthy and added value food ingredients from Lupin kernels, the European protein-rich grain legume**

This project aims to optimise economically competitive processes for preparing food ingredients with optimal technological, sensory, and nutritional characteristics, from lupin kernels. It will develop protocols for preparing food items with lupin ingredients that may be well accepted by EU consumers for sensory and nutritional characteristics. It will evaluate nutritional characteristics and assess potential health benefits. It will assure traceability of lupin based ingredients in food items and assess allergenic potential. Model foods will be sensory evaluated in collaboration with EU consumer associations. It will produce a survey with statistical data on protein ingredients in EU and trends of consumers and industrialists on novel products. Finally, it will promote lupin based ingredients and food items in Europe through involvement of consumer associations.

**Enzyme and Protein Chemistry**  
**Department of Systems Biology**  
**Period:** 01/01/2003 → 31/12/2005  
**Number of participants:** 1  
**Project Manager, organisational:** Frøkiær, Hanne (Intern)  
**Financing sources**  
Source: Forsk. EU - Rammeprogram  
Name of research programme: Forsk. EU - Rammeprogram  
Amount: 355,407.00 Danish Kroner  
**Project**

**Bakterial Adhæsion og Biofilm dannelse: Global Gen Ekspression**

**Department of Systems Biology**  
**Period:** 15/10/2002 → 01/02/2008  
**Number of participants:** 6  
**Phd Student:** Zeuthen, Louise (Intern)  
**Supervisor:** Christensen, Hanne Risager (Intern)  
**Main Supervisor:** Frøkiær, Hanne (Intern)  
**Examiner:**
Parlesak, Alexandr (Intern)
Claesson, Mogens H. (Ekstern)
Wold, Agnes E. S. (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: DTU-lønnet stipendie
Project: PhD

Marint fedt i Vestgrønland - Human ernæring og trofiske relationer
Department of Systems Biology
Period: 01/10/2002 → 22/09/2006
Number of participants: 8
Phd Student:
Møller, Per (Intern)
Supervisor:
Born, Erik W. (Ekstern)
Dietz, Rune (Ekstern)
Johansen, Paul (Ekstern)
Main Supervisor:
Hellgren, Lars (Intern)
Examiner:
Frøkiær, Hanne (Intern)
Hop, Haakon (Ekstern)
Walton, Michael J. (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: Ansat eksternt
Project: PhD

The Role of T Regulatory Cells 1 in Specific Immunotherapy
Department of Systems Biology
Period: 01/05/2002 → 08/05/2006
Number of participants: 7
Phd Student:
Liu, Anting (Ekstern)
Supervisor:
Millner, Anders (Ekstern)
Würtzen, Peter Adler (Ekstern)
Main Supervisor:
Søndergaard, Ib (Intern)
Examiner:
Frøkiær, Hanne (Intern)
Hoffmann, Hans Jürgen H. (Ekstern)
Poulsen, Lars Kærgaard (Intern)

Financing sources
Source: Internal funding (public)
Name of research programme: ErhvervsPhD-ordningen VTU
Project: PhD

Sialinsyreholdige mælkeproteiner - relationer mellem struktur og funktion
Department of Systems Biology
Period: 15/07/2001 → 08/06/2005
Number of participants: 6
Phd Student:
In vivo studier af kødproteiners og -lipiders indvirken på intestinal jernabsorption

Department of Systems Biology
Period: 01/09/2000 → 03/03/2005
Number of participants: 6
Phd Student: Hansen, Lotte Fynbo (Intern)
Supervisor: Bukhave, Klaus (Intern)
Main Supervisor: Søndergaard, Ib (Intern)
Examiner: Frøkiær, Hanne (Intern)
Financing sources
Source: Internal funding (public)
Name of research programme: Blandet Finansiering
Project: PhD

New downstream processing of antibodies

Department of Systems Biology
Period: 01/04/2000 → 12/08/2003
Number of participants: 6
Phd Student: Bak, Hanne (Intern)
Supervisor: Christophersen, Kim B. (Ekstern)
Main Supervisor: Thomas, Owen R. T. (Ekstern)
Examiner: Frøkiær, Hanne (Intern)
Boschetti, Egisto (Ekstern)
Johansen, Jesper Sonne (Ekstern)
Financing sources
Source: Internal funding (public)
Name of research programme: DTU-lønnet stipendie
Project: PhD

Biologisk aktive kostkomponenters betydning for immunforsvarets celler - naturlige komponenter i unaturlige sammensætninger
Characterization of immune stimulating components in milk

Milk contains components which are claimed to either stimulate or suppress immunological reactions. Enrichment of foods with an immune-stimulating milk fraction may contribute to a higher health status. On the other hand, immunoactive components may contribute to development of food allergy. The aim of the project is identification and characterization of immunoactive components in milk. The project is closely related to "immune analyses".

Department of Biochemistry and Nutrition

Department of Systems Biology
Period: 01/01/1999 → 01/01/2002
Number of participants: 4
Project participant:
Barkholt, Vibeke (Intern)
Pedersen, Susanne Brix (Intern)
Nielsen, Dorthe (Intern)
Project Manager, organisational:
Frøkiær, Hanne (Intern)

Financing sources
Source: Unknown
Name of research programme: Ukendt
Amount: 3,000,000.00 Danish Kroner
Project
Immune analyses

Immune analyses cover a broad range of activities related to the hybridoma laboratory of the department. A major task is production of monoclonal antibodies against e.g. different components in food and designing sensitive immunochemical analyses based on the monoclonal antibodies. Another major task is studies of the influences of various food components on the immune system. An experimental animal model for studies on immunological oral tolerance and food allergy has been established. Together with various immunological, physiological and chemical methodologies this animal model is employed to study factors in the diet which may be responsible for a breakdown in oral tolerance or in the lack of development as well as studies on the cellular and physiological mechanisms leading to the induction of oral tolerance against a food protein.

Department of Biochemistry and Nutrition
Period: 01/01/1998 → …
Number of participants: 7
Project participant:
Bahrenscheer, Jesper Glarborg (Intern)
Christensen, Hanne Risager (Intern)
Gärtnert, Thea Isidora (Intern)
Hendriksen, Lone Roland (Intern)
Kjær, Tanja (Intern)
Barkholt, Vibeke (Intern)
Project Manager, organisational:
Frøkiær, Hanne (Intern)

Financing sources
Source: Unknown
Name of research programme: Ukendt
Amount: 2,100,000.00 Danish Kroner
Source: Unknown
Name of research programme: Ukendt
Amount: 2,000,000.00 Danish Kroner

Udvikling af en cellebaseret. Skal have 4 klip i oktober 2000.

Udvikling af en cellebaseret. Skal have 4 klip i oktober 2000.

Department of Systems Biology
Period: 01/02/1996 → 16/07/2002
Number of participants: 6
PhD Student:
Kjær, Tanja (Intern)
Supervisor:
Frøkiær, Hanne (Intern)
Main Supervisor:
Barkholt, Vibeke (Intern)
Examiner:
Søndergaard, Ib (Intern)
Houen, Gunnar (Ekstern)
Larsen, Jørgen Nedergaard (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: DTU-Su Stipendium, Eksperiment
Project: PhD

NUTRIPEA
New technologies for improved and functional value of pea protein

Department of Biochemistry and Nutrition
SIK
Provital
Semper AB
VTT - Technical Research Centre of Finland
ADRIA Food safety and Quality

ETH Zurich
Period: 01/01/1996 → 31/12/1998
Number of participants: 7
Project participant:
Frøkiær, Hanne (Intern)
Nielsen, Dorthe (Intern)
Follmann, Frank (Intern)
Pedersen, Susanne Brix (Intern)
Sørensen, Anne Dorthe (Intern)
Milora, Nina (Intern)
Project Manager, organisational:
Barkholt, Vibeke (Intern)

Financing sources
Source: Unknown
Name of research programme: Ukendt
Amount: 1,540,000.00 Danish Kroner

Characterisation of hypoallergenic milk formulas
Department of Biochemistry and Nutrition
Period: 01/02/1994 → 31/01/1999
Number of participants: 5
Project participant:
Frøkiær, Hanne (Intern)
Larsen, Annette Rosendal (Intern)
Follmann, Frank (Intern)
Sørensen, Tine Mette (Intern)
Project Manager, organisational:
Barkholt, Vibeke (Intern)

Financing sources
Source: Unknown
Name of research programme: Ukendt
Amount: 2,800,000.00 Danish Kroner

Allergenicity of food
Development of analyses for evaluation of allergenicity. Investigations on the importance of carbohydrate residues for the allergenicity of food.

Department of Biochemistry and Nutrition
Period: 01/11/1988 → …
Number of participants: 5
Project participant:
Frøkiær, Hanne (Intern)
Milora, Nina (Intern)
Frisner, Henrik (Intern)
Sørensen, Tine Mette (Intern)
Project Manager, organisational:
Barkholt, Vibeke (Intern)