A novel Dual Amylin and Calcitonin Receptor Agonist (DACRA), KBP-089, induces weight loss through a reduction in fat, but not lean mass, while improving food preference

Background and Purpose

Obesity and associated co-morbidities, such as type 2 diabetes and non-alcoholic fatty liver disease, are major health challenges – hence, development of weight loss therapies with the ability to reduce the co-morbidities is key.

Experimental Approach

The effect of the dual amylin and calcitonin receptor agonist (DACRA), KBP-089, on bodyweight, glucose homeostasis, and fatty acid accumulation in liver and muscle tissue, food preference was investigated. Further, we elucidate weight-independent effects of KBP-089 using a weight-matched group.

Key Results

High fat diet fed rats were treated with KBP-089 s.c., at 0.625, 1.25, 2.5 µg·kg⁻¹ and vehicle resulting in a dose-dependent and sustained ~17% weight loss by the 2.5 µg·kg⁻¹ (p < 0.001). Moreover, KBP-089 reduced fat depot size and reduced lipid accumulation in muscle and liver.

In Zucker Diabetic Fatty rats, KBP-089 improved glucose homeostasis through improved insulin action. To obtain a weight-matched group, significantly less food was offered (9% less than in the KBP-089 group). Weight-matching led to improved glucose homeostasis through lowered plasma insulin; however, these were inferior to the effect of KBP-089.

In the food preference test, normal diet rats obtained 74% of their calories from chocolate. KBP-089 administration reduced total caloric intake, and induced a relative increase in chow consumption while drastically lowering the chocolate compared to vehicle.

Conclusion

The novel DACRA, KBP-089 induces a sustained weight loss, leading to improved metabolic parameters including food preference, and these are beyond those observed simply by diet-induced weight loss.
A safflower oil-based high fat/high-sucrose diet modulates the gut microbiota and liver phospholipid profiles associated with early glucose intolerance in the absence of tissue inflammation

n-6 PUFA-rich diets are generally considered obesogenic in rodents. Here we examined how long-term intake of a high fat/high sucrose (HF/HS) diet based on safflower oil affected metabolism, inflammation and gut microbiota composition. We fed male C57BL/6J mice a HF/HS diet based on safflower oil - rich in n-6 PUFAs - or low-fat/low-sucrose (LF/LS) diet for 40 weeks. Compared to the LF/LS diet, intake of the safflower-based HF/HS diet only led to moderate weight gain, while glucose intolerance developed at week 5 prior to signs of inflammation, but concurrent with increased levels of linoleic acid and arachidonic acid in hepatic phospholipids. Intake of the HF/HS diet resulted in early changes in the gut microbiota, including an increased abundance of Blautia, while late changes coincided with altered inflammatory profiles and increased fasting plasma insulin. Analysis of immune cells in visceral fat and liver revealed no differences between diets before week 40, where the number of immune cells decreased in the liver of HF/HS-fed mice. We suggest that a
diet-dependent increase in the n-6 to n-3 PUFA ratio in hepatic phospholipids together with gut microbiota changes contributed to early development of glucose intolerance without signs of inflammation. This article is protected by copyright. All rights reserved.
A study of associations between early DHA status and fatty acid desaturase (FADS) SNP and developmental outcomes in children of obese mothers

DHA from diet or endogenous synthesis has been proposed to affect infant development, however, results are inconclusive. In this study, we aim to verify previously observed fatty acid desaturase gene cluster (FADS) SNP-specific associations with erythrocyte DHA status in 9-month-old children and sex-specific association with developmental outcomes. The study was performed in 166 children (55 % boys) of obese mothers. Erythrocyte fatty acid composition was analysed in blood-samples obtained at 9 months of age, and developmental outcomes assessed by the Ages and Stages Questionnaire at 3 years. Erythrocyte DHA level ranged from 4·4 to 9·9 % of fatty acids, but did not show any association with FADS SNP or other potential determinants. Regression analysis showed associations between erythrocyte DHA and scores for personal-social skills (β 1·8 (95 % CI 0·3, 3·3), P=0·019) and problem solving (β 3·4 (95 % CI 1·2, 5·6), P=0·003). A tendency was observed for an association in opposite direction between minor alleles (G-variant) of rs1535 and rs174575 and personal-social skills (P=0·062 and 0·068, respectively), which became significant when the SNP were combined based on their previously observed effect on erythrocyte DHA at 9 months of age (β 2·6 (95 % CI 0·01, 5·1), P=0·043). Sex-SNP interaction was indicated for rs174575 genotype on fine motor scores (P=0·016), due to higher scores among minor allele carrying girls (P=0·043), whereas no effect was seen among boys. In conclusion, DHA-increasing FADS SNP and erythrocyte DHA status were consistently associated with improved personal-social skills in this small cohort of children of obese mothers irrespective of sex, but the sample was too small to verify potential sex-specific effects.
n-3 PUFA, FADS fatty acid desaturase gene cluster, FA% percentage of the overall chromatogram area, LCPUFA long-chain PUFA (≥20 carbon atoms and ≥3 double bonds), SKOT Småbørns Kost Og Trivsel, equivalent to percentage of fatty acids by weight, Child development, Cognitive function, Fish oil, Programming

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Dual Amylin and Calcitonin Receptor Agonists: A Novel Treatment for Obesity and Related Co-Morbidities

Amylin and/or calcitonin receptor agonists such as pramlintide and davalintide have shown promise on weight reduction in preclinical models and clinical settings, albeit with limited efficacy on glucose homeostasis.
The overall aim of this Ph.D. project was to investigate the metabolic effect of the dual amylin and calcitonin receptor agonists (DACRA), KBP-042, KBP-088, KBP-089, focusing on the weight reducing and glucoregulatory potential in preclinical animal models of obesity and related morbidities like type 2 diabetes (T2D) and nonalcoholic steatohepatitis (NASH). Both synthetic and naturally occurring DACRAs exert prolonged receptor activation and it is hypothesized that this prolonged receptor activation will improve the in vivo efficacy. Furthermore, it is hypothesized that DACRAs have beneficial metabolic effects beyond caloric intake and simple diet-induced weight loss.

In this series of studies, the focus was on metabolic effects of KBPs. Effects on body weight and adipose tissue as well as glucose metabolism were thoroughly explored in experimental rat models resembling the phenotypes of obesity, T2D and NASH, to address whether these beneficial effects were solely due to suppression of food intake and the subsequent weight loss. As amylin agonism induces a well-known anorexic effect at dose initiation, these studies also focused on different dosing regimens including dose escalation and dosing frequency. Finally, we compared KBPs to a second-generation amylinomimetic, davalintide, and combination of KBPs with the GLP-1 analogue, liraglutide.

KBPs potently activated both the amylin and calcitonin receptors in vitro, and demonstrated a prolonged receptor activation when compared to second-generation amylinomimetic, davalintide.

KBPs transiently suppressed caloric intake, and induced and sustained a dose-dependent weight loss compared to vehicle and pair-fed rats. Concomitantly, overall adiposity was decreased and obesity related adipocyte hypertrophy were improved – findings superior to the effects obtained with davalintide treatment. The inappropriate high fat diet-induced lipid accumulation was eliminated by KBP treatment, and interestingly, KBPs alleviated hyperinsulinaemia and improved glucose tolerance even with significantly lower insulin levels. KBP treatment increased the glucose infusion rate during a hyperinsulinaemic euglycemic clamp indicating enhanced insulin action. Importantly, KBPs also improved glucose homeostasis and enhanced insulin action in Zucker Diabetic Fatty rats.

To investigate beneficial effects beyond weight loss, a weight-matched group was implemented. Of interest, weight matching led to improved glucose homeostasis through lowered plasma insulin; however, these were inferior to the effect of KBPs.

KBPs were introduced using various dosing regimens and frequencies. Dosing every day and every second day resulted in an equal weight loss at study end; however, with a later onset of maximal weight loss. To optimize tolerability, KBPs were introduced by dose escalation. In a 4-fold dose escalation, KBPs induced a transient reduction in food intake at every escalation step – with reducing magnitude over time. Two-fold and linear escalations suppressed body weight evenly with no significant reduction in food intake at either escalation step; however, with a delayed onset of maximum efficacy.

Interestingly, when KBP and liraglutide were combined, the effect on acute food intake was superior to either of peptides as single-dose. Chronically, KBP-089 (1.25 μg/kg) and liraglutide (50 μg/kg) lowered body weight 8% and 2% in HFD rats, respectively, while the combination resulted in a 12% body weight reduction. Moreover, the combination improved glucose tolerance.

In a rat model resembling the phenotype of human NASH, KBP treatment led to a reduction of the high fat, high cholesterol and cholate diet induced increase in liver weight and circulating aspartate transaminase (AST) levels. Finally, at the histological level KBP treatment reduced hepatic steatosis, ballooning and inflammation, hence resulting in a reduced NAS score in combination with a lowered fibrosis stage.

In conclusion, KBPs induce and sustain weight loss, leading to improved metabolic parameters including food preference, and these are beyond those observed simply by dietinduced weight loss. Additionally, these peptides are well tolerated when introduced by dose escalation. Finally, KBPs reduce liver steatosis in both obese and NASH rats, and importantly reduced inflammation and fibrosis scores in NASH, hence underscoring the DACRA potential as an anti-obesity agent with benefits on glucose control and NASH.

**General information**

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Effects of Gliadin consumption on the Intestinal Microbiota and Metabolic Homeostasis in Mice Fed a High-fat Diet

Dietary gluten causes severe disorders like celiac disease in gluten-intolerant humans. However, currently understanding of its impact in tolerant individuals is limited. Our objective was to test whether gliadin, one of the detrimental parts of gluten, would impact the metabolic effects of an obesogenic diet. Mice were fed either a defined high-fat diet (HFD) containing 4% gliadin (n = 20), or a gliadin-free, isocaloric HFD (n = 20) for 23 weeks. Combined analysis of several parameters including insulin resistance, histology of liver and adipose tissue, intestinal microbiota in three gut compartments, gut barrier function, gene expression, urinary metabolites and immune profiles in intestinal, lymphoid, liver and adipose tissues was performed. Mice fed the gliadin-containing HFD displayed higher glycated hemoglobin and higher insulin resistance as evaluated by the homeostasis model assessment, more hepatic lipid accumulation and smaller adipocytes than mice fed the gliadin-free HFD. This was accompanied by alterations in the composition and activity of the gut microbiota, gut barrier function, urine metabolome, and immune phenotypes within liver and adipose tissue. Our results reveal that gliadin disturbs the intestinal environment and affects metabolic homeostasis in obese mice, suggesting a detrimental effect of gluten intake in gluten-tolerant subjects consuming a high-fat diet.
Environmental spread of microbes impacts the development of metabolic phenotypes in mice transplanted with microbial communities from humans

Microbiota transplantation to germ-free animals is a powerful method to study involvement of gut microbes in the aetiology of metabolic syndrome. Owing to large interpersonal variability in gut microbiota, studies with broad coverage of donors are needed to elucidate the establishment of human-derived microbiotas in mice, factors affecting this process and resulting impact on metabolic health. We thus transplanted faecal microbiotas from humans (16 obese and 16 controls) separately into 64 germ-free Swiss Webster mice caged in pairs within four isolators, with two isolators assigned to each phenotype, thereby allowing us to explore the extent of microbial spread between cages in a well-controlled environment. Despite high group-wise similarity between obese and control human microbiotas, transplanted mice in the four isolators developed distinct gut bacterial composition and activity, body mass gain, and insulin resistance. Spread of microbes between cages within isolators interacted with establishment of the transplanted microbiotas in mice, and contributed to the transmission of metabolic phenotypes. Our findings highlight the impact of donor variability and reveal that inter-individual spread of microbes contributes to the development of metabolic traits. This is of major importance for design of animal studies, and indicates that environmental transfer of microbes between individuals may affect host metabolic traits.

General information
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Fatty acid composition and phospholipid types used in infant formulas modifies the establishment of human gut bacteria in germ-free mice

Human milk fat contains high concentrations of medium-chained fatty acids (MCFA) and triacylglycerols emulsified by a sphingomyelin-rich phospholipid membrane (milk phospholipids, MPL). Infant formula comprises mainly long-chained fatty acids (LCFA) emulsified with dairy proteins and soy lecithin (SL) lacking sphingomyelin. Sphingomyelin content and saturation level of phospholipids affect the gut lipase activity, which alters the concentrations of lipid hydrolysis products in ileum and colon, and hereby putatively affects the competitive advantage of specific gut bacteria. Thus, differences in phospholipid and FA composition may modulate the establishment of the gut microbiota. We investigated effects of fatty acid (FA) composition and emulsification (MPL vs SL) ingested during establishment of human gut microbiota in germ-free mice, and found that cecal microbiotas from mice given MCFA-rich emulsions were characterized by high relative abundances of Bacteroidaceae and Desulfovibrionaceae, while LCFA-rich emulsions caused higher abundances of Enterobacteriaceae, Erysipelotrichaceae, Coriobacteriaceae and Enterococcaceae. Consumption of SL-emulsified lipids skewed the community towards more Enterococcaceae and Enterobacteriaceae, while MPL increased Bacteroidaceae, Desulfovibrionaceae, Rikenellaceae and Porphyromonadaceae. Intake of SL increased cecal concentrations of iso-valeric and iso-butyric acids. This suggests that fat-type and emulsifiers applied in infant formula may have distinct effects on the establishment of the gut microbiota in formula-fed infants.

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Gene expression profiling in persons with multiple chemical sensitivity before and after a controlled n-butanol exposure session

To investigate the pathophysiological pathways leading to symptoms elicitation in multiple chemical sensitivity (MCS) by comparing gene expression in MCS participants and healthy controls before and after a chemical exposure optimised to cause symptoms among MCS participants. The first hypothesis was that unexposed and symptom-free MCS participants have similar gene expression patterns to controls and a second hypothesis that MCS participants can be separated from controls based on differential gene expression upon a controlled n-butanol exposure. Participants were exposed to 3.7 ppm n-butanol while seated in a windowed exposure chamber for 60 min. A total of 26 genes involved in biochemical pathways found in the literature have been proposed to play a role in the pathogenesis of MCS and other functional somatic syndromes were selected. Expression levels were compared between MCS and controls before, within 15 min after being exposed to and 4 hours after the exposure. Participants suffering from MCS and healthy controls were recruited through advertisement at public places and in a local newspaper. 36 participants who considered themselves sensitive were prescreened for eligibility. 18 sensitive persons fulfilling the criteria for MCS were enrolled together with 18 healthy controls. 17 genes showed sufficient transcriptional level for analysis. Group comparisons were conducted for each gene at the 3 times points and for the computed area under the curve (AUC) expression levels. MCS participants and controls displayed similar gene expression levels both at baseline and after the exposure and the computed AUC values were likewise comparable between the 2 groups. The intragroup variation in expression levels among MCS participants was noticeably greater than the controls. MCS participants and controls have similar gene expression levels at baseline and it was not possible to separate MCS participants from controls based on gene expression measured after the exposure.

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Interactions between host metabolism, immune regulation, and the gut microbiota in diet-associated obesity and metabolic dysfunction

The increase in the prevalence of obesity and obesity-associated complications such as the metabolic syndrome is becoming a global challenge. Dietary habits and nutrient consumption modulates host homeostasis, which manifests in various diet-induced complications marked by changes in host metabolism and immune regulation, which are intricately linked. In addition, diet effectively shapes the gut microbiota composition and activity, which in turn interacts with the host to modulate host metabolism and immune regulation.

In the three studies included in this PhD thesis, we have explored the impact of specific dietary components on host metabolic function, immune regulation and gut microbiota composition and activity.

In the first study, we have characterized the effect of a combined high-fat and gliadin-rich diet, since dietary gliadin has been reported to be associated with intestinal inflammation and permeability. The combination of gliadin with an obesogenic diet allowed us to investigate the long-term effects of a single dietary component on host function of obese mice, resulting in identification of notable changes in host metabolic and immune function, as well as in the gut microbiota composition.

In the second study, the effect of a safflower-based high-fat diet on host homeostasis is evaluated, and we show that intake of this n-6 polyunsaturated fatty acid-rich diet exerts only minor host metabolic and inflammatory changes even after 40 weeks intake. Although potentially proinflammatory n-6 polyunsaturated fatty acids are effectively contributing to the liver phospholipids and glucose intolerance manifested after 5 weeks intake, body weight gain, insulin resistance and adipose tissue inflammation are delayed and detectable only after 40 weeks feeding.

In the last study, we evaluated the effect of short-term fasting of obese mice. By applying a coabundance cluster analysis that identifies fasting-induced changes in urine metabolites, gut microbiome and liver lipid composition; we identified defining factors that integrate with the host response to propagate a fasting-induced metabolic shift.

The use of multivariate analyses allows for a better understanding of the interplay between diet, host metabolic regulation, immune function and gut microbiota composition and activity. These studies indicate new directions in which to focus further studies to increase our knowledge of host-diet-microbiome interactions.

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Optimization of tolerability and efficacy of the novel dual amylin and calcitonin receptor agonist KBP-089 through dose escalation and combination with a GLP-1 analog

Amylin and GLP-1 agonism induce a well-known anorexic effect at dose initiation, which is managed by dose escalation. In this study we investigated how to optimize tolerability while maintaining efficacy of a novel, highly potent dual amylin and calcitonin receptor agonist (DACRA), KBP-089. Furthermore, we tested the GLP-1 add-on potential of KBP-089 in high-fat diet (HFD)-fed rats. KBP-089 potently activated both the amylin and calcitonin receptors in vitro and demonstrated a prolonged receptor activation as well as a potent reduction of acute food intake. HFD rats dosed every day or every second day obtained equal weight loss at study end, albeit with an uneven reduction in both food intake and body weight in rats dosed every second day. In a 4-fold dose escalation, KBP-089 induced a transient reduction in food intake at every escalation step, with reducing magnitude over time, and the following treatment with 2.5, 10, and 40 µg/kg resulted in an ~15% vehicle-corrected weight loss, a corresponding reduction in adipose tissue (AT), and, in all treatment groups, improved oral glucose tolerance (P < 0.01). Twofold and linear escalations suppressed body weight evenly with no significant reduction in food intake at either escalation step. KBP-089 (1.25 µg/kg) and liraglutide (50 µg/kg) reduced 24-h food intake by 29% and 37% compared with vehicle, respectively; however, when they were combined, 24-h food intake was reduced by 87%. Chronically, KBP-089 (1.25 µg/kg) and liraglutide (50 µg/kg) lowered body weight 8% and 2% in HFD rats, respectively, whereas the combination resulted in a 12% body weight reduction. Moreover, the combination improved glucose tolerance (P < 0.05). In conclusion, DACRAs act complementarily with GLP-1 on food intake and body weight. Furthermore, on escalation, KBP-089 was well tolerated and induced and sustained a significant weight loss and a reduction in AT in lean and HFD rats, underscoring the potential of KBP-089 as an anti-obesity agent.
Supplementation of docosahexaenoic acid (DHA), vitamin D$_3$ and uridine in combination with six weeks of cognitive and motor training in prepubescent children: a pilot study

Background Learning and memory have been shown to be influenced by combination of dietary supplements and exercise in animal models, but there is little available evidence from human subjects. The aim of this pilot study was to investigate the effect of combining a motor- and cognitive exercise program with dietary supplementation consisting of 500 mg docosahexaenoic acid (DHA), 10 μg vitamin D3 and 1000 mg uridine (DDU-supplement) in 16 prepubescent children (age 8–11 years). Methods We designed a randomized, placebo-controlled, double-blinded study lasting 6 weeks in which DDU-supplement or placebo was ingested daily. During the intervention period, all children trained approximately 30 min 3 days/week using an internet-based cognitive and motor training program (Mitii). Prior to and post the intervention period dietary record, blood sampling, physical exercise tests and motor and cognitive tests were performed. Results Fourteen of the 16 children completed the intervention and ingested the supplement as required. 6 weeks DDU-supplementation resulted in a significant increase in the blood concentration of vitamin D2+3 and DHA (p = 0.023 and p < 0.001, respectively). Power calculation based on one of the cognitive tasks revealed a proper sample size of 26 children. Conclusion All children showed improved performance in the trained motor- and cognitive tasks, but it was not possible to demonstrate any significant effects on the cognitive tests from the dietary supplementation. However, DDU-supplementation did result in increased blood concentration of DHA and vitamin D2+3. Trial registration Clinical registration ID: NCT02426554 (clinical Trial.gov). January 2015 retrospectively registered.

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Do very small adipocytes in subcutaneous adipose tissue (a proposed risk factor for insulin insensitivity) have a fetal origin?

Previous studies have shown that fetal life malnutrition affects preferences for fat deposition in the body thereby predisposing for visceral adiposity and associated disorders in glucose-insulin regulation. In this study, we aimed to test the hypotheses that late-gestation undernutrition 1) has long-term differential impacts on development, expandability and metabolic features in subcutaneous as compared to perirenal and mesenteric adipose tissues, which 2) will predispose for visceral obesity upon exposure to an obesogenic diet in early postnatal life.

Fish oil supplementation from 9 to 18 months of age affects the insulin-like growth factor axis in a sex-specific manner in Danish infants

Several studies have investigated the effects of fish oil (FO) on infant growth, but little is known about the effects of FO and sex on insulin-like growth factor-1 (IGF-1), the main regulator of growth in childhood. We explored whether FO v. sunflower oil (SO) supplementation from 9 to 18 months of age affected IGF-1 and its binding protein-3 (IGFBP-3) and whether the potential effects were sex specific. Danish infants (n 115) were randomly allocated to 5 ml/d FO (1·2 g/d n-3 long-chain PUFA (n-3 LCPUFA)) or SO. We measured growth, IGF-1, IGFBP-3 and erythrocyte EPA, a biomarker of n-3 LCPUFA intake and status, at 9 and 18 months. Erythrocyte EPA increased strongly with FO compared with SO (P <0·001). There were no effects of FO compared with SO on IGF-1 in the total population, but a sex×group interaction (P =0·02). Baseline-adjusted IGF-1 at 18 months was 11·1 µg/l (95 % CI 0·4, 21·8; P=0·04) higher after FO compared with SO supplementation among boys only. The sex×group interaction was borderline significant in the model of IGFBP-3 (P =0·09), with lower IGFBP-3 with FO compared with SO among girls only (P=0·03). The results were supported by sex-specific dose–response associations between changes in erythrocyte EPA and changes in IGF-1 and IGFBP-3 (both P <0·03). Moreover, IGF-1 was sex specifically associated with BMI and length. In conclusion, FO compared with SO
resulted in higher IGF-1 among boys and lower IGFBP-3 among girls. The potential long-term implications for growth and body composition should be investigated further.
Human gut microbes impact host serum metabolome and insulin sensitivity

Insulin resistance is a forerunner state of ischaemic cardiovascular disease and type 2 diabetes. Here we show how the human gut microbiome impacts the serum metabolome and associates with insulin resistance in 277 non-diabetic Danish individuals. The serum metabolome of insulin-resistant individuals is characterized by increased levels of branched-chain amino acids (BCAAs), which correlate with a gut microbiome that has an enriched biosynthetic potential for BCAAs and is deprived of genes encoding bacterial inward transporters for these amino acids. *Prevotella copri* and *Bacteroides vulgatus* are identified as the main species driving the association between biosynthesis of BCAAs and insulin resistance, and in mice we demonstrate that *P. copri* can induce insulin resistance, aggravate glucose intolerance and augment circulating levels of BCAAs. Our findings suggest that microbial targets may have the potential to diminish insulin resistance and reduce the incidence of common metabolic and cardiovascular disorders.

**General information**

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Plasma acylcarnitine profiling indicates increased fatty acid oxidation relative to tricarboxylic acid cycle capacity in young, healthy low birth weight men

We hypothesized that an increased, incomplete fatty acid beta-oxidation in mitochondria could be part of the metabolic events leading to insulin resistance and thereby an increased type 2 diabetes risk in low birth weight (LBW) compared with normal birth weight (NBW) individuals. Therefore, we measured fasting plasma levels of 45 acylcarnitine species in 18 LBW and 25 NBW men after an isocaloric control diet and a 5-day high-fat, high-calorie diet. We demonstrated that LBW men had higher C2 and C4-OH levels after the control diet compared with NBW men, indicating an increased fatty acid beta-oxidation relative to the tricarboxylic acid cycle flux. Also, they had higher C6-DC, C10-OH/C8-DC, and total hydroxyl-/dicarboxyl-acylcarnitine levels, which may suggest an increased fatty acid omega-oxidation in the liver. Furthermore, LBW and NBW men decreased several acylcarnitine levels in response to overfeeding, which is likely a result of an upregulation of fatty acid oxidation due to the dietary challenge. Moreover, C10-OH/C8-DC and total hydroxyl-/dicarboxyl-acylcarnitine levels tended to be negatively associated with the serum insulin level, and the total hydroxyl-/dicarboxyl-acylcarnitine level additionally tended to be negatively associated with the hepatic insulin resistance index. This indicates that an increased fatty acid omega-oxidation could be a compensatory mechanism to prevent an accumulation of lipid species that impair insulin signaling.
Plasma amino acid levels are elevated in young, healthy low birth weight men exposed to short-term high-fat overfeeding

Low birth weight (LBW) individuals exhibit a disproportionately increased, incomplete fatty acid oxidation and a decreased glucose oxidation, compared with normal birth weight (NBW) individuals, and furthermore have an increased risk of developing insulin resistance and type 2 diabetes. We hypothesized that changes in amino acid metabolism may occur parallel to alterations in fatty acid and glucose oxidation, and could contribute to insulin resistance. Therefore, we measured fasting plasma levels of 15 individual or pools of amino acids in 18 LBW and 25 NBW men after an isocaloric control diet and after a 5-day high-fat, high-calorie diet. We demonstrated that LBW and NBW men increased plasma alanine levels and decreased valine and leucine/isoleucine levels in response to overfeeding. Also, LBW men had higher alanine, proline, methionine, citrulline, and total amino acid levels after overfeeding compared with NBW men. Alanine and total amino acid levels tended to be negatively associated with the insulin-stimulated glucose uptake after overfeeding. Furthermore, the alanine level was negatively associated with the plasma acetylcarnitine level and positively associated with the hepatic glucose production after overfeeding. Thus, the higher alanine level in LBW men could be accompanied by an increased anaplerotic formation of oxaloacetate and thereby an enhanced tricarboxylic acid cycle activity and as well an increased gluconeogenesis.
Regulation of host metabolism and immunity by the gut microbiome

During recent years, central roles of the gut microbiome in metabolic and immunological diseases have been uncovered, and multiple studies have shown that bacterial-derived components shape host physiology and immune responses via direct cellular interactions. The intestinal immune system is crucial for the induction of effective immune responses against invading pathogens while simultaneously being vital for maintenance of homeostatic conditions. This balancing act requires a tightly regulated system that might be influenced by bacterial metabolites such as butyrate, since reduced frequencies of butyrate-producing species associate with various lifestyle-associated disorders.

In the present work, we used systems biology approaches to understand how bacterial components may associate with metabolic disease and mediate phenotypic shifts in pro-inflammatory immune cells. First, we developed a computational framework for identifying bacteria that produce specific endotoxin variants with opposing immunological effects in metagenomic fecal samples. This framework was used to identify the endotoxin variant distribution amongst bacteria in the gut microbiome of Danes and Chinese with obesity and type 2 diabetes. We show for the first time that species producing pro-inflammatory endotoxin variants are vastly underrepresented in the gut microbiome compared to species producing non-inflammatory endotoxin and we identify country-specific gram-negative bacterial modules associated with insulin resistance. Second, we show that when the short-chain fatty acid butyrate is present under proinflammatory conditions, it induces a phenotypic switch in monocyte-derived dendritic cells to promote homeostasis through a potent inhibition of a type 1 immune response and induction of tissue-sustaining transcriptional programs. Collectively, these studies give insight into how intestinal microbes can affect their human host in a context-specific manner.
The Dual Amylin- and Calcitonin-Receptor Agonist KBP-042 Increases Insulin Sensitivity and Induces Weight Loss in Rats with Obesity

Objective: In this study, KBP-042, a dual amylin- and calcitonin-receptor agonist, was investigated as a treatment of obesity and insulin resistance in five different doses (0.625 μg/kg-10 μg/kg) compared with saline-treated and pair-fed controls. Methods: Rats with obesity received daily s.c. administrations for 56 days, and glucose tolerance was assessed after one acute injection, 3 weeks of treatment, and again after 7 weeks of treatment. To assess the effect on insulin sensitivity, rats received 5 μg/kg KBP-042 for 21 days before hyperinsulinemic-euglycemic clamp. Results: KBP-042 induced a sustained weight loss of up to 20% without any significant weight reduction in the pair-fed groups. Decreases in adipose tissues and lipid deposition in the liver were observed, while plasma adiponectin was increased and plasma leptin levels were decreased. Acute administration of KBP-042 led to impaired glucose tolerance and increased plasma lactate, while this diabetogenic effect was reversed by chronic treatment. Finally, assessment of insulin sensitivity using the hyperinsulinemic-euglycemic clamp showed that KBP-042 increased the glucose infusion rate. Conclusions: The study indicates that KBP-042 combines two highly relevant features, namely weight loss and insulin sensitivity, and is thus an excellent candidate for chronic treatment of obesity and insulin resistance.
Adaptation of Lactococcus lactis to high growth temperature leads to a dramatic increase in acidification rate

Lactococcus lactis is essential for most cheese making, and this mesophilic bacterium has its growth optimum around 30 °C. We have, through adaptive evolution, isolated a mutant TM29 that grows well up to 39 °C, and continuous growth at 40 °C is possible if pre-incubated at a slightly lower temperature. At the maximal permissive temperature for the wild-type, 38 °C, TM29 grows 33% faster and has a 12% higher specific lactate production rate than its parent MG1363, which results in fast lactate accumulation. Genome sequencing was used to reveal the mutations accumulated, most of which were shown to affect thermal tolerance. Of the mutations with more pronounced effects, two affected expression of single proteins (chaperone; riboflavin transporter), two had pleiotropic effects (RNA polymerase) which changed the gene expression profile, and one resulted in a change in the coding sequence of CDP-diglyceride synthase. A large deletion containing 10 genes was also found to affect thermal tolerance significantly. With this study we demonstrate a simple approach to obtain non-GMO derivatives of the important L. lactis that possess properties desirable by the industry, e.g. thermal robustness and increased rate of acidification. The mutations we have identified provide a genetic basis for further investigation of thermal tolerance.

General information
State: Published
Organisations: National Food Institute, Research Group for Microbial Biotechnology and Biorefining, Department of Systems Biology
Authors: Chen, J. (Intern), Shen, J. (Intern), Hellgren, L. (Intern), Jensen, P. R. (Intern), Solem, C. (Intern)
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BFI (2018): BFI-level 1
Emulsifying triglycerides with dairy phospholipids instead of soy lecithin modulates gut lipase activity: Emulsifying triglycerides with dairy phospholipids

A high energy supply and appropriate amount of polyunsaturated fatty acids is crucial for proper growth and development in neonates. The capacity for fatty acid absorption in newborns is however hampered due to an undeveloped pancreatic function combined with a low bile output. This seems in particular to limit fatty acid absorption in babies given infant formulas. Since interaction between the lipid droplet and the gastric and duodenal lipases occur through the hydrophobic/hydrophilic interface, the composition of the emulsifier may be crucial for efficient hydrolysis. We therefore determined hydrolytic rate of gastric lipase and pancreatic lipase, on their own or pancreatic lipase after gastric lipase on TAG droplets of similar size emulsified in either soy lecithin (SL) or in bovine milk phospholipids (MPL), more similar to human milk globule membrane lipids than soy lecithin. Gastric lipase activity was substantially higher on MPL-emulsified particles, while SL emulsification caused a higher rate of pancreatic lipase hydrolysis, on particles that had not been pre-treated with gastric lipase. MPL emulsification did however cause higher pancreatic lipase activity, when the particles had been pre-treated with gastric lipase. The attenuating effect of MPL-emulsification on pancreas lipase activity was validated in vivo in mice.

Practical application: Our results show that the activity of gastric lipase, a key enzyme in lipid absorption in neonates, is highly dependent on the phospholipid composition of the surface layer on the emulsion droplets. We furthermore show that increasing gastric lipase activity by modifying the phospholipid composition on the droplet surface, also enhance the subsequent activity of the pancreatic lipase acting in the duodenum. This implies that it is possible to strategically design the surface layer of lipid droplets in infant formulas to maximize gastric lipase activity, and that this could improve total fatty acid absorption in formula-fed neonates. This is of particular importance in the development of formula aimed at pre-mature babies, but is also highly relevant for formulas for term-born infants.

General information

State: Published
Organisations: Department of Systems Biology, Technical University of Denmark, University of Copenhagen, Lund University Hospital
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Gliadin affects glucose homeostasis and intestinal metagenome in C57BL6 mice fed a high-fat diet

Dietary gluten and its component gliadin are well-known environmental triggers of celiac disease and important actors in type-1 diabetes, and are reported to induce alterations in the intestinal microbiota. However, research on the impact of gluten on type-2 diabetes in non-celiac subjects is more limited. The aim of this study was to investigate the effect of gliadin on glucose homeostasis and intestinal ecology in the mouse.

Forty male C57BL/6 mice were fed a high-fat diet containing either 4% gliadin or no gliadin for 22 weeks. Gliadin consumption significantly increased the HbA1c level over time, with a borderline significance of higher HOMA-IR (homeostasis model assessment of insulin resistance) after 22 weeks. Sequencing of the V3 region of the bacterial 16S rRNA genes showed that gliadin altered the abundance of 81 bacterial taxa, separating the intestinal microbial profile of the gliadin consuming mice from the control mice in the principal coordinate analysis (PCoA) of weighted UniFrac distance. Moreover, gliadin reduced the ileal gene expression of tight junction protein 1, occludin, cadherin 1, mucin 2 and mucin 3, indicating an impaired intestinal barrier function. No difference was found in body weight gain, feed consumption or circulating cytokines (IL-1β, IL-6, IFN-γ, TNF-α and IL-10).

Our study is the first to show that gliadin as part of a defined synthetic feed exacerbates the glycaemia and alters the intestinal microbiota composition. Comprehensive analyses of metabolites, histological sections and the profile of specific immune cells are in progress to elucidate the mechanism behind the observed effects.

Gliadin intake alters intestinal microbiota, glucose and lipid metabolism, and adipose tissue and liver immune cells

General information
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Organisations: National Food Institute, Division of Food Microbiology, Department of Systems Biology, Center for Biological Sequence Analysis, University of Copenhagen
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Gliadin intake alters intestinal microbiota, glucose and lipid metabolism, and adipose tissue and liver immune cells

General information
State: Published
Organisations: Center for Biological Sequence Analysis, Department of Systems Biology, Division of Food Microbiology, National Food Institute, Research Group for Gut Microbiology and Immunology, University of Copenhagen
Pages: 314-314
Publication date: 2015
Main Research Area: Technical/natural sciences
Background: Hand eczema (HE) is a multifactorial disease, comprising different aetiological conditions and different morphologies. There are two aetiologically distinct groups of HE recognised: exogenous, such as contact dermatitis (allergic and/or irritant HE) and endogenous, such as the classic hyperkeratotic HE. Differences in the skin barrier
properties of these two conditions could theoretically be expected.

Aim: To examine whether differences exist in the lipid profile and the susceptibility of the stratum corneum (SC) in patients with allergic/irritant HE and those with hyperkeratotic HE.

Methods: Using cyanoacrylate, SC samples were taken from 23 patients with allergic/irritant HE and 15 with hyperkeratotic HE for lipid analysis by high-performance thin-layer chromatography (HPTLC). Samples were also taken from adjacent, unaffected skin. Severity of HE was assessed by the Hand Eczema Severity Index (HECSI), and skin barrier susceptibility was assessed by measuring transepidermal water loss (TEWL) after a 24-hour patch test with sodium lauryl sulfate (SLS).

Results: No statistically significant difference was found between groups for the lipid analysis or for skin susceptibility to SLS. We found a significantly higher HECSI score for hyperkeratotic HE compared with irritant or allergic HE (P=0.02).

Conclusions: There appears to be no difference in skin barrier between allergic/irritant HE (exogenous eczema) and hyperkeratotic HE (endogenous eczema) with regard to SC lipids or susceptibility to SLS.

General information
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Organisations: Department of Systems Biology, Center for Biological Sequence Analysis, Roskilde Hospital, Newcastle University, Bispebjerg University Hospital
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Scopus rating (2016): SJR 0.522 SNIP 0.764 CiteScore 1.02
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BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.611 SNIP 0.887 CiteScore 1.08
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Scopus rating (2013): SJR 0.647 SNIP 0.812 CiteScore 1.11
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Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.597 SNIP 0.829 CiteScore 1.01
ISI indexed (2011): ISI indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 0.552 SNIP 0.904
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 0.601 SNIP 0.938
BFI (2008): BFI-level 2
Scopus rating (2008): SJR 0.637 SNIP 0.955
Scopus rating (2007): SJR 0.604 SNIP 0.962
Scopus rating (2006): SJR 0.632 SNIP 0.858
Lipid hydrolysis products affect the composition of infant gut microbial communities in vitro.

Some lipid hydrolysis products such as medium-chained NEFA (MC-NEFA), sphingosine and monoacylglycerols (MAG) possess antibacterial activity, while others, including oleic acid, are essential for the optimal growth of Lactobacillus species. Thus, changes in the concentrations of NEFA and MAG in the distal ileum and colon can potentially selectively modulate the composition of the gut microbiota, especially in early life when lipid absorption efficacy is reduced. As medium-chained fatty acids are enriched in mothers’ milk, such effects may be highly relevant during gut colonisation. In the present study, we examined the effect of selected NEFA, MAG and sphingosine on the composition of faecal microbial communities derived from infants aged 2–5 months during a 24 h anaerobic in vitro fermentation. We tested lipid mixtures in the concentration range of 0–200 mM, either based on MC-NEFA (10 : 0 to 14 : 0 and MAG 12 : 0) or long-chained NEFA (LC-NEFA; 16 : 0 to 18 : 1 and MAG 16 : 0) with and without sphingosine, representing lipid hydrolysis products characteristic for intestinal hydrolysis of breast milk lipids. Ion Torrent sequencing of the bacterial 16S ribosomal RNA gene revealed that the relative abundance of lactic acid-producing genera, including Lactobacillus and Bifidobacterium, was generally increased in the presence of 50mM or higher concentrations of MC-NEFA. For Bifidobacterium, the same effect was also observed in the presence of a mixture containing LC-NEFA with sphingosine. On the contrary, the relative abundance of Enterobacteriaceae was significantly decreased in the presence of both lipid mixtures. Our findings suggest that the high concentration of medium-chained fatty acids in breast milk might have functional effects on the establishment of the gut microbiota in early life.
Long-chain polyunsaturated fatty acids in breast-milk and erythrocytes and neurodevelopmental outcomes in Danish late-preterm infants

Background: The supply of long-chain polyunsaturated fatty acids (LC-PUFA) during pregnancy and early lactation has been shown to affect cognitive development in preterm infants, but the effect on early neurodevelopment of late-preterm infants has not yet been examined. Aim: To examine the fatty acid composition of late-preterm human milk and identify possible associations between infant LC-PUFA status and perinatal as well as 1-year neurobehavioral outcomes.

Methods: Mother’s milk and erythrocytes (RBC) were sampled from 53 Danish late-preterm infants (33-36 weeks of gestation) 1 week and 1 month after delivery, and 3 months corrected age. Fatty acid composition was determined by gas-
liquid chromatography. Neurodevelopmental outcomes were assessed by the Nicu Network Neurobehavioral Scale (NNNS) at 1 week and 1 month and the Bayley Scales (BSID-III) at 1 year corrected age. Results: We found that breast-milk content of arachidonic acid (AA) and docosahexaenoic acid (DHA) was similar to reported fatty acid compositions of term human milk. Infant RBC-AA decreased from 1 week to 1 month of age and the size of the decrease was associated with better NNNS-scores at 1 month, specifically on regulation (p=0.03). Infant RBC-AA at 1 month was also associated with a lower 1-year corrected age BSID-III score of receptive language (p=0.05) and fine motor development (p=0.03). Infant RBC-DHA did not decrease significantly after delivery and was not associated with any of the developmental outcomes. Conclusion: Breast-milk LC-PUFA content was reflected in the RBC LC-PUFA status of the infant. Early RBC-AA status was associated with both early and long-term neurobehavioral development, but not in a consistent way.

General information
State: Published
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Publication: Research - peer-review › Journal article – Annual report year: 2015

Multiple Chemical Sensitivity: Baseline cytokine profiling and characterization of airway immunological response and gene expression profiling upon chemical exposure
Multiple chemical sensitivity (MCS) is a chronic disorder characterized by reports of symptoms from various organ systems attributed by the individuals to exposure to common odors and airborne chemicals in doses far below those known to induce toxic effects. There exists a general lack of knowledge about the mechanisms underpinning the disorder and no diagnostic tools or evidence-based treatment strategies are currently available. Little progress has been made in regards to clarifying the pathophysiology of MCS, and it remains a controversial topic with many opposing opinions. For further progress in the field, it is thus essential, that more evidence about the pathophysiological mechanisms is generated. The objectives of the thesis were thus to review the existing knowledge on immunology, genetics and metabolic abnormalities in MCS as presented in manuscript I and to investigate levels of primarily immunological biomarkers in MCS via three separate studies presented in manuscript IIIV. A complementary investigation of selected biomarkers associated with alternative modes of actions was likewise examined by gene expression measures, as part of manuscript IV.
The study presented in Manuscript II compared blood plasma levels of 14 cytokines, chemokines and growth factors between a MCS group (N = 150) and a sex and age-matched healthy control group (N = 149). The study observed significantly increased levels of cytokines interleukin (IL)-1β, IL-2, IL-4, IL-6, tumor necrosis factor-α in the MCS group, significantly reduced levels of IL-13 in the MCS group and no group differences in the allergen specific IgE measures. The differences were independent of factors such as sex, age, Body Mass Index, asthma, smoking, depression, anxiety and allergen-specific IgE. In conclusion, the study identified a distinct systemic immune mediator profile suggestive of low-grade systemic inflammation, along with a deviating Th2-associated cytokine response not involving IgE-mediated mechanisms. The two studies presented in manuscript III and IV are both based on biological samples collected from MCS subjects and matched controls at baseline, immediately after and four hours after a controlled chemical (n-butanol) exposure, in an exposure chamber previously verified to induce symptom elicitation in MCS subjects. In manuscript III, mucosal lining fluid samples were collected and levels of 19 cytokines and chemokines were quantified.
and compared between MCS subjects and healthy controls. The investigation did not identify any group associated
differences in mediator levels, either at baseline or upon the exposure session. However, time dependent changes were
identified for four of the 19 mediators, with decreasing mediator levels observed over time in both MCS subjects and
healthy controls. Overall, the findings suggest that the exposure session did not trigger a local inflammatory response and
that symptom elicitation in MCS is not dependent or affected by secretion of immunological mediators from epithelial or
immune cells in the upper airways.

Manuscript IV presents an explorative study investigating the feasibility of using gene expression profiling as an analytical
tool for biomarker discovery in MCS and to study the pathogenic mechanisms, based on differential gene expression
regulation upon the symptom elicitation. Expression levels of 26 genes associated with MCS were quantified in white
blood cells, nine genes showed low expression levels and were excluded while expression levels of the remaining genes
were compared between the groups at each time of sampling. The study did not identify any significant group differences
in gene expression levels of unexposed subjects or in the samples collected after the exposure session. As an effective
measure of the longitudinal responses to the exposure session, an integrated area under the curve (AUC) value was
computed for each gene and the AUC data revealed an increase in IL-6 expression in the MCS group and a tendency
toward increased expression of in IL-10 and acid ceramidase. In general, the data revealed a non-significant overall
increase in transcription rates associated with MCS and a larger intragroup variation among MCS subjects, indicative of a
diversified physiological reaction to the exposure. Overall, the findings presented in this thesis support the hypothesis of
abnormal regulation of the immune system in MCS subjects as a component in MCS pathophysiology, but were unable to
reveal new correlations between symptom elicitation and gene transcription in MCS.

**General information**

State: Published
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Main Research Area: Technical/natural sciences

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Projects:

Multiple Chemical Sensitivity

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**Obesity-associated fecal microbiota from human modulates body mass and metabolites in mice**

**General information**

State: Published
Organisations: National Food Institute, Research Group for Gut Microbiology and Immunology, Department of Systems
Biology, Holbæk University Hospital, University of Copenhagen
Authors: Zhang, L. (Intern), Bahl, M. I. (Intern), Hellgren, L. (Intern), Roager, H. M. (Intern), Fonvig, C. E. (Ekstern), Holm,
J. (Ekstern), Hansen, T. (Ekstern), Pedersen, O. (Ekstern), Licht, T. R. (Intern)
Publication date: 2015
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Main Research Area: Technical/natural sciences
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**Relations**

Activities:

Obesity-associated fecal microbiota from human modulates body mass and metabolites in mice

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Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2015

**Plasma phospholipid very-long-chain saturated fatty acids: a sensitive marker of metabolic dysfunction or an indicator of
specific healthy dietary components?**
Pregnancy induces an insulin resistance promoting hepatic ceramide phenotype in mice

General information
State: Published
Organisations: Department of Systems Biology
Authors: Hellgren, L. (Intern), Ingvorsen, C. (Intern)
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Publication date: 2015
Main Research Area: Technical/natural sciences

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Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 5.23 SJR 3.158 SNIP 1.732
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 3.609 SNIP 1.923 CiteScore 5.57
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 3.215 SNIP 1.97 CiteScore 5.57
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 3.216 SNIP 2.029 CiteScore 6
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 3.144 SNIP 1.916 CiteScore 5.76
ISI indexed (2012): ISI indexed yes
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Scopus rating (2011): SJR 3.068 SNIP 1.87 CiteScore 5.47
ISI indexed (2011): ISI indexed yes
Reduced ex vivo stimulated IL-6 response in infants randomized to fish oil from 9 to 18 months, especially among PPARG2 and COX2 wild types

We investigated whether n-3 LCPUFA affected immune function in late infancy and explored effect-modification by single nucleotide polymorphisms (SNPs) and links to intestinal microbiota. Infants (n=105) were randomized to fish oil (FO, 1.2 g/d n-3 LCPUFA) or sunflower oil (SO)-supplements from age 9-18 months. Immune function was assessed by ex vivo cytokine production in stimulated blood and plasma immunoglobulin E (IgE). We genotyped functional SNPs in PPARG2 and COX2 and analyzed fecal microbiota by 16S-rRNA terminal restriction fragment length polymorphism. FO compared to SO reduced Lactobacillus paracasei-stimulated IL-6 at 18 months (P=0.03, n=104). This effect was most pronounced among infants wild-type for PPARG2-Pro12Ala and/or COX2-T8473C (P<0.05). Predominant bacterial fragments were associated with 18 months IgE in all infants (P=0.004) (bp100) and with IL-6 production among infants weaned before 9 months (P=0.047) (bp102). Thus, FO reduced IL-6 in a genotype-modified manner. The microbiota was partly linked to IL-6 and IgE, not directly to FO.

General information
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Organisations: Department of Systems Biology, Center for Biological Sequence Analysis, University of Copenhagen, National Research Center for Working Environment
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Number of pages: 7
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Web of Science (2017): Indexed Yes
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Scopus rating (2016): SJR 1.345 SNIP 1.055 CiteScore 3.17
The effect of a short-term high-fat overfeeding on plasma levels of acylcarnitines in young, healthy men with low or normal birth weight

General information
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Organisations: Department of Systems Biology, Copenhagen University Hospital, Duke University
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Publication date: 2015
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Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.095 SNIP 0.804 CiteScore 2.54
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.066 SNIP 0.935 CiteScore 2.94
ISI indexed (2013): ISI indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 1.172 SNIP 1.155 CiteScore 3.19
ISI indexed (2012): ISI indexed yes
BFI (2011): BFI-level 1
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ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.052 SNIP 0.916
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 0.906 SNIP 0.91
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 1.079 SNIP 0.865
Scopus rating (2007): SJR 1.069 SNIP 0.92
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 1.067 SNIP 0.873
Scopus rating (2005): SJR 0.992 SNIP 0.739
Scopus rating (2004): SJR 0.965 SNIP 0.695
Scopus rating (2003): SJR 0.694 SNIP 0.601
Scopus rating (2002): SJR 0.52 SNIP 0.485
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Scopus rating (2016): CiteScore 5.23 SJR 3.158 SNIP 1.732
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 3.609 SNIP 1.923 CiteScore 5.57
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 3.215 SNIP 1.97 CiteScore 5.57
Web of Science (2014): Indexed yes
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Scopus rating (2013): SJR 3.216 SNIP 2.029 CiteScore 6
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 3.144 SNIP 1.916 CiteScore 5.76
ISI indexed (2012): ISI indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 3.068 SNIP 1.87 CiteScore 5.47
ISI indexed (2011): ISI indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 3.182 SNIP 1.828
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 2
Scopus rating (2009): SJR 2.948 SNIP 1.643
BFI (2008): BFI-level 2
Scopus rating (2008): SJR 3.198 SNIP 1.859
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 2.761 SNIP 1.611
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 2.641 SNIP 1.444
Web of Science (2006): Indexed yes
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Scopus rating (2004): SJR 2.415 SNIP 1.882
Scopus rating (2003): SJR 1.959 SNIP 1.82
Scopus rating (2002): SJR 1.935 SNIP 1.747
Scopus rating (2001): SJR 2.245 SNIP 1.782
Scopus rating (2000): SJR 2.015 SNIP 1.524
Scopus rating (1999): SJR 2.026 SNIP 1.619
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The effect of maternal Inflammation on foetal programming of metabolic disease

Maternal obesity during pregnancy increases the child’s risk of developing obesity and obesity-related diseases later in life. Key components in foetal programming of metabolic risk remain to be identified; however, chronic low-grade inflammation associated with obesity might be responsible for metabolic imprinting in the offspring. We have therefore surveyed the literature to evaluate the role of maternal obesity-induced inflammation in foetal programming of obesity and related diseases. The literature on this topic is limited, so this review also includes animal models where maternal inflammation is mimicked by single injections with lipopolysaccharide (LPS). An LPS challenge results in an immunological response that resembles the obesity-induced immune profile, although LPS injections provoke a stronger response than the subclinical obesity-associated response. Maternal LPS or cytokine exposures result in increased adiposity and impaired metabolic homeostasis in the offspring, similar to the phenotype observed after exposure to maternal obesity. The cytokine levels might be specifically important for the metabolic imprinting, as cytokines are both transferable from maternal to foetal circulation and have the capability to modulate placental nutrient transfer. However, the immune response associated with obesity is moderate and therefore potentially weakened by the pregnancy-driven immune modulation, dominated by anti-inflammatory Treg and Th2 cells. We know from other low-grade inflammatory diseases, such as rheumatoid arthritis, that pregnancy can improve disease state. If pregnancy is also capable of suppressing the obesity-associated inflammation, the immunological markers might be less likely to affect metabolic programming in the developing foetus than otherwise implied.

General information
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Organisations: Department of Systems Biology, Center for Biological Sequence Analysis, University of Cambridge
Authors: Ingvorsen, C. (Intern), Pedersen, S. B. (Intern), Ozanne, S. E. (Ekstern), Hellgren, L. (Intern)
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Scopus rating (2016): CiteScore 2.99 SJR 1.547 SNIP 1.063
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.611 SNIP 1.049 CiteScore 2.78
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.793 SNIP 1.241 CiteScore 3.5
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.613 SNIP 1.066 CiteScore 3.66
ISI indexed (2013): ISI indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 1.507 SNIP 1.19 CiteScore 4.05
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
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Scopus rating (2011): SJR 1.427 SNIP 1.055 CiteScore 2.64
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.236 SNIP 1.12
Whey-reduced weight gain is associated with a temporary growth reduction in young mice fed a high-fat diet

Whey protein consumption reportedly alleviates parameters of the metabolic syndrome. Here, we investigated the effects of whey protein isolate (whey) in young mice fed a high-fat diet. We hypothesized that whey as the sole protein source reduced early weight gain associated with retarded growth and decreased concentration of insulin-like growth factor-1. Moreover, we hypothesized that these changes were explained by increased nitrogen loss via elevated urea production and/or increased energy expenditure. Male 5-week-old C57BL/6 mice were fed high-fat diets with the protein source being either whey, casein or a combination of both for 5 weeks. After 1, 3 or 5 weeks, respectively, the mice were subjected to a meal challenge with measurements of blood and urinary urea before and 1 and 3 h after eating a weighed meal of their respective diets. In a subset of mice, energy expenditure was measured by indirect calorimetry during the first week of dietary intervention. Observed exclusively during the first week of intervention, whey significantly reduced body length \((P < 0.01)\) and weight gain \((P < 0.001)\) correlating positively with plasma concentrations of insulin-like growth factor-1. The combination diet displayed intermediate results indicating an interactive effect. Urea production, urea cycle activity, food intake and energy expenditure were unaffected by protein source. In conclusion, whey decreased growth-related parameters exclusively during the first week of dietary intervention. The early effect of whey could not be explained by food intake, energy expenditure, urea production or urea cycle activity but was correlated with plasma levels of insulin-like growth factor-1.

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Authors: Tranberg, B. (Ekstern), Madsen, A. N. (Ekstern), Hansen, A. K. (Ekstern), Hellgren, L. (Intern)
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ISSN (Print): 0955-2863
Objective. Maternal high-fat intake during pregnancy may have long-term consequences in the offspring. Since this might relate to the capacity of mitochondrial metabolic adaptation and hepatic lipid metabolism, we investigated how maternal high-fat intake affected mitochondrial function and hepatic steatosis in the offspring. Design. Sprague-Dawley rats were fed a high-fat (20% w/w) or a control diet (chow, C) from 10 days before pregnancy and throughout lactation. At weaning the litters were split into two groups; one was continued on the maternal diet and the other was fed low-fat chow. Sample. Skeletal muscle mitochondria and liver lipids. Methods. Mitochondrial respiration and hepatic lipid content were determined during and after weaning, on days 20 and 70 postpartum. Main outcome measures. Mitochondrial function and hepatic lipids. Results. At 20 days, maternal high-fat diet caused increased VO2max with pyruvate as substrate \((p = 0.047)\), at 70 days, pups born by C-dams, but not those born by highfat-dams, showed increased oxidation of
palmitoylcarnitine in the absence of ADP ($p = 0.018$). Rates of ADP-stimulated oxygen consumption, maximal respiratory capacity and mitochondrial respiratory control ratio with pyruvate, increased post weaning ($p < 0.001$), whereas respiratory control ratio with palmitoylcarnitine decreased ($p = 0.013$). The increase in respiratory control ratio was most pronounced in pups from C-dams ($p = 0.05$). The high-fat-diet caused pronounced hepatic steatosis in pups at weaning ($p < 0.001$), without concomitant ceramide accumulation, while high-fat-feeding after weaning induced triacylglycerol and ceramide accumulation ($p < 0.01$), regardless of maternal diet. Conclusion. Intake of a fat-rich diet during pregnancy and lactation reduced the age-induced increases in un-coupled fat oxidation.

General information
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Organisations: Department of Systems Biology, Center for Biological Sequence Analysis, Technical University of Denmark, University of Copenhagen
Authors: Hellgren, L. (Intern), Jensen, R. I. (Ekstern), Waterstradt, M. S. G. (Ekstern), Quistorff, B. (Ekstern), Lauritzen, L. (Ekstern)
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Scopus rating (2014): SJR 1.197 SNIP 1.294 CiteScore 2
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Scopus rating (2013): SJR 1.092 SNIP 1.136 CiteScore 1.82
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Web of Science (2013): Indexed yes
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ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.952 SNIP 1.077 CiteScore 1.72
ISI indexed (2011): ISI indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 0.911 SNIP 1.009
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 0.896 SNIP 1.028
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 0.736 SNIP 0.923
Scopus rating (2007): SJR 0.796 SNIP 0.972
Scopus rating (2006): SJR 0.887 SNIP 1.014
Scopus rating (2005): SJR 0.902 SNIP 1.148
Scopus rating (2004): SJR 0.762 SNIP 1.104
Scopus rating (2003): SJR 0.757 SNIP 1.175
Scopus rating (2002): SJR 0.735 SNIP 0.998
Adipose tissue trans fatty acids and changes in body weight and waist circumference

Previous studies have suggested that the intake of trans-fatty acids (TFA) plays a role in the development of obesity. The proportions of adipose tissue fatty acids not synthesised endogenously in humans, such as TFA, usually correlate well with the dietary intake. Hence, the use of these biomarkers may provide a more accurate measure of habitual TFA intake than that obtained with dietary questionnaires. The objective of the present study was to investigate the associations between the proportions of specific TFA in adipose tissue and subsequent changes in weight and waist circumference (WC). The relative content of fatty acids in adipose tissue biopsies from a random sample of 996 men and women aged 50–64 years drawn from a Danish cohort study was determined by GC. Baseline data on weight, WC and potential confounders were available together with information on weight and WC 5 years after enrolment. The exposure measures were total trans-octadecenoic acids (18 : 1t), 18 : 1 D6-10t, vaccenic acid (18 : 1 D11t) and rumenic acid (18 : 2 D9c, 11t). Data were analysed using multiple regression with cubic spline modelling. The median proportion of total adipose tissue 18 : 1t was 1.52% (90% central range 0.98, 2.19) in men and 1.47% (1.01, 2.19) in women. No significant associations were observed between the proportions of total 18 : 1t, 18:1 D6-10t, vaccenic acid or rumenic acid and changes in weight or WC. The present study suggests that the proportions of specific TFA in adipose tissue are not associated with subsequent changes in weight or WC within the exposure range observed in this population.
Effects of pregnancy on obesity-induced inflammation in a mouse model of fetal programming

Objective
Maternal obesity is associated with increased risk of metabolic dysfunction in the offspring. It is not clear whether it is the metabolic changes or chronic low-grade inflammation in the obese state that causes this metabolic programming. We therefore investigated whether low-grade inflammation was present in obese dams compared to controls dams at gestation day 18.

Methods
Female mice were fed either a standard chow diet or a highly palatable obesogenic diet for 6 weeks prior to conception. Mice were either euthanized before mating (n=12 in each group), or euthanized on gestation day 18 (n=8 in each group).
Blood and tissues were collected for analysis.

Results

The obesogenic diet increased body weight and decreased insulin sensitivity prior to conception, while there was no difference between the groups at gestation day 18. Local inflammation was assayed by macrophage count in adipose tissue and liver. Macrophage count in the adipose tissue was increased significantly by the obesogenic diet, and the hepatic count also showed a tendency to increased macrophage infiltration prior to gestation. This was further supported by a decreased population of monocytes in the blood of the obese animals, which suggested that monocytes are being recruited from the blood to the liver and adipose tissue in the obese animals. Gestation reversed macrophage infiltration, such that obese dams showed a lower adipose tissue macrophage count at the end of gestation compared to pre-pregnancy obese mice, and there were no longer a tendency towards increased hepatic macrophage count. Placental macrophage count was also similar in the two groups.

Conclusion

At gestation day 18, obese dams were found to have similar macrophage infiltration in placenta, adipose tissue and liver as lean dams, despite an incipient infiltration before gestation. Thus, the obesity-induced inflammation was reversed during gestation.

General information

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BFI (2015): BFI-level 1
Scopus rating (2015): SJR 2.943 SNIP 1.604 CiteScore 4.93
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 2.663 SNIP 1.706 CiteScore 4.72
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 2.436 SNIP 1.676 CiteScore 4.81
ISI indexed (2013): ISI indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 2.273 SNIP 1.61 CiteScore 4.71
ISI indexed (2012): ISI indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 2.527 SNIP 1.831 CiteScore 4.9
ISI indexed (2011): ISI indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 2.45 SNIP 1.586
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 2
Scopus rating (2009): SJR 1.977 SNIP 1.448
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 2.172 SNIP 1.536
Effects on metabolic markers are modified by PPARG2 and COX2 polymorphisms in infants randomized to fish oil.

Long-chain n-3 fatty acids (n-3 LCPUFA) improve blood pressure (BP) and lipid profile in adults and improve insulin sensitivity in rodents. We have previously shown that n-3 LCPUFA reduces BP and plasma triacylglycerol (TAG) in infants. Few studies have found effects on glucose homeostasis in humans. We explored possible effect modification by FADS, PPARG2, and COX2 genotypes to support potential effects of n-3 LCPUFA on metabolic markers in infants. Danish infants (133) were randomly allocated to daily supplementation with a teaspoon (~5 mL/day) of fish oil (FO) or sunflower oil (SO) from 9 to 18 months of age. Before and after the intervention, we assessed BP, erythrocyte n-3 LCPUFA, plasma lipid profile, insulin, and glucose in addition to functional single nucleotide polymorphisms in FADS, PPARG2, and COX2. At 18 months, plasma TAG was lower in the FO compared with SO group (p = 0.014). This effect was modified by PPARG2-Pro12Ala, as TAG only decreased among heterozygotes. FO supplemented PPARG2 Pro12Ala heterozygotes also had decreased plasma glucose compared with the SO group (p = 0.043). The effect of FO on mean arterial BP at 18 months was gender dependent (p = 0.020) and reduced in boys only (p = 0.028). Diastolic BP was, however, lower among all FO supplemented homozygous COX2-T8473C variant allele carriers compared with the SO group (p = 0.001). In conclusion, our results confirm that FO supplementation in late infancy reduces TAG and BP and indicates that the effects are mediated via peroxisome proliferator-activated receptor-γ and cyclooxygenase-2. Furthermore, FO reduced plasma glucose only in PPARG2 heterozygotes.
Environmental factors influencing neonatal immunity and development of diseases later in life

The prevalence of chronic inflammatory diseases in children, including childhood asthma, has increased during the past decades resulting in reduced quality of life for the implicated child and family, and an increased socioeconomic burden. Complex interactions between genetic factors (genetic predisposition) and the exposed environment, beginning as early as in perinatal life, are recognized causes of chronic inflammatory diseases.

This PhD thesis focuses on two potential environmental risk exposures for development of childhood asthma, namely maternal parity, and postpartum bacterial colonisation of the upper respiratory tract. The aim with this thesis was to investigate how maternal parity history affected neonatal immunity; and whether hereditary and environmental risk factors affected bacterial diversity in the upper respiratory tract of asymptomatic neonates. The study is based on clinical material from the birth cohorts of Copenhagen Prospective Studies on Asthma in Childhood (COPSAC).

The first study in the PhD thesis assessed how purified cord blood T cells from newborns of primiparous versus multiparous mothers react upon polyclonal activation in vitro. These data showed a reduced anti-inflammatory T cell function in first-born children as the IL-10 secretion and CD25 expression on CD4+ helper T cells were diminished as opposed to second- or later-born children. The result suggested that in utero T cell programing is responsible for this finding, which could be one of the explanations for the well-known epidemiological observations of enhanced risk for development of immune-mediated diseases in first-born children.

The second study assessed the associations between bacterial diversity and genetic predisposition for atopy and environmental risk factors relevant to establishment of a microbiota in the upper airways of newborns. The study showed a high diversity of nasopharyngeal bacterial in asymptomatic 1-month old infants. Moreover, season of birth was found to associate to nasopharyngeal bacterial diversity, with a higher bacterial diversity as well as specific bacteria profiles representing Gram-negative alphaproteobacteria and Gram-positive Bacilli in the nasopharynx of summer-born children. The result suggested that early postnatal colonization of the upper airways may reflect surrounding air at birth. A focus on the aspect of seasonality in modelling the impact of early dynamic changes in airway communities in relation to later disease development should be included in future studies.

Overall, these findings contribute to our understanding of how common environmental factors, such as maternal parity and season of birth are associated to the development of the newborn’s immune system and nasal microbiota. These environmental factors tend to be overlooked both in the study design, statistical analysis and reporting of scientific studies. This may result in misinterpretations and errors in our search for causes of childhood asthma and other chronic inflammatory diseases.

General information
State: Published
Organisations: Department of Systems Biology, Center for Biological Sequence Analysis
Gliadin affects glucose homeostasis and intestinal metagenome in C57BL/6 mice fed a high-fat diet

Dietary gluten and its component gliadin are well-known environmental triggers of celiac disease and important actors in type-1 diabetes, and are reported to induce alterations in the intestinal microbiota. However, research on the impact of gluten on type-2 diabetes in non-celiac subjects is more limited. The aim of this study was to investigate the effect of gliadin on glucose homeostasis and intestinal ecology in the mouse. Forty male C57BL/6 mice were fed a high-fat diet containing either 4% gliadin or no gliadin for 22 weeks. Gliadin consumption significantly increased the HbA1c level over time, with a borderline significance of higher HOMA-IR (homeostasis model assessment of insulin resistance) after 22 weeks. Sequencing of the V3 region of the bacterial 16S rRNA genes showed that gliadin changed the abundance of 81 bacterial taxa, separating the intestinal microbial profile of the gliadin consuming mice from the control mice in the principal coordinate analysis (PCoA) of weighted UniFrac distance. No difference was found in body weight gain, feed consumption or circulating cytokines (IL-1β, IL-6, IFN-γ, TNF-α and IL-10). Our study is the first to show that gliadin as part of a defined synthetic feed exacerbates the glycaemia and alters the intestinal microbiota composition. Comprehensive analyses of the profile of specific immune cells, metabolites and intestinal permeability are in progress to elucidate the mechanism behind the observed effects.

Phytol: A chlorophyll component with anti-inflammatory and metabolic properties

The naturally occurring dipterpenol molecule Phytol is an alcohol that can be extracted from the chlorophyll of green plants. Phytol has been studied for decades and has been suggested to have both metabolic properties as well as potent anti-inflammatory effects. Phytol represents a molecule derived by nature with lipid regulating properties, in line with today's need for new drugs to control for diseases that follow the westernized diet and lifestyle. The beneficial effects of phytol on health is in this chapter presented as one interesting naturally derived component in new natural remedies and functional food products to tackle the rapidly increasing global health problems caused by cardiovascular and chronic inflammatory diseases.

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Pre-natal undernutrition and post-natal overnutrition are associated with permanent changes in hepatic metabolism markers and fatty acid composition in sheep

Determine the impacts of pre- and early-post-natal nutrition on selected markers of hepatic glucose and fat metabolism. Twin-bearing ewes were fed 100% (NORM) or 50% (LOW) of protein and energy requirements during the last 6-weeks of gestation. Twin-lambs received either a high-carbohydrate high-fat (HCHF) or conventional (CONV) diet from 3 days to 6 months of age (around puberty), thereafter lambs from the four subgroups were slaughtered (16 males/3 females). Remaining lambs (19 females) were fed a moderate diet and slaughtered at 2 years of age (young adults). Pre-natal LOW nutrition was associated with increased hepatic triglyceride, ceramide and free fatty acid content in adulthood (not observed in lambs), which was accompanied by up-regulated early-stage insulin signalling as reflected by increased INSRβ and PI3K-p110 protein expression. The HCHF diet increased hepatic triglyceride content in lambs, associated with down-regulated expressions of energy-metabolism-related genes (GLUT1, PPARα, SREBP1c, PEPCK). These post-natal effects were not observed in adult HCHF sheep, after they had received a moderate (body-fat correcting) diet for 1.5 years. Interestingly, pre-natal LOW nutrition induced permanent alterations in hepatic phospholipids' fatty acid composition. Thus, the amount of linoleic acid (C18 : 2 Δ9,12) was significantly increased and composition of rumen-derived fatty acids were altered, indicating changed composition of rumenal microbiota. Hepatic insulin signalling and linoleic and microbial-derived fatty acid content in phospholipids are targets of foetal programming induced by late-gestation undernutrition. Future studies are required to explain their cause–effect associations with increased risks of developing hepatic steatosis and insulin insensitivity in adulthood.

General information
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Organisations: Department of Systems Biology, Center for Biological Sequence Analysis, Centre for Fetal Programming, University of Copenhagen
Authors: Hou, L. (Ekstern), Hellgren, L. (Intern), Kongsted, A. H. (Ekstern), Vaag, A. (Ekstern), Nielsen, M. O. (Ekstern)
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Scopus rating (2015): SJR 1.611 SNIP 1.049 CiteScore 2.78
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BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.793 SNIP 1.241 CiteScore 3.5
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The effect of a short-term high-fat overfeeding on plasma levels of amino acids in young, healthy men with low or normal birth weight

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Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2014

The effect of a short-term high-fat overfeeding on plasma levels of amino acids in young, healthy men with low or normal birth weight

General information
State: Published
Organisations: Department of Systems Biology, Center for Biological Sequence Analysis, Duke University, Copenhagen University Hospital
Adipose tissue trans fatty acids and changes in body weight and waist circumference

Previous studies have suggested that intake of trans fatty acids (TFA) may play a role in the development of obesity. For fatty acids not synthesized endogenously in humans, such as TFA, the proportions in adipose tissue tend to correlate well with the habitual dietary intake. Biomarkers may provide a more accurate measure of habitual TFA intake than dietary questionnaires. Our objective was to investigate the associations between specific TFA in adipose tissue and subsequent changes in body weight and waist circumference (WC).

Content and distribution of phytanic acid diastereomers in organic milk as affected by feed composition

Phytanic acid (PA) is a bioactive compound found in milk that is derived from the phytol chain of chlorophyll, and the content of PA in milk fat depends on the availability of phytol from feed. In this study, the content of PA diastereomers was analyzed in milk sampled from five organic herds twice during the grazing season (May and September). The total content of PA was higher in September compared to May, but was not affected by breed (Danish Holstein or Danish Jersey). Total PA could not be directly related to intake of green feed items. The distribution between diastereomers was closely related to the amount of grazed clovers, where a higher intake resulted in a higher share of the RRR isomer. © 2012 American Chemical Society.
Docosahexaenoic acid status at 9 months is inversely associated with communicative skills in 3-year-old girls

The objective of the present observational study was to investigate if the docosahexaenoic acid (DHA) status assessed in infant erythrocytes (RBC) at 9 months was associated with the age when the infants reach developmental milestones and their psychomotor function at 3 years of age. Three hundred eleven healthy Danish children were followed from 9 months to 3 years of age (the SKOT cohort). RBC fatty acid composition was analysed by gas chromatography in 272 of the children. Milestone age was collected by questionnaires at 9 and 18 months and psychomotor development at 3 years of age was assessed by the parents using third edition of the Ages and Stages Questionnaire (ASQ-3). RBC DHA levels ranged from 2.2% to 12.6% of the RBC fatty acids. The age of reaching milestones correlated with psychomotor development, particularly with gross motor function at 3 years. An association between milestones and later personal and social skills was also observed, but only for girls. In girls, RBC-DHA was found to be inversely correlated with communication at 3 years of age (odds ratio = 0.69, 95% confidence interval: 0.56-0.86, P = 0.001), but no other associations with psychomotor development or milestones were found. The results from study indicate that DHA status at 9 months may not have a pronounced beneficial effect on psychomotor development in early childhood and that communicative skills at 3 years of age may even be inversely associated with early RBC-DHA levels in girls.

General information
State: Published
Organisations: Department of Systems Biology, Center for Biological Sequence Analysis, University of Copenhagen
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Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 1.453 SNIP 1.351 CiteScore 2.57
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.841 SNIP 1.798 CiteScore 2.94
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.273 SNIP 1.282 CiteScore 2.35
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.303 SNIP 1.155 CiteScore 2.37
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.844 SNIP 0.876 CiteScore 1.78
ISI indexed (2012): ISI indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 1.176 SNIP 1.022 CiteScore 2.02
ISI indexed (2011): ISI indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.103 SNIP 1.076
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 0.832 SNIP 0.865
BFI (2008): BFI-level 2
Scopus rating (2008): SJR 0.592 SNIP 0.796
Scopus rating (2007): SJR 0.455 SNIP 0.819
Effects of butter from mountain-pasture grazing cows on risk markers of the metabolic syndrome compared with conventional Danish butter: a randomized controlled study.

There is considerable interest in dairy products from low-input systems, such as mountain-pasture grazing cows, because these products are believed to be healthier than products from high-input conventional systems. This may be due to a higher content of bioactive components, such as phytanic acid, a PPAR-agonist derived from chlorophyll. However, the effects of such products on human health have been poorly investigated. Objective: To compare the effect of milk-fat from mountain-pasture grazing cows (G) and conventionally fed cows (C) on risk markers of the metabolic syndrome. Design: In a double-blind, randomized, 12-week, parallel intervention study, 38 healthy subjects replaced part of their habitual dietary fat intake with 39 g fat from test butter made from milk from mountain-pasture grazing cows or from cows fed conventional winter fodder. Glucose-tolerance and circulating risk markers were analysed before and after the intervention. Results: No differences in blood lipids, lipoproteins, hsCRP, insulin, glucose or glucose-tolerance were observed. Interestingly, strong correlations between phytanic acid at baseline and total (P

General information
State: Published
Organisations: Department of Systems Biology, Center for Biological Sequence Analysis, Aarhus University, University of Copenhagen
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Number of pages: 10
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Scopus rating (2016): SJR 0.864 SNIP 0.845 CiteScore 2.33
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.954 SNIP 0.973 CiteScore 2.68
Effects of maternal energy intake during gestation and lactation on leptin levels in the young and adult pups

General information
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Organisations: Department of Systems Biology, Center for Biological Sequence Analysis
Authors: Ingvorsen, C. (Intern), Hellgren, L. (Intern)
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Event: Abstract from Annual meeting in Dansk Selskab for Adipositasforskning, Odense, Denmark.
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FADS genotype and diet are important determinants of DHA status: a cross-sectional study in Danish infants

Background: Infant docosahexaenoic acid (DHA) status is supported by the DHA content of breast milk and thus can decrease once complementary feeding begins. Furthermore, it is unclear to what extent endogenous DHA synthesis contributes to status. Objective: We investigated several determinants, including FADS genotypes on DHA status at 9 mo and 3 y. Design: This was a cross-sectional study with Danish infants from 2 prospective studies [Essentielle Fedtsyrer i Overgangskost (EFION) and the Småbørns Kost Og Trivsel (SKOT) cohort] in which we measured red blood cell (RBC) DHA status at 9 mo (n = 409) and 3 y (n = 176) and genotyped 4 FADS tag single nucleotide polymorphisms (SNPs): rs3834458, rs1535, rs174575, and rs174448 (n = 401). Information about breastfeeding was obtained by using questionnaires, and fish intake was assessed by using 7-d precoded food diaries. Results: FADS genotype, breastfeeding,
and fish intake explained 25% of the variation in infant RBC DHA status [mean ± SD: 6.6 ± 1.9% of fatty acids (FA%)]. Breastfeeding explained most of the variation (~20%), and still being breastfed at 9 mo was associated with a 0.7 FA% higher DHA compared with no longer being breastfed (P < 0.001). The FADS SNPs rs1535 and rs3834458 were highly correlated (r = 0.98). Homozygous carriers of the minor allele of rs1535 had a DHA increase of 1.8 FA% (P = 0.001) relative to those with the wild-type allele, whereas minor allele carriers of rs174448 and rs174575 had a decrease of 1.1 FA% (P = 0.005) and 2.0 FA% (P = 0.001), respectively. Each 10-g increment in fish intake was associated with an increased DHA status of 0.3 FA%. At 3 y, fish intake was the only significant determinant of DHA status (0.2 FA%/10 g).

Conclusion: Breastfeeding, FADS genotype, and fish intake are important determinants of DHA status in late infancy. The EFiON study was registered at clinicaltrials.gov as NCT 00631046.

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Web of Science (2016): Indexed yes
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Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 3.799 SNIP 2.417 CiteScore 5.71
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Scopus rating (2013): SJR 4.045 SNIP 2.579 CiteScore 6.38
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Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 3.675 SNIP 2.435 CiteScore 6.05
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 3.519 SNIP 2.473 CiteScore 6.23
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BFI (2010): BFI-level 2
Scopus rating (2010): SJR 3.261 SNIP 2.231
BFI (2009): BFI-level 2
Scopus rating (2009): SJR 3.213 SNIP 2.457
BFI (2008): BFI-level 2
Scopus rating (2008): SJR 3.291 SNIP 2.265
Web of Science (2008): Indexed yes
Lipid hydrolysis products affect the composition of microbiota isolated from infant fecal samples after in vitro fermentation

Some lipid hydrolysis products such as medium-chained free fatty acids (FFA) and monoacylglycerols (MAG) have antibacterial activity, while others, including oleic acid, have been reported to be essential for optimal growth of Lactobacillus species. Thus, the FFA and MAG concentration in the distal ileum and in colon can be expected to selectively modulate the growth rate and hereby the composition of the microbiota.

In earlier studies, we have shown that this concentration is dependent on the type of emulsification of the triglycerides, which deviates between breast milk and formula milk.

Here, we have determined effects of selected combinations of FFA and MAG on microbial composition during a 24-hour anaerobic in vitro fermentation in microbiota obtained from infant fecal samples (age 2-5 months). PCR-based quantification of 11 different bacterial taxa revealed that the growth of Firmicutes, Lactobacillus and B. longum is significantly increased in the presence of a mixture of C10-C14 FFAs.

Lipid hydrolysis products affect the composition of microbiota isolated from infant fecal samples after in vitro fermentation

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General information

State: Published
Organisations: Department of Systems Biology, Center for Biological Sequence Analysis, National Food Institute, Division of Food Microbiology
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Lipid hydrolysis products affect the composition of microbiota isolated from infant fecal samples after in vitro fermentation

**General information**

State: Published
Organisations: Department of Systems Biology, Center for Biological Sequence Analysis, National Food Institute, Division of Food Microbiology
Authors: Bennike, R. M. G. (Intern), Licht, T. R. (Intern), Hellgren, L. (Intern)
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Mapping Condition-Dependent Regulation of Lipid Metabolism in Saccharomyces cerevisiae.

Lipids play a central role in cellular function as constituents of membranes, as signaling molecules, and as storage materials. Although much is known about the role of lipids in regulating specific steps of metabolism, comprehensive studies integrating genome-wide expression data, metabolite levels, and lipid levels are currently lacking. Here, we map condition-dependent regulation controlling lipid metabolism in Saccharomyces cerevisiae by measuring 5636 mRNAs, 50 metabolites, 97 lipids, and 57 13C-reaction fluxes in yeast using a three-factor full-factorial design. Correlation analysis across eight environmental conditions revealed 2279 gene expression level-metabolite/lipid relationships that characterize the extent of transcriptional regulation in lipid metabolism relative to major metabolic hubs within the cell. To query this network, we developed integrative methods for correlation of multi-omics datasets that elucidate global regulatory signatures. Our data highlight many characterized regulators of lipid metabolism and reveal that sterols are regulated more at the transcriptional level than are amino acids. Beyond providing insights into the systems-level organization of lipid metabolism, we anticipate that our dataset and approach can join an emerging number of studies to be widely used for interrogating cellular systems through the combination of mathematical modeling and experimental biology.

**General information**

State: Published
Organisations: Department of Systems Biology, Center for Biological Sequence Analysis, Department of Biotechnology, Technical University of Denmark
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Publication: Research - peer-review › Journal article – Annual report year: 2013
Obesity-induced hepatic and placental inflammation are absent in obese gestating mice compared to control fed dams

General information
State: Published
Organisations: Department of Systems Biology, Center for Biological Sequence Analysis, University of Cambridge
Number of pages: 1
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Event: Abstract from 15th European Congress of Endocrinology 2013, Copenhagen, Denmark.
Main Research Area: Technical/natural sciences
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Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2013

Introduction: Maternal diet during gestation and lactation has been implicated as a factor that modifies the risk of developing metabolic diseases later in life. Hepatic lipid accumulation is strongly linked to development of metabolic diseases. Free fatty acids induce ER stress, mitochondrial stress and are the substrate for formation of other lipotoxic species, such as ceramide, diacylglycerol and acyl-CoA. We have therefore investigated if the maternal intake of a high fat diet combined with sucrose-rich beverage alters the offspring’s ability to metabolically cope with a high-fat challenge in adult life. In this poster, we report data on hepatic lipid content.

Methods: Rat dams were fed a 60 E% fat diet and given 15% sucrose (HFHS) in the drinking water or chow and pure water (C) six weeks before mating as well as during gestation and lactation. After birth, male pups were cross-fostered by the dams, so that half of the pups born by HFHS mothers was lactated by C dams and vice versa, generating four groups; CC, CH, HC and HH (first letter maternal diet during pregnancy and the second diet during lactation). At weaning all pups were transferred to chow-diet and kept on this diet until the age of 20 weeks. At 20 weeks of age, all pups, with the exception of one control group, were transferred to a high fat diet (45E% fat). After 6 weeks on this diet, all rats were sacrificed and hepatic lipid content and composition was analyzed using GC-FID.

Results: The high fat intervention caused strongly increased levels of hepatic free fatty acids (FFA) in rats both born and lactated by HFHS-dams. Principal component analysis of the FFA fatty acid composition showed that there were in particular dietary PUFA that accumulated, indicating that it is the ability to metabolize these fatty acids that are hampered in these animals.

Conclusion: Maternal high fat/high sucrose intake during gestation and lactation makes the offspring less able to metabolize dietary PUFA, which cause accumulation of these as FFA. This might make them more prone to develop metabolic diseases when exposed to energy dense diets.

Offspring from rat mothers fed a high-fat/high-sucrose diet during gestation and lactation accumulate free fatty acids in the liver when exposed to high fat diet as adults.

Introduction: Maternal diet during gestation and lactation has been implicated as a factor that modifies the risk of developing metabolic diseases later in life. Hepatic lipid accumulation is strongly linked to development of metabolic diseases. Free fatty acids induce ER stress, mitochondrial stress and are the substrate for formation of other lipotoxic species, such as ceramide, diacylglycerol and acyl-CoA. We have therefore investigated if the maternal intake of a high fat diet combined with sucrose-rich beverage alters the offspring’s ability to metabolically cope with a high-fat challenge in adult life. In this poster, we report data on hepatic lipid content.

Methods: Rat dams were fed a 60 E% fat diet and given 15% sucrose (HFHS) in the drinking water or chow and pure water (C) six weeks before mating as well as during gestation and lactation. After birth, male pups were cross-fostered by the dams, so that half of the pups born by HFHS mothers was lactated by C dams and vice versa, generating four groups; CC, CH, HC and HH (first letter maternal diet during pregnancy and the second diet during lactation). At weaning all pups were transferred to chow-diet and kept on this diet until the age of 20 weeks. At 20 weeks of age, all pups, with the exception of one control group, were transferred to a high fat diet (45E% fat). After 6 weeks on this diet, all rats were sacrificed and hepatic lipid content and composition was analyzed using GC-FID.

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Conclusion: Maternal high fat/high sucrose intake during gestation and lactation makes the offspring less able to metabolize dietary PUFA, which cause accumulation of these as FFA. This might make them more prone to develop metabolic diseases when exposed to energy dense diets.

Perinatal programming of metabolic dysfunction and obesity-induced inflammation

The number of obese women in the childbearing age is drastically increasing globally. As a consequence, more children are born by obese mothers. Unfortunately, maternal obesity and/ or high fat intake during pregnancy increase the risk of developing obesity, type-2 diabetes, cardiovascular disease and non-alcoholic fatty liver disease in the children, which passes obesity and metabolic dysfunction on from generation to generation. Several studies try to elucidate causative effects of maternal metabolic markers on the metabolic imprinting in the children; however diet induced obesity is also associated with chronic low grade inflammation. Nobody have yet investigated the role of this inflammatory phenotype, but here we demonstrate that obesity induced inflammation is reversed during pregnancy in mice, and is therefore less likely to affect the fetal programming of metabolic dysfunction. Instead, we suggest that an early elevated lipid exposure caused by a maternal high fat feeding might be more important for long term metabolic imprinting in the offspring. Therefore, we study the effect of maternal high fat/high sucrose diet during gestation, lactation or both to elucidate if perinatal adaptations to a high fat/high sucrose diet makes the offspring more capable of dealing with a high fat diet later in life. We
demonstrate that a dietary mismatch between pre- and post-natal life alters the phenotype in an obese prone rat model at weaning. Thus, exposure to a control diet in utero and a high fat/high sucrose diet during lactation cause more severe phenotypic alteration in the offspring at weaning than pups exposed to the high fat/high sucrose diet both in utero and during lactation. The same pattern is seen in the adult offspring after being challenged with a high fat diet for 6 weeks. However HFHS exposure during fetal life protected against hyperleptinemia in the adult offspring during the challenge. Additionally, offspring exposed to high fat/high sucrose diet during lactation displayed a decrease level of inflammatory genes in the blood, which could indicate that perinatal HFHS exposure protect against the detrimental effects of high fat feeding leading to metabolic disease.

Phytanic acid stimulates glucose uptake in a model of skeletal muscles, the primary porcine myotubes

ABSTRACT: BACKGROUND: Phytanic acid (PA) is a chlorophyll metabolite with potentials in regulating glucose metabolism, as it is a natural ligand of the peroxisome proliferator-activated receptor (PPAR) that is known to regulate hepatic glucose homeostasis. This study aimed to establish primary porcine myotubes as a model for measuring glucose uptake and glycogen synthesis, and to examine the impact of physiological amounts of PA on glucose uptake and glycogen synthesis either alone or in combination with insulin. METHODS: Porcine satellite cells were cultured into differentiated myotubes and tritiated 2-deoxyglucose (2-DOG) was used to measure glucose uptake, in relation to PA and 2-DOG exposure times and also in relation to PA and insulin concentrations. The MIXED procedure model of SAS was used for statistical analysis of data. RESULTS: PA increased glucose uptake by approximately 35%, and the presence of insulin further increased the uptake, but this further increase in uptake was non-additive and less pronounced at high insulin concentrations. There was no effect of PA alone on glycogen synthesis, while the insulin stimulation of glycogen synthesis was increased by 20% in the presence of PA. PA neither stimulated glucose uptake nor glycogen synthesis in insulin-resistant myotubes generated by excess glucose exposure. CONCLUSIONS: Primary porcine myotubes were established as a model of skeletal muscles for measuring glucose uptake and glycogen synthesis, and we showed that PA can play a role in stimulating glucose uptake at no or inadequate insulin concentrations.
Polymorphism in the fatty acid desaturase genes and diet are important determinants of infant n-3 fatty acid status.

**Background and objectives:** Tissue docosahexaenoic acid (DHA) accretion in early infancy has been shown to be supported by the DHA-content of breast-milk and thus may decrease once complementary feeding takes over. Endogenous synthesis of DHA from alpha-linolenic acid has been shown to be very low and polymorphism in the genes that encodes the fatty acid desaturases (FADS) has little effect on DHA-status in adults. It is however unclear to what extent endogenous DHA-synthesis contributes to infant DHA-status.

**Aim:** To investigate the role of diet and FADS polymorphism on DHA-status at 9 months and 3 years.

**Methods:** This cross-sectional study with Danish infants use data from two prospective studies (EFION and the SKOT cohort). We measured erythrocyte (RBC) DHA-status at 9 months (n=409) and 3 years (n=176) and genotyped 4 FADS tagSNPs, rs3834458, rs1535, rs174575 and rs174448 (n=401). Information about breastfeeding was obtained by questionnaires and fish intake was assessed by 7-day pre-coded food diaries.

**Results:** FADS-genotype, breastfeeding, and fish intake were found to explain 25% of the variation in infant RBC DHA-status (mean±SD: 6.6±1.9% of the fatty acids (FA%)). Breastfeeding was the most important contributor and still being breast-fed at 9 months was associated with 0.8 FA% higher DHA vs. no longer breast-fed (p<0.001). Two of the examined FADS-SNPs were highly correlated (rs1535 and rs3834458; r=0.98). Homozygous carriers of the minor allele of rs1535 had an increase in RBC DHA of 1.6 FA% relative to those with wild type, whereas minor allele carriers of rs174448 and rs174575 had a decrease of 0.9 (p=0.017) and 1.9 FA% (p=0.001), respectively. Each 10-gram increment in fish intake was associated with an increase in DHA-status of 0.3 FA%. At 3 years, fish intake was the only significant determinant of DHA-status (0.2 FA%/10g).
Conclusions: FADS-genotype and diet are both important determinants of DHA-status in late infancy.

General information
State: Published
Organisations: Department of Systems Biology, Center for Biological Sequence Analysis, National Research Center for Working Environment, University of Copenhagen
Authors: Harsløf, L. (Ekstern), Larsen, L. (Ekstern), Ritz, C. (Ekstern), Hellgren, L. (Intern), Michaelsen, K. F. (Ekstern), Vogel, U. (Ekstern), Lauritzen, L. (Ekstern)
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Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2013

Polymorphisms in the fatty acid desaturase genes and diet are important determinants of infant docosahexaenoic acid status
Tissue docosahexaenoic acid (DHA) accretion in early infancy is supported by DHA in breast-milk and may thus decrease once complementary feeding takes over. Endogenous synthesis of DHA from alphalinolenic acid is low and polymorphisms in the genes that encodes the fatty acid desaturases (FADS) has been shown to have little effect on DHA-status in adults. It is unclear to what extent endogenous DHA-synthesis contributes to infant DHA-status. We aim to investigate the role of diet and FADS-polymorphisms on DHA-status at 9 months and 3 years. Methods: This cross-sectional study with Danish infants use data from two prospective studies (EFiON and the SKOTcohort). We measured erythrocyte (RBC) DHA-status at 9 months (n=409) and 3 years (n=176) and genotyped 4 FADS tagSNPs, rs3834458, rs1535, rs174575 and rs174448 (n=401).

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Organisations: Department of Systems Biology, Center for Biological Sequence Analysis, National Research Center for Working Environment, University of Copenhagen
Authors: Lauritzen, L. (Ekstern), Harsløf, L. (Ekstern), Larsen, L. (Ekstern), Ritz, C. (Ekstern), Hellgren, L. (Intern), Michaelsen, K. F. (Ekstern), Vogel, U. (Ekstern)
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Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
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Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.284 SNIP 1.12 CiteScore 2.64
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.949 SNIP 1.014 CiteScore 2.46
ISI indexed (2013): ISI indexed yes
Pre- and early-postnatal nutrition modify gene and protein expressions of muscle energy metabolism markers and phospholipid fatty acid composition in a muscle type specific manner in sheep.

We previously reported that undernutrition in late fetal life reduced whole-body insulin sensitivity in adult sheep, irrespective of dietary exposure in early postnatal life. Skeletal muscle may play an important role in control of insulin action. We therefore studied a range of putative key muscle determinants of insulin signalling in two types of skeletal muscles (longissimus dorsi (LD) and biceps femoris (BF)) and in the cardiac muscle (ventriculus sinister cordis (VSC)) of sheep from the same experiment. Twin-bearing ewes were fed either 100% (NORM) or 50% (LOW) of their energy and protein requirements during the last trimester of gestation. From day-3 postpartum to 6-months of age (around puberty), twin offspring received a high-carbohydrate-high-fat (HCHF) or a moderate-conventional (CONV) diet, whereafter all males were slaughtered. Females were subsequently raised on a moderate diet and slaughtered at 2-years of age (young adults). The only long-term consequences of fetal undernutrition observed in adult offspring were lower expressions of the insulin responsive glucose transporter 4 (GLUT4) protein and peroxisome proliferator-activated receptor gamma, coactivator 1a (PGC1α) mRNA in BF, but increased PGC1α expression in VSC. Interestingly, the HCHF diet in early postnatal life was associated with somewhat paradoxically increased expressions in LD of a range of genes (but not proteins) related to glucose uptake, insulin signalling and fatty acid oxidation. Except for fatty acid oxidation genes, these changes persisted into adulthood. No persistent expression changes were observed in BF and VSC. The HCHF diet increased phospholipid ratios of n-6/n-3 polyunsaturated fatty acids in all muscles, even in adults fed identical diets for 1 1/2 years. In conclusion, early postnatal, but not late gestation, nutrition had long-term consequences for a number of determinants of insulin action and metabolism in LD. Tissues other than muscle may account for reduced whole body insulin sensitivity in adult LOW sheep.

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Organisations: Department of Systems Biology, Center for Biological Sequence Analysis, University of Jiroft, Technical University of Denmark, Copenhagen University Hospital, University of Copenhagen
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Whey protein reduces early life weight gain in mice fed a high-fat diet.

An increasing number of studies indicate that dairy products, including whey protein, alleviate several disorders of the metabolic syndrome. Here, we investigated the effects of whey protein isolate (whey) in mice fed a high-fat diet hypothesising that the metabolic effects of whey would be associated with changes in the gut microbiota composition. Five-week-old male C57BL/6 mice were fed a high-fat diet ad libitum for 14 weeks with the protein source being either whey or casein. Faeces were collected at week 0, 7, and 13 and the fecal microbiota was analysed by denaturing gradient gel electrophoresis analyses of PCR-derived 16S rRNA gene (V3-region) amplicons. At the end of the study, plasma samples were collected and assayed for glucose, insulin and lipids. Whey significantly reduced body weight gain during the first four weeks of the study compared with casein (P<0.001–0.05). Hereafter weight gain was similar resulting in a 15% lower final body weight in the whey group relative to casein (34.0±1.0 g vs. 40.2±1.3 g, P<0.001). Food intake was unaffected by protein source throughout the study period. Fasting insulin was lower in the whey group (P<0.01) and glucose clearance was improved after an oral glucose challenge (P<0.05). Plasma cholesterol was lowered by whey compared to casein (P<0.001). The composition of the fecal microbiota differed between high- and low-fat groups at 13 weeks (P<0.05) whereas no difference was seen between whey and casein. In conclusion, whey initially reduced weight gain in young C57BL/6 mice fed a high-fat diet compared to casein. Although the effect on weight gain ceased, whey alleviated glucose intolerance, improved insulin sensitivity and reduced plasma cholesterol. These findings could not be explained by changes in food intake or gut microbiota composition. Further studies are needed to clarify the mechanisms behind the metabolic effects of whey.

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Ceramide profile in hypohidrotic ectodermal dysplasia

Background. Hypohidrotic ectodermal dysplasia (HED) is a rare genetic disease. The clinical presentation includes lack of sweating ability, and an often widely spread dermatitis resembling atopic dermatitis (AD). In AD, the skin-barrier defect is partly ascribed to the altered lipid profile in the stratum corneum and partly to mutations of the filaggrin genes. To our knowledge, no data are available about the epidermal lipid profile of HED. Aim. To compare the ceramide profile for patients with HED and AD. Methods. The ceramide profile and ceramide/cholesterol ratio were compared between patients with HED (n = 7) and patients with AD (n = 21), using cyanoacrylate to take biopsy samples from the stratum corneum. Lipids were extracted from the biopsies and analysed using high-performance thin-layer chromatography. Results. The lipid profiles of HED and AD were similar in distribution, apart from ceramide 1, which was significantly higher in HED (P = 0.04). Conclusions. The increased ceramide 1 level found in HED compared with AD is known to play a role in the structure of the lipid bilayers. However, further studies are needed to identify the functional significance of these observations and thereby elucidate differences in the skin barrier between HED and AD.
Effects of Butter and Phytanic acid intake on metabolic parameters and T-cell polarization

The still growing obesity epidemic is a major risk for our society, as it is associated with the development of the so called metabolic syndrome, which is a clinical diagnosis correlated to development of metabolic disorders. Lack of physical activity, excess energy intake, and nutritional factors e.g. fatty acid composition of the diet, are important factors with regard to development of metabolic syndrome. There is a controversy between the fact that several studies has shown that intake of saturated fatty acids are strongly correlated to the development of metabolic related diseases, such as cardiovascular diseases and type 2 diabetes, and against the fact that other studies has shown that intake of dairy fat, which has high saturated fatty acid content, correlates negatively with risk factors. Hence, it has even been suggested that dairy fat might have beneficial impacts in relation to metabolic disorders. Dairy fat is the most complex type of fat occurring in the nature, with more than 400 identified fatty acids. Several of these fatty acids that occur in low amounts have been suggested to have beneficial properties with regard to metabolic disorders. The concentrations of certain of these minor fatty acids are raised in dairy fat along with the amount of green plant material intake of the cattle. Phytanic acid is one of these minor fatty acids, due to agonist activities for nuclear receptors with central roles in among others the lipid and glucose metabolism.

To determine the effects of both dairy fat in general and phytanic acid on metabolic parameters, we performed several studies. First, we investigated effects on hepatic lipid metabolism, glucose homeostasis, and circulating metabolic markers, of high fat diets based on butter from high- or low-yield production, a diet based on high oleic acid sunflower oil, and a diet based on grape-seed oil with high amount of linoleic acid, in diet induced obese mice. Second, we investigated phytanic acid effects on similar parameters in obese mice, both as dose response in butter based diets, and in grape-seed oil based diets with and without addition of phytanic acid. Third, we investigated butter and phytanic acid effects on human T-cell polarization, both by in vitro incubation with phytanic acid, and by a 12 weeks intervention with intake of butter. Finally, we performed two human interventions, first one with intake of butter and cheese, and the second with intake of butter. In these studies we investigated whether it is possible to alter the human plasma concentration of phytanic acid due
to dairy fat intake, and if butter from different feeding regimes, and production forms has different effects on metabolic parameters upon intake.

Fat type intervention in mice

Obesity was induced in mice, by addition of sucrose to the drinking water, and giving high fat diets, based on butter from either grazing or conventional fed cattle, high oleic acid (monounsaturated fatty acid) sunflower oil, or finally from grape-seed oil with high content of the n-6 poly unsaturated fatty acid linoleic acid, along with having a lean reference group. Oral glucose tolerance test was performed after 10 weeks intervention, and animals sacrificed two days later. Parameters relevant to glucose metabolism, and hepatic lipid metabolism e.g. lipid deposition, were measured, just as RT-qPCR were used to measure expression of genes relevant for lipid metabolism in the liver. Plasma lipids, adipokines, and a marker of inflammation were also measured. We found that the hyper caloric diet based on oleic acid had the most detrimental effects on metabolic parameters, of the tested fats, as it led to increased hepatic lipid deposition, and reduced glucose tolerance. The butter based diets had more unfavorable effects on concentration of blood lipids, observed as raised triacylglycerol and total cholesterol. Compared to the literature the results with regard to oleic acid are controversial, as the common advice is to substitute SFA by MUFA in the diet.

Phytanic acid effects in mice

Two human dairy fat interventions was conducted, with healthy subjects divided into groups and given dairy fat (as butter and cheese) from cattle under different feeding regimes, resulting in among others difference in phytic acid content. From the first intervention, we found that it is possible to alter the human plasma phytic acid concentration due to four weeks dairy fat intervention. From the second intervention we found that butter from grazing cattle, which among others have increased phytic acid content, increase plasma LDL cholesterol and insulin, compared to conventional butter. From a subpopulation of the second intervention, T-cells were isolated from blood before and after the intervention, to analyze the effect on T-cell polarization. Furthermore we performed an in vitro incubation of T-cells, from eight donors, with phytic- and palmitic acid, to investigate if phytic acid affects T-cell polarization as hypothesized. Phytic acid was not found to change the T-cell polarization, neither in the incubation study nor due to the difference in concentrations in the butter intervention. We saw up regulation in mRNA expression of both IL-4 and IFN-gamma due to the butter intervention, when the groups were regarded as one. This was more pronounced for IL-4 than IFN-gamma, and we observed increase in the ratio IL-4: IFN-gamma due to the intervention. This is pointing towards a general effect towards Th2 polarization of human T-cells due to increased intake of butter. These results add to the understanding of potential phytic acid and butter effects, on the immune system as similar studies have not been performed on T-cells before.

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**Fish intake, erythrocyte n-3 fatty acid status and metabolic health in Danish adolescent girls and boys**

Marine n-3 long-chain PUFA (n-3 LCPUFA) may have a beneficial effect on several aspects of the metabolic syndrome (dyslipidaemia, insulin resistance, hypertension and abdominal obesity). The metabolic syndrome is increasing in prevalence during adolescence, but only few studies have investigated the effects of n-3 LCPUFA in adolescence. The present study examines associations between fish intake (assessed by a 7 d pre-coded food diary), erythrocyte (RBC) DHA status (analysed by GC) and metabolic syndrome measures (anthropometry, blood pressure and plasma lipids, insulin and glucose) in 109 17-year-old children from the Copenhagen Birth Cohort Study. Of the children, 8% were overweight or obese and few showed signs of the metabolic syndrome, but all the metabolic syndrome variables were correlated. Median fish intake was 10-7 (interquartile range 3-6–21-2) g/d. Boys tended to have a higher fish intake (P=0-052), but girls had significantly higher RBC levels of DHA (P=0-001). Sex and fish intake explained 37% of the variance in RBC-DHA (P=0-001). After adjusting for confounders, high DHA status was found to be significantly correlated
with higher systolic blood pressure (P<0.014) and increased fasting insulin (P<0.018), but no adverse association was observed with the mean metabolic syndrome z-score. Overall, the present study showed the expected association between fish intake and RBC-DHA, which in contrast to our expectations tended to be associated with a poorer metabolic profile. Whether these results reflect the physiological function of n-3 LCPUFA, lifestyle factors associated with fish intake in Denmark, or mere chance remains to be investigated.

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Maternal high-fat/high-sucrose diet during lactation results in increased adipose tissue mass, and altered hepatic fatty acid metabolism at weaning

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Maternal high-fat/high-sucrose diet during lactation results in increased adipose tissue mass, and altered hepatic fatty acid metabolism at weaning

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Maternal high-fat/high-sucrose diet during lactation results in increased adipose tissue mass, and altered hepatic fatty acid metabolism at weaning
Muscle ceramide content is similar after 3 weeks’ consumption of fat or carbohydrate diet in a crossover design in patients with type 2 diabetes

This study aimed at investigating the effect of prolonged adaptation to fat- or carbohydrate-rich diet on muscle ceramide in type 2 diabetes patients, using a longitudinal crossover study. Eleven type 2 diabetes patients consumed isocaloric fat- or carbohydrate-rich diet for 3 weeks in random order. After each dietary intervention period, muscle glycogen, triacylglycerol and ceramide content and plasma concentrations of insulin, adiponectin, glucose and FFA were determined. Insulin resistance was assessed by HOMA2 calculation. After the dietary period, plasma glucose and insulin, insulin sensitivity, muscle glycogen, triacylglycerol and ceramide content were similar. Plasma adiponectin concentration was significantly higher after fat compared with carbohydrate-rich diet. Results indicated that following fat-rich diet intake muscle ceramide and triacylglycerol concentrations were not different compared with that after carbohydrate-rich diet. Furthermore, plasma adiponectin concentration was higher after fat-rich compared with carbohydrate-rich diet, but insulin sensitivity remained similar despite the major difference in dietary macronutrient composition.
A randomized controlled intervention with fish oil versus sunflower oil from 9 to 18 months of age: exploring changes in growth and skinfold thicknesses

n-3 long-chain polyunsaturated fatty acids (n-3 LCPUFA), from fish oil (FO), in rodents have been shown to reduce adipogenesis. Evidence of an effect on adipose tissue mass in humans is limited, and no studies have specifically aimed to elucidate this in infancy. To explore whether n-3 LCPUFA intake affects adipose tissue growth, we randomly allocated 154 healthy infants to daily supplementation with FO or sunflower oil (SO) from 9 to 18 mo of age and measured z-score changes in various anthropometric assessments of body size and skinfold thicknesses and plasma adipokine concentrations. Among the 133 completing infants, erythrocyte n-3 PUFA increased more in those receiving FO than in infants receiving SO [12.2 ± 0.7 (mean ± SE) versus 2.0 ± 0.4 fatty acid percentage (FA%), p <0.001] with a concomitant larger decrease in n-6 PUFA (-8.9 ± 0.7 versus -0.9 ± 0.6 FA%, p <0.001). We found no association between FO consumption relative to SO consumption and any of the anthropometric measures related to the size of the fat mass, but infants in the FO group had a lower skinfold ratio (triceps/subscapular) at 18 mo than those in SO group (p = 0.02). Our findings do not support the hypothesis that dietary n-3 LCPUFA is important for infant fat mass, but future studies testing this specifically are warranted. ABBREVIATIONS:
Effect of dairy fat on plasma phytanic acid in healthy volunteers - a randomized controlled study

BACKGROUND: Phytanic acid produced in ruminants from chlorophyll may have preventive effects on the metabolic syndrome, partly due to its reported RXR and PPAR-α agonist activity. Milk from cows fed increased levels of green plant material, contains increased phytanic acid concentrations, but it is unknown to what extent minor increases in phytanic acid content in dairy fat leads to higher circulating levels of phytanic acid in plasma of the consumers. OBJECTIVE: To investigate if cow feeding regimes affects concentration of plasma phytanic acid and risk markers of the metabolic syndrome in human. DESIGN: In a double-blind, randomized, 4 wk, parallel intervention study 14 healthy young subjects were given 45 g milk fat/d from test butter and cheese with 0.24 wt% phytanic acid or a control diet with 0.13 wt% phytanic acid. Difference in phytanic acid was obtained by feeding roughage with low or high content of chlorophyll. RESULTS: There tended to be a difference in plasma phytanic acid (P = 0.0730) concentration after the dietary intervention. Plasma phytanic acid increased significantly within both groups with the highest increase in control group (24%) compared to phytanic acid group (15%). There were no significant effects of phytanic acid on risk markers for the metabolic syndrome. CONCLUSIONS: The results indicate that increased intake of dairy fat modify the plasma phytanic acid concentration, regardless of cows feeding regime and the minor difference in dietary phytanic acid. Whether the phytanic acid has potential to affects the risk markers of the metabolic syndrome in human still remain to be elucidated.
Effect of industrially produced trans fat on markers of systemic inflammation: evidence from a randomized trial in women

Consumption of industrially produced trans fatty acids (IP-TFA) has been positively associated with systemic markers of low-grade inflammation and endothelial dysfunction in cross-sectional studies, but results from intervention studies are inconclusive. Therefore, we conducted a 16 week double-blind parallel intervention study with the objective to examine the...
The effect of IP-TFA intake on biomarkers of inflammation, oxidative stress, and endothelial dysfunction. Fifty-two healthy overweight postmenopausal women (49 completers) were randomly assigned to receive either partially hydrogenated soybean oil (15.7 g/day IP-TFA) or control oil without IP-TFA. After 16 weeks, IP-TFA intake increased baseline-adjusted serum tumor necrosis factor (TNF) α by 12% [95% confidence interval (CI): 5–20; P = 0.002] more in the IP-TFA group compared with controls. Plasma soluble TNF receptors 1 and 2 were also increased by IP-TFA [155 pg/ml (CI: 72–887); P <0.001 and 480 pg/ml (CI: 72–887); P = 0.02, respectively]. Serum C-reactive protein, interleukin (IL) 6 and adiponectin and subcutaneous abdominal adipose tissue mRNA expression of IL6, IL8, TNFα, and adiponectin as well as ceramide content were not affected by IP-TFA, nor was urinary 8-iso-prostaglandin-F2α. In conclusion, this dietary trial indicates that the mechanisms linking dietary IP-TFA to cardiovascular disease may involve activation of the TNFα system.

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Effects of Topical Corticosteroid and Tacrolimus on Ceramides and Irritancy to Sodium Lauryl Sulphate in Healthy Skin

The skin barrier, located in the stratum corneum, is influenced mainly by the lipid and protein composition of this layer. In eczematous diseases impairment of the skin barrier is thought to be of prime importance. Topical anti-inflammatory drugs and emollients are the most widely used eczema treatments. The aim of this study was to examine the effects of topically applied corticosteroid, tacrolimus and emollient on stratum corneum lipids and barrier parameters. Nineteen healthy volunteers participated in the study. Both forearms of the subjects were divided into four areas, which were treated twice daily for one week with betamethasone, tacrolimus, emollient, or left untreated, respectively. After one week each area was challenged with a 24 h sodium lauryl sulphate patch test. The lipids were collected using the cyanoacrylate method and evaluated by high performance thin layer chromatography. For evaluation of the skin barrier, transepidermal water loss, erythema and electrical capacitance were measured. The ceramide/cholesterol ratio was increased in betamethasone- (p = 0.008) and tacrolimus-treated (p = 0.025) skin compared with emollient-treated skin. No differences in ceramide subgroups were found between treatment regimes. Pretreatment with betamethasone (p = 0.01) or with tacrolimus (p = 0.001) causes a decreased inflammatory response to sodium lauryl sulphate compared with emollient. In conclusion, treatment with betamethasone and tacrolimus has a positive effect on the ceramide/cholesterol ratio and susceptibility to irritant reaction compared with an emollient.
Fish oil combined with SCFA synergistically prevent tissue accumulation of NEFA during weight loss in obese mice

Based on their proposed metabolic effects, we examined whether fish oil (FO) and SCFA, alone or in combination, accelerate weight loss and the resultant metabolic improvements. Obesity was induced in male C57BL/6J mice by high-energy feeding for 10 weeks. The mice were transferred to a low-fat diet (2.5% w%) for 4 weeks, the source of fat being either FO, a lard–safflower oil mix (control), or both types combined with SCFA. Weight, fasting insulin, tissue and serum lipid concentrations, as well as mRNA amount of genes related to adipose inflammation and hepatic fat oxidation were determined. All groups lost weight and showed reduced fasting insulin concentrations and reduced liver TAG. However, weight loss on the control-fat diet caused significant increase in hepatic and cardiac NEFA. Substituting 20 % of the fat with SCFA increased weight loss by 48 % and reduced fasting insulin 1.5-fold more than the no-SCFA diets. It furthermore significantly increased the amount of mRNA for PPAR-α, and decreased the mRNA amount for NF-κB in the liver and white adipose tissue. The FO diets enhanced improvement of tissue lipid levels. Thus, FO improved liver TAG and NEFA levels compared with weight loss on the control diet. Combining FO and SCFA further reduced tissue NEFA accumulation. In conclusion, we found that dietary SCFA had a significant impact on gene expression in the liver and adipose tissue, and that the effect of FO on tissue NEFA content was modified by SCFA. Thus, interactions between fatty acids should be considered when studying the effects of specific fatty acids.

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"Good teaching practice" at DTU Systems Biology - sustaining quality in teaching and learning

Success in developing teaching and learning in engineering education in general, as well as in a CDIO context, depends on continuous development of teaching competences among faculty members. Thus, it is essential to develop systems that promote understanding of how teaching and assessment can support student learning within disciplinary knowledge as well as development of professional skills. Development and maintenance of high quality teaching and learning furthermore requires that teachers have the ability to reflect critically on their teaching activities and understand its impact on the students' learning process. To succeed in reaching these goals, development of teaching competences and knowledge in the fields of teaching and learning must be combined with continuous possibilities to reflect on teaching practice in a structured way. Development of successful teaching also requires that faculty members are inspired and encouraged to try new ways and methods in teaching, and gaining an extended understanding in how students learning can be efficiently supported. In this paper we describe a novel initiative, a concept of Good Teaching Practice, that has been developed through a process involving faculty at the department of Systems Biology at the Technical University of Denmark. The GTP initiative addresses important factors for effective teaching and enhancement of student learning. On the surface GTP is structured as an online tool, which makes six statements about important factors that support student learning that the teachers at the department are supposed to consider. This is coupled to a wiki-based web resource for sharing good examples from teaching practice among faculty. By formulating a teaching and learning profile at the department level the importance of teaching for the department are emphasized and at the same time, the wiki-based resource for sharing teaching experience shows that teaching is a shared responsibility among the entire faculty. On the website, the theoretical framework underlying GTP provides a shorthand introduction to the important prerequisites for students learning and provides definitions that provide the faculty members with a common language to use in discussions of teaching and learning. The GTP concept addresses standard 10 in the CDIO context which focuses on the enhancement of the development of teaching and learning at department level and provides the teachers with tools to conduct teaching proficiently.

Improved glucose tolerance after intensive life style intervention occurs without changes in muscle ceramide or triacylglycerol in morbidly obese subjects

Aim: This study investigated the effect of a 15-week life style intervention (hypocaloric diet and regular exercise) on glucose tolerance, skeletal muscle lipids and muscle metabolic adaptations in 14 female and 9 male morbidly obese subjects (age: 32.5 +/- 2.3 years, BMI: 46.1 +/- 1.9 kg m(-2)). Method: Before and after the life style intervention an oral glucose tolerance test (OGTT) was performed and a muscle biopsy was obtained in the fasted state. Maximal oxygen uptake was measured by an indirect test. Results: After the intervention body weight was decreased (P
Leptin levels in the young offspring from dams fed hypercaloric diets during gestation are decoupled from body-weight, regardless of maternal post-natal diets

General information
State: Published
Organisations: Department of Systems Biology, Center for Biological Sequence Analysis
Authors: Ingvorsen, C. (Intern), Hellgren, L. (Intern)
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Publication date: 2011
Event: Poster session presented at Scientific meeting in Centre for Fetal Programming, Statens Serum Institut, Copenhagen, Denmark.
Main Research Area: Technical/natural sciences
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http://www.cfp-research.com/
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Maternal energy intake during lactation and gestation has an effect on leptin levels in the young and adult pups

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Organisations: Department of Systems Biology, Center for Biological Sequence Analysis
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Main Research Area: Technical/natural sciences
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Source-ID: u::9007
Publication: Research › Conference abstract for conference – Annual report year: 2011

The Effect of Dietary Fish Oil in addition to Lifestyle Counselling on Lipid Oxidation and Body Composition in Slightly Overweight Teenage Boys

Objective. n-3 long-chain polyunsaturated fatty acids (LCPUFAs) have shown potential to increase lipid oxidation and prevent obesity. Subjects. Seventy-eight boys aged 13–15 y with whole-body fat% of 30 ± 9% were randomly assigned to consume bread with fish oil (FO) (1.5 g n-3 LCPUFA/d) or vegetable oil for 16 weeks. All boys were counselled to improve diet and exercise habits. Results. Lifestyle counselling resulted in decreased sugar intake but did not change the physical activity level. Whole-body fat% decreased 0.7 ± 2.5% and 0.6 ± 2.2%, resting metabolic rate after the intervention was 7150 ± 1134 kJ/d versus 7150 ± 1042 kJ/d, and the respiratory quotient was 0.89 ± 0.05 versus 0.88 ± 0.05, in the FO and control group, respectively. No group differences were significant. Conclusion. FO-supple

General information
State: Published
Organisations: Center for Biological Sequence Analysis, Department of Systems Biology, Division of Nutrition, National Food Institute, Technical University of Denmark, University of Copenhagen
Authors: Pedersen, M. H. (Intern), Mølgaard, C. (Ekstern), Hellgren, L. (Intern), Matthiessen, J. (Intern), Holst, J. J. (Ekstern), Lauritzen, L. (Ekstern)
Pages: 348368
Publication date: 2011
Main Research Area: Technical/natural sciences

Publication information
Journal: Journal of Nutrition and Metabolism
The impact of ultraviolet therapy on stratum corneum ceramides and barrier function
The ceramide profile as well as the barrier function is known to be deteriorated in atopic eczema and psoriasis, and ultraviolet (UV) light is known to improve the barrier function. The impact of UV light on ceramides, however, is not clarified. The aim of this study was to examine the effect of UV therapy in dermatological patients on ceramides and skin barrier function. We found that UV light treatment does not change the ratio of important stratum corneum lipids, but we confirm earlier findings of decreased susceptibility to irritants after UV-therapy.
UV light therapy, Ceramides, Skin barrier measurements

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Milk Bioactives to Prevent Gut Inflammation

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State: Published
Organisations: Center for Biological Sequence Analysis, Department of Systems Biology
Authors: Møller, H. K. (Intern), Frøkiær, H. (Intern), Hellgren, L. (Intern)
Publication date: Sep 2010

Publication information
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Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 271230
Publication: Research › Ph.D. thesis – Annual report year: 2010

Antioxidant properties of modified rutin esters by DPPH, reducing power, iron chelation and human low density lipoprotein assays
Practical limitations exist regarding the effectiveness of flavonoids as antioxidants in many food systems, possibly due to their poor solubility and miscibility in lipidic environments. Current strategies to improve these properties include enzymatically acylating flavonoids with lipophilic moieties. Herein, two derivatives of rutin (possessing C12:0 or C16:0 acyl groups) were assessed for their antioxidant properties, and compared with their parent compound, rutin and with butylated hydroxytoluene (BHT). While all compounds exhibited relatively strong radical scavenging abilities, modified rutin
compounds exhibited decreased reducing power and metal chelating abilities as compared to rutin. Conversely, investigations on the oxidation of human low density lipoprotein (LDL) revealed that rutin laurate was most effective in inhibiting oxidation by prolonging LDL lag time for an in vitro system. With regards to in vivo considerations, a pre-treatment step confirmed that the ester bond linking rutin and acyl moieties was most susceptible to hydrolysis by digestive enzymes, while rutin itself was not degraded. Thus, acylation of rutin with medium or long chain fatty acids may result in improved antioxidant abilities in more complex systems, including LDL-oxidation assays. Likely reasons may include improved lipophilic solubility and partitioning properties allowing for better accessibility to the actual site of oxidation. (C) 2010 Elsevier Ltd. All rights reserved.

General information
State: Published
Organisations: National Food Institute, Division of Seafood Research, Center for Biological Sequence Analysis, Department of Systems Biology, Department of Chemistry, Center for BioProcess Engineering, Department of Chemical and Biochemical Engineering
Authors: Lue, B. (Intern), Nielsen, N. S. (Intern), Jacobsen, C. (Intern), Hellgren, L. (Intern), Guo, Z. (Intern), Xu, X. (Intern)
Pages: 221-230
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BFI (2015): BFI-level 2
Scopus rating (2015): SJR 1.597 SNIP 1.962 CiteScore 4.31
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 1.595 SNIP 2.027 CiteScore 3.92
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 1.548 SNIP 2.069 CiteScore 3.87
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 1.805 SNIP 2.357 CiteScore 3.98
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Scopus rating (2011): SJR 1.909 SNIP 2.395 CiteScore 4.17
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 1.965 SNIP 2.261
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 2
Scopus rating (2009): SJR 1.776 SNIP 2.024
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 2
Scopus rating (2008): SJR 1.488 SNIP 1.703
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.
Ceramides and barrier function in healthy skin

Lipids in the stratum corneum are key components in the barrier function of the skin. Changes in lipid composition related to eczematous diseases are well known, but limited data are available on variations within healthy skin. The objective of the present study was to compare ceramide subgroups and ceramide/cholesterol ratios in young, old, male and female healthy skin. A total of 55 participants with healthy skin was included in the study. Lipid profiles were correlated with transepidermal water loss and with information on dry skin from a questionnaire including 16 people. No statistically
significant differences were found between young and old skin for ceramide subgroups or ceramide/cholesterol ratios, and there was no statistically significant correlation between answers about dry skin and ceramide levels. Interestingly, a statistically significant higher ceramide/cholesterol ratio was found for men than for women (p = 0.02).

**General information**
- **State:** Published
- **Organisations:** Center for Biological Sequence Analysis, Department of Systems Biology
- **Authors:** Jungerstedt, J. (Ekstern), Hellgren, L. (Intern), Drachmann, T. (Intern), Høgh, J. K. (Intern), Jemec, G. (Ekstern), Agner, T. (Ekstern)
- **Pages:** 350-353
- **Publication date:** 2010

**Main Research Area:** Technical/natural sciences

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- **Volume:** 90
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- Web of Science (2018): Indexed yes
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- BFI (2016): BFI-level 1
- Scopus rating (2016): SJR 0.908 SNIP 1.151 CiteScore 1.59
- BFI (2015): BFI-level 1
- Scopus rating (2015): SJR 1.082 SNIP 1.293 CiteScore 1.58
- BFI (2014): BFI-level 1
- Scopus rating (2014): SJR 1.078 SNIP 1.204 CiteScore 1.5
- BFI (2013): BFI-level 1
- Scopus rating (2013): SJR 1.203 SNIP 1.271 CiteScore 1.67
- ISI indexed (2013): ISI indexed yes
- BFI (2012): BFI-level 1
- Scopus rating (2012): SJR 1.124 SNIP 1.428 CiteScore 1.53
- ISI indexed (2012): ISI indexed yes
- BFI (2011): BFI-level 1
- Scopus rating (2011): SJR 0.102 SNIP 0 CiteScore 1.35
- Web of Science (2011): Indexed yes
- Scopus rating (2010): SJR 0.102 SNIP 0
- Web of Science (2010): Indexed yes
- Scopus rating (2009): SJR 0.102 SNIP 0.489
- BFI (2008): BFI-level 2
- Scopus rating (2008): SJR 0.232 SNIP 0.907
- Scopus rating (2007): SJR 0.116 SNIP 0.017
- Scopus rating (2006): SJR 0.266 SNIP 1.073
- Scopus rating (2005): SJR 0.248 SNIP 0.595
- Scopus rating (2004): SJR 0.613 SNIP 4.037
- Scopus rating (2003): SJR 0.669 SNIP 1.634
- Scopus rating (2002): SJR 0.32 SNIP 1.09
- Scopus rating (2001): SJR 0.266 SNIP 0.55
- Web of Science (2001): Indexed yes
- Scopus rating (2000): SJR 0.203 SNIP 0.426
- Scopus rating (1999): SJR 0.191 SNIP 2.051

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**ceramides, age, gender, ceramide/cholesterol ratio, TEWL, stratum corneum**

**Electronic versions:**
3247.pdf
Changes in skin barrier during treatment with systemic alitretinoin: focus on skin susceptibility and stratum corneum ceramides

Alitretinoin is a new drug for systemic treatment of chronic hand eczema. Previous functional tests of skin topically treated with retinoids have indicated impaired skin barrier function, but no data are available on barrier parameters after systemic alitretinoin treatment. To investigate the effect of systemic alitretinoin on skin barrier function and response to irritants, a secondary objective was to determine if changes occur in the lipid profile of stratum corneum after treatment with systemic alitretinoin. We conducted an open clinical intervention study on eight people ascribed to systemic alitretinoin treatment. The criteria for being ascribed to alitretinoin were chronic hand eczema and insufficient therapeutic response to potent topical corticosteroids. Before initiation and after 2 months of systemic treatment with 30 mg alitretinoin, a challenge with sodium lauryl sulphate (SLS) was performed on the volar forearm and evaluated by trans-epidermal water loss (TEWL), erythema, and a cyanoacrylate skin sample was obtained for lipid analysis. We found no significant changes in response to SLS irritation as evaluated by TEWL and erythema, after treatment with alitretinoin for 2 months. No significant changes in stratum corneum lipids were found after 2 months of treatment. In conclusion, systemic alitretinoin does not influence skin susceptibility to irritants or the ceramide profile of stratum corneum.

General information

State: Published
Organisations: Department of Systems Biology, Center for Biological Sequence Analysis
Authors: Jungersted, J. (Ekstern), Høgh, J. K. (Intern), Hellgren, L. (Intern), Jemec, G. (Ekstern), Agner, T. (Ekstern)
Pages: 653-656
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Main Research Area: Technical/natural sciences

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Journal: Archives of Dermatological Research
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Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 0.996 SNIP 0.895 CiteScore 2.37
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.962 SNIP 0.92 CiteScore 2.24
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.944 SNIP 0.919 CiteScore 2.21
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.031 SNIP 0.983 CiteScore 2.64
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 1.107 SNIP 1.104 CiteScore 2.74
ISI indexed (2012): ISI indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 1.03 SNIP 1.142 CiteScore 2.44
ISI indexed (2011): ISI indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 0.876 SNIP 1.069
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Chronic exposure of adults and embryos of Pandalus borealis to oil causes PAH accumulation, initiation of biomarker responses and an increase in larval mortality

General information
State: Published
Organisations: Section for Aquaculture, National Institute of Aquatic Resources, Center for Biological Sequence Analysis, Department of Systems Biology
Authors: Bechmann, R. (Ekstern), Larsen, B. K. (Intern), Taban, I. (Ekstern), Hellgren, L. (Intern), Møller, P. (Intern), Sanni, S. (Ekstern)
Pages: 2087-2098
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Scopus rating (2016): CiteScore 3.46 SJR 1.302 SNIP 1.331
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 1.245 SNIP 1.277 CiteScore 3.23
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 1.304 SNIP 1.425 CiteScore 3.04
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.208 SNIP 1.546 CiteScore 2.89
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Effects of Fish Oil Supplementation on Markers of the Metabolic Syndrome

OBJECTIVE: To investigate whether fish oil affects cardiovascular risk factors during the adolescent growth spurt. STUDY DESIGN: A total of 78 boys age 13-15 years with a mean body fat percentage of 30% +/- 9% were randomly assigned to consume fish oil (providing 1.5 g of n-3 long-chain polyunsaturated fatty acid/day) or vegetable oil (control) for 16 weeks. The oils were included in bread. RESULTS: After the intervention, the red blood cell (RBC) content of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) were 1.2% +/- 0.5% and 6.7% +/- 1.6%, respectively, in the those receiving fish oil (FO group), compared with 0.6% +/- 0.3% and 4.1% +/- 0.9% in the control group. Systolic blood pressure (SBP) was 3.8 +/- 1.4 mm Hg lower (P <.006) and diastolic blood pressure (DBP) was 2.6 +/- 1.1 mm Hg lower (P <.01) in the FO group compared with the control group. Plasma triacylglycerol (TAG) concentration and insulin sensitivity were unaffected by either of the treatments. Plasma high-density lipoprotein (HDL) and non-HDL cholesterol were increased by 5% and 7%, respectively, in the FO group, compared with 0.6% +/- 0.3% and 4.1% +/- 0.9% in the control group. Systolic blood pressure (SBP) was 3.8 +/- 1.4 mm Hg lower (P <.006) and diastolic blood pressure (DBP) was 2.6 +/- 1.1 mm Hg lower (P <.01) in the FO group compared with the control group. Plasma triacylglycerol (TAG) concentration and insulin sensitivity were unaffected by either of the treatments. Plasma high-density lipoprotein (HDL) and non-HDL cholesterol were increased by 5% and 7%, respectively, in the FO group, compared with 0.6% +/- 0.3% and 4.1% +/- 0.9% in the control group. Systolic blood pressure (SBP) was 3.8 +/- 1.4 mm Hg lower (P <.006) and diastolic blood pressure (DBP) was 2.6 +/- 1.1 mm Hg lower (P <.01) in the FO group compared with the control group. Plasma triacylglycerol (TAG) concentration and insulin sensitivity were unaffected by either of the treatments. Plasma high-density lipoprotein (HDL) and non-HDL cholesterol were increased by 5% and 7%, respectively, in the FO group, compared with 0.6% +/- 0.3% and 4.1% +/- 0.9% in the control group. Systolic blood pressure (SBP) was 3.8 +/- 1.4 mm Hg lower (P <.006) and diastolic blood pressure (DBP) was 2.6 +/- 1.1 mm Hg lower (P <.01) in the FO group compared with the control group. Plasma triacylglycerol (TAG) concentration and insulin sensitivity were unaffected by either of the treatments. Plasma high-density lipoprotein (HDL) and non-HDL cholesterol were increased by 5% and 7%, respectively, in the FO group, compared with 0.6% +/- 0.3% and 4.1% +/- 0.9% in the control group. Systolic blood pressure (SBP) was 3.8 +/- 1.4 mm Hg lower (P <.006) and diastolic blood pressure (DBP) was 2.6 +/- 1.1 mm Hg lower (P <.01) in the FO group compared with the control group. Plasma triacylglycerol (TAG) concentration and insulin sensitivity were unaffected by either of the treatments. Plasma high-density lipoprotein (HDL) and non-HDL cholesterol were increased by 5% and 7%, respectively, in the FO group, compared with 0.6% +/- 0.3% and 4.1% +/- 0.9% in the control group. Systolic blood pressure (SBP) was 3.8 +/- 1.4 mm Hg lower (P <.006) and diastolic blood pressure (DBP) was 2.6 +/- 1.1 mm Hg lower (P <.01) in the FO group compared with the control group. Plasma triacylglycerol (TAG) concentration and insulin sensitivity were unaffected by either of the treatments. Plasma high-density lipoprotein (HDL) and non-HDL cholesterol were increased by 5% and 7%, respectively, in the FO group, compared with 0.6% +/- 0.3% and 4.1% +/- 0.9% in the control group. Systolic blood pressure (SBP) was 3.8 +/- 1.4 mm Hg lower (P <.006) and diastolic blood pressure (DBP) was 2.6 +/- 1.1 mm Hg lower (P <.01) in the FO group compared with the control group. Plasma triacylglycerol (TAG) concentration and insulin sensitivity were unaffected by either of the treatments. Plasma high-density lipoprotein (HDL) and non-HDL cholesterol were increased by 5% and 7%, respectively, in the FO group, compared with 0.6% +/- 0.3% and 4.1% +/- 0.9% in the control group. Systolic blood pressure (SBP) was 3.8 +/- 1.4 mm Hg lower (P <.006) and diastolic blood pressure (DBP) was 2.6 +/- 1.1 mm Hg lower (P <.01) in the FO group compared with the control group. Plasma triacylglycerol (TAG) concentration and insulin sensitivity were unaffected by either of the treatments. Plasma high-density lipoprotein (HDL) and non-HDL cholesterol were increased by 5% and 7%, respectively, in the FO group, compared with 0.6% +/- 0.3% and 4.1% +/- 0.9% in the control group. Systolic blood pressure (SBP) was 3.8 +/- 1.4 mm Hg lower (P <.006) and diastolic blood pressure (DBP) was 2.6 +/- 1.1 mm Hg lower (P <.01) in the FO group compared with the control group.

CONCLUSION: Fish oil improves BP in normotensive and normolipidemic slightly overweight adolescent boys. Copyright © 2010 Mosby, Inc. All rights reserved.
Ethnicity and stratum corneum ceramides

BACKGROUND: The barrier function of the skin is dependent on an optimal composition of the stratum corneum lipids, exemplified by the altered lipid profile in patients with atopic eczema (AE). Differences in the global prevalence of AE point to the environment as an important factor in AE. Studies on filaggrin point to a genetic aspect in AE. The influence of environment and genes needs to be explored. OBJECTIVES: To investigate possible differences in stratum corneum lipids between different healthy ethnicities living in the same environment. METHODS: Healthy participants without any major skin diseases were enrolled in the study. Twenty-five participants of Asian origin (Asians), 18 of African origin (Africans) and 28 of Danish origin (white-skinned), all students at universities in the Copenhagen area of Denmark, had the ceramide profile of their stratum corneum examined using the cyanoacrylate method and analysed using high-performance thin layer chromatography. RESULTS: For the ceramide/cholesterol ratio we found statistically significant differences between groups, with Asians having the highest ratio (P <0.001 as compared with both white-skinned individuals and Africans), white-skinned individuals having intermediate values, and Africans having the lowest values. No statistically significant
differences were found between any of the ceramide subgroups. CONCLUSIONS: We found different ceramide/cholesterol ratios in comparable groups of different ethnicity, pointing to unknown genetic differences.
Lipid asymmetry in plant plasma membranes: phosphate deficiency-induced phospholipid replacement is restricted to the cytosolic leaflet

As in other eukaryotes, plant plasma membranes contain sphingolipids, phospholipids, and free sterols. In addition, plant plasma membranes also contain sterol derivatives and usually 5 mol% DGDG was included. As both the apoplastic plasma membrane leaflet (probably the major water permeability barrier) and rafts both contain only trace amounts of DGDG, we conclude that this lipid class is not compatible with membrane functions requiring a high degree of lipid order. By not replacing phospholipids site specifically with DGDG, negative functional effects of this lipid in the plasma membrane are avoided.

Tjellström, H., Hellgren, L. I., Wieslander, A., Sandelius, A. S. Lipid asymmetry in plant plasma membranes: phosphate deficiency-induced phospholipid replacement is restricted to the cytosolic leaflet.

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Organisations: Center for Biological Sequence Analysis, Department of Systems Biology
Authors: Tjällström, H. (Ekstern), Hellgren, L. (Intern), Wieslander, Å. (Ekstern), Sandelius, A. (Ekstern)
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BFI (2017): BFI-level 2
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 4.68 SJR 2.57 SNIP 1.22
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 2.788 SNIP 1.249 CiteScore 4.68
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 2.993 SNIP 1.342 CiteScore 4.92
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 3.116 SNIP 1.4 CiteScore 5.5
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 3.071 SNIP 1.441 CiteScore 5.6
ISI indexed (2012): ISI indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 3.042 SNIP 1.525 CiteScore 5.4
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
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Scopus rating (2010): SJR 3.414 SNIP 1.572
Phytanic acid—an overlooked bioactive fatty acid in dairy fat?

Phytanic acid is a multibranched fatty acid with reported retinoid X receptor (RXR) and peroxisome proliferator-activated receptor-alpha (PPAR-alpha) agonist activity, which have been suggested to have preventive effects on metabolic dysfunctions. Serum level in man is strongly correlated to the intake of red meat and dairy products and the concentration in these products is strongly correlated to the chlorophyll content in the feed of the cattle. Available data suggest that phytanic acid is a natural agonist for RXR at physiological concentrations, while it is more likely that it is the metabolite pristanic acid, rather than phytanic acid itself, that acts as PPAR-a agonist. Animal studies show increased expression of genes involved in fatty acid oxidation, after intake of phytol, the metabolic precursor of phytanic acid, but it is at present not possible to deduce whether phytanic acid is useful in the prevention of ectopic lipid deposition. Phytanic acid is an efficient inducer of the expression of uncoupler protein 1 (UCP1). UCP1 is expressed in human skeletal muscles, were it might be important for the total energy balance. Therefore, phytanic acid may be able to stimulate energy dissipation in skeletal muscles. Phytanic acid levels in serum are associated with an increased risk of developing prostate cancer, but the available data do not support a general causal link between circulating phytanic acid and prostate cancer risk. However, certain individuals, with specific single-nucleotide polymorphisms in the gene for the enzyme alpha-methylacyl-CoA racemase, might be susceptible to raised phytanic acid levels.

General information

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Authors: Hellgren, L. (Intern)
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BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Web of Science (2017): Indexed Yes
Skin barrier response to occlusion of healthy and irritated skin: Differences in trans-epidermal water loss, erythema and stratum corneum lipids

Background: Occlusion of the skin is a risk factor for development of irritant contact dermatitis. Occlusion may, however, have a positive effect on skin healing. No consensus on the effect of occlusion has been reached. Objectives: To investigate skin barrier response to occlusion on intact and damaged skin. Methods: In study A, the response to occlusion (nitrile glove material) for either 8 hr daily for 7 days or for 72 consecutive hours, respectively, was determined and compared with that of non-occluded skin. In study B, the response to occlusion of for 72 consecutive hours of skin that had been damaged by either sodium lauryl sulfate (SLS) or tape stripping, respectively, was determined and compared with that of non-occluded pre-damaged skin. Skin barrier function was assessed by measurements of trans-epidermal water loss (TEWL) and erythema. In study A, stratum corneum lipids were analysed. Results: Occlusion of healthy skin did not significantly influence skin barrier function, ceramide profile or the ceramide/cholesterol ratio. Occlusion of the skin after SLS irritation resulted in higher TEWL than in the control (P = 0.049). Occlusion of the skin after tape stripping resulted in lower TEWL than in control skin (P = 0.007). Conclusions: A week of occlusion did not significantly affect healthy skin, but was found to decrease healing of SLS-damaged skin, and to improve healing of tape-stripped skin.
Stratum corneum lipids, skin barrier function and filaggrin mutations in patients with atopic eczema

Background: Prior to the discovery of filaggrin (FLG) mutations, evidence for an impaired skin barrier in atopic dermatitis (AD) has been documented, and changes in ceramide profile, altered skin pH and increased trans-epidermal water loss (TEWL) in patients with AD have been reported. Until now, no studies have analysed stratum corneum (SC) lipids combined with skin barrier parameters in subjects of known FLG genotype. Methods: A cohort of 49 German individuals genotyped for the most common FLG mutations (R501X, 2282del4) had SC samples taken for lipid analysis by high-performance thin layer chromatography. In addition, TEWL, erythema, skin hydration and pH were measured. In 27 of the 49 individuals, a 24-h irritation patch test with sodium lauryl sulphate was performed. For the analysis, both the AD group and the control group were stratified by FLG mutation status (FLGmut/FLGwt). Results: In the FLGmut AD group, significantly lower levels of ceramide 4 and significantly higher levels of ceramide 7 were observed when compared to both healthy control groups. However, ceramide 7 levels also significantly differed between FLGwt AD and FLGwt controls, as did ceramide 1 levels. No significant differences were observed for ceramide 2, 3, 5 and 6. FLGmut individuals had significantly higher skin pH values than individuals not carrying FLG mutations. Patients with AD with FLG mutations had significantly higher erythema compared to patients with AD without FLG mutations. Conclusion: Our results confirm previous observations of altered ceramide levels in AD, which however appear to show no clear relationship with FLG mutations.

General information
State: Published
Organisations: Department of Systems Biology, Center for Biological Sequence Analysis
Authors: Høgh, J. K. (Intern), Hellgren, L. (Intern), Jungersted, J. (Ekstern), Scheer, H. (Ekstern), Mempel, M. (Ekstern), Baurecht, H. (Ekstern), Cifuentes, L. (Ekstern), Jemec, G. (Ekstern), Agner, T. (Ekstern), Weidinger, S. (Ekstern)
Pages: 911-918
Publication date: 2010
Main Research Area: Technical/natural sciences

Publication information
Journal: Allergy
Volume: 65
Issue number: 7
ISSN (Print): 0105-4538
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 6.23 SJR 2.724 SNIP 2.475
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 3.13 SNIP 2.127 CiteScore 5.73
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 2.464 SNIP 2.121 CiteScore 5.51
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 2.195 SNIP 1.902 CiteScore 4.91
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 2.008 SNIP 1.818 CiteScore 4.81
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 2.328 SNIP 1.781 CiteScore 4.89
ISI indexed (2011): ISI indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.826 SNIP 1.845
Validation of Cyanoacrylate Method for Collection of Stratum Corneum in Human Skin for Lipid Analysis

Background and Objective: Lipids in the stratum corneum (SC) are of major importance for the skin barrier function. Many different methods have been used for the collection of SC for the analysis of SC lipids. The objective of the present study was to validate the cyanoacrylate method for the collection of SC in relation to lipid analysis. Methods: The results of the lipid analysis (ceramide/cholesterol and ceramide profile) of SC samples obtained by the cyanoacrylate method were compared to the results of the lipid analysis of mechanically removed SC samples. The intra- and interindividual variations in lipid composition were assessed when using the cyanoacrylate method, and lipid compositions in cyanoacrylate samples and samples taken from different depths of SC were compared. Results: No statistically significant differences were found between mean values of lipids from the mechanically removed total thickness of the SC and cyanoacrylate samples. With respect to the cyanoacrylate samples, the intraindividual variation was significantly smaller than the interindividual variation, and the results did not indicate a change in lipid profile related to the depth of SC. The results clearly indicate that the cyanoacrylate method used for obtaining SC for lipid analysis is a useful and valid method for the purpose.
Enzymatic Production of Ceramide

General information
State: Published
Organisations: Department of Systems Biology, Center for Biological Sequence Analysis
Authors: Zhang, L. (Intern), Hellgren, L. (Intern), Xu, X. (Intern)
Number of pages: 145
Publication date: Apr 2009

Publication information
Place of publication: Kgs. Lyngby, Denmark
Publisher: Technical University of Denmark (DTU)
Original language: English
Main Research Area: Technical/natural sciences
Sphingomyelin, Ceramide, Phospholipase C, Hydrolysis
Electronic versions:
Thesis.pdf
Source: orbit
Fedtstof-forskere samles om erstatning for transfedtsyrer

General information
State: Published
Organisations: Division of Food Production Engineering, National Food Institute, Center for Biological Sequence Analysis, Department of Systems Biology
Authors: Jørgensen, S. B. (ed.) (Intern), Hellgren, L. (Intern)
Publication date: 2009
Main Research Area: Technical/natural sciences

Publication information
Journal: FoodDTU Midt i Ugen
Issue number: 86
Original language: Danish
Source: orbit
Source-ID: 257971
Publication: Communication › Journal article – Annual report year: 2009

Dansk-amerikansk forskningssamarbejde om sundhed og livsstilssygdomme

General information
State: Published
Organisations: Division of Food Production Engineering, National Food Institute, Center for BioProcess Engineering, Department of Chemical and Biochemical Engineering, Center for Biological Sequence Analysis, Department of Systems Biology
Authors: Jørgensen, S. B. (ed.) (Intern), Meyer, A. S. (Intern), Hellgren, L. (Intern)
Publication date: 2008
Main Research Area: Technical/natural sciences

Publication information
Journal: FoodDTU Midt i Ugen
Original language: Danish
Source: orbit
Source-ID: 258217
Publication: Communication › Journal article – Annual report year: 2008

Effect of gender on lipid-induced insulin resistance in obese subjects

Objective: In obese subjects, chronically elevated plasma concentrations of non-esterified fatty acids (NEFAs) exert a marked risk to contract insulin resistance and subsequently type 2 diabetes. When NEFA is acutely increased due to i.v. infusion of lipid, glucose disposal during a hyperinsulinemic-euglycemic clamp is reduced. This effect has been explained by a NEFA-induced decrease in skeletal muscle insulin sensitivity caused by accumulation of the lipid intermediates such as ceramide and diacylglycerol in the myocytes. However, neither the lipid-induced reduction of glucose disposal nor the intramyocellular lipid deposition has been compared directly in obese females and males. Design: We studied eight obese females and eight obese males (body mass index (BMI): 32.6+/−1.4 and 32.8+/−0.8 respectively, non significant (NS)) matched for cardiorespiratory fitness relative to lean body mass (43.7+/−1.6 and 47.6+/−1.3 ml/kg min respectively, NS). Methods: Each subject underwent two hyperinsulinemic-euglycemic clamps with infusion of lipid or saline respectively. Furthermore, the subjects exercised during the last half an hour of each clamp. Results: The lipid-induced reduction in glucose disposal during the clamp was similar in females and males (46+/−10 and 60+/−4%, respectively, NS). However, whole-body insulin sensitivity as well as non-oxidative glucose disposal was higher in obese females compared with obese males both during lipid and saline infusion (P

General information
State: Published
Organisations: Center for Biological Sequence Analysis, Department of Systems Biology, University of Copenhagen
Authors: Vistisen, B. (Ekstern), Hellgren, L. (Intern), Vadset, T. (Ekstern), Scheede-Bergdahl, C. (Ekstern), Helge, J. (Ekstern), Dela, F. (Ekstern), Stallknecht, B. (Ekstern)
Pages: 61-68
Publication date: 2008
Main Research Area: Technical/natural sciences

Publication information
Fedtsyrebalancen påvirker livsstilssygdomme og allergi

General information
State: Published
Organisations: Division of Food Production Engineering, National Food Institute, Center for Biological Sequence Analysis, Department of Systems Biology
Authors: Jørgensen, S. B. (ed.) (Intern), Hellgren, L. (Intern), Pedersen, S. B. (Intern)
Publication date: 2008
Main Research Area: Technical/natural sciences

Publication information
Journal: FoodDTU Midt i Ugen
Original language: Danish
Source: orbit
Source-ID: 258490
Publication: Communication › Journal article – Annual report year: 2008

Fedtsyrebalance påvirker livsstilssygdomme og allergi

General information
State: Published
Organisations: Center for Biological Sequence Analysis, Department of Systems Biology
Authors: Hellgren, L. (Intern), Pedersen, S. B. (Intern)
Publication date: 2008
Main Research Area: Technical/natural sciences

Publication information
Journal: FoodDTU
Volume: 44
Original language: Danish
Source: orbit
Source-ID: 231385
Publication: Research › Journal article – Annual report year: 2008

Influence of dietary fatty acids on endocannabinoid and N-acylethanolamine levels in rat brain, liver and small intestine

Endocannabinoids and N-acylethanolamines are lipid mediators regulating a wide range of biological functions including food intake. We investigated short-term effects of feeding rats five different dietary fats (palm oil (PO), olive oil (OA), safflower oil (LA), fish oil (170) and arachidonic acid (AA)) on tissue levels of 2-arachidonoylglycerol, anandamide, oleoyl ethanolamide, palmitoyl ethanolamide, stearoyl ethanolamide, linoleoyl ethanolamide, eicosapentaenoyl ethanolamide, docosahexaenoylethanolamide and tissue fatty acid composition. The LA-diet increased linoleoyl ethanolamide and linoleic acid in brain, jejunum and liver. The OA-diet increased brain levels of anandamide and oleoyl ethanolamide (not 2-arachidonoylglycerol) without changing tissue fatty acid composition. The same diet increased oleoyl ethanolamide in liver. All five dietary fats decreased oleoyl ethanolamide in jejunum without changing levels of anandamide, suggesting that dietary fat may have an orexigenic effect. The AA-diet increased anandamide and 2-arachidonoylglycerol in jejunum without effect on liver. The FO-diet decreased liver levels of all N-acylethanolamines (except eicosapentaenoylethanolamide and docosahexaenoylethanolamide) with similar changes in precursor lipids. The AA-diet and FO-diet had no effect on N-acylethanolamines, endocannabinoids or precursor lipids in brain. All N-acylethanolamines activated PPAR-alpha. In conclusion, short-term feeding of diets resembling human diets (Mediterranean diet high in monounsaturated fat, diet high in saturated fat, or diet high in polyunsaturated fat) can affect tissue levels of endocannabinoids and N-acylethanolamines.

General information
State: Published
Organisations: Department of Environmental Engineering, Center for Biological Sequence Analysis, Department of Systems Biology, Division of Toxicology and Risk Assessment, National Food Institute, National Veterinary Institute
Authors: Artmann, A. (Ekstern), Petersen, G. (Ekstern), Hellgren, L. (Intern), Boberg, J. (Intern), Skonberg, C. (Ekstern), Nellemann, C. L. (Intern), Hansen, S. H. (Ekstern), Hansen, H. S. (Ekstern)
Pages: 200-212
Publication date: 2008
Main Research Area: Technical/natural sciences

Publication information
Journal: Biochimica et Biophysica Acta - Molecular and Cell Biology of Lipids
Kinetic study of sphingomyelin hydrolysis for ceramide production

Kinetic study of sphingomyelin hydrolysis catalyzed by Clostridium perfringens phospholipase C was, at the first time, conducted for ceramide production. Ceramide has the major role in maintaining the water-retaining properties of the epidermis. Hence, it is of great commercial potential in cosmetic and pharmaceutical industries such as in hair and skin care products. The enzymatic hydrolysis of sphingomyelin has been proved to be a feasible method to produce ceramide. The kinetic performance of sphingomyelin hydrolysis in the optimal two-phase (water:organic solvent) reaction system was investigated to elucidate the possible reaction mechanism and also to further improve the hydrolysis performance.
Enzyme in solution had less thermal stability than the enzyme powder and the immobilized enzyme. The thermal inactivation of phospholipase C in all the three forms did not follow the first order reaction at 65 °C. The reactions for both the soluble and immobilized enzymes followed Michaelis–Menten kinetics. Km's for the soluble and immobilized enzymes were 1.07 ± 0.32 and 1.26 ± 0.19 mM, respectively. The value of Vmax was markedly decreased by the immobilization without much change in Km, as if the immobilization functioned as the non-competitive inhibition. Ceramide as product activated the hydrolysis reaction, however, and its addition mainly caused the increase in the affinity of the enzyme–substrate complex.

General information
State: Published
Organisations: Department of Systems Biology, Center for Biological Sequence Analysis, Food Production Engineering, National Food Institute
Authors: Zhang, L. (Intern), Hellgren, L. (Intern), Xu, X. (Intern)
Pages: 93-99
Publication date: 2008
Main Research Area: Technical/natural sciences

Publication information
Journal: Journal of Molecular Catalysis. B, Enzymatic
Volume: 51
ISSN (Print): 1381-1177
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BFI (2018): BFI-level 1
BFI (2017): BFI-level 1
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 2.39 SJR 0.63 SNIP 0.855
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.66 SNIP 0.802 CiteScore 2.12
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.744 SNIP 1.044 CiteScore 2.5
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.038 SNIP 1.38 CiteScore 3.09
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 1.12 SNIP 1.347 CiteScore 2.98
ISI indexed (2012): ISI indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 1.026 SNIP 1.126 CiteScore 2.74
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 0.797 SNIP 1.032
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 0.898 SNIP 1.136
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 0.975 SNIP 1.021
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 0.835 SNIP 1.007
Scopus rating (2006): SJR 0.723 SNIP 1.069
Scopus rating (2005): SJR 0.742 SNIP 0.955
Web of Science (2005): Indexed yes
Lipids and skin barrier function - a clinical perspective

The stratum corneum (SC) protects us from dehydration and external dangers. Much is known about the morphology of the SC and penetration of drugs through it, but the data are mainly derived from in vitro and animal experiments. In contrast, only a few studies have the human SC lipids as their focus and in particular, the role of barrier function in the pathogenesis of skin disease and its subsequent treatment protocols. The 3 major lipids in the SC of importance are ceramides, free fatty acids, and cholesterol. Human studies comparing levels of the major SC lipids in patients with atopic dermatitis and healthy controls have suggested a possible role for ceramide 1 and to some extent ceramide 3 in the pathogenesis of the disease. Therapies used in diseases involving barrier disruption have been sparingly investigated from a lipid perspective. It has been suggested that ultraviolet light as a treatment increases the amount of all 3 major SC lipids, while topical glucocorticoids may lead to a decrease. Such effects may influence the clinical outcome of treatment in diseases with impaired barrier function. We have, therefore, conducted a review of the literature on SC lipids from a clinical perspective. It may be concluded that the number of human studies is very limited, and in the perspective of how important diseases of impaired barrier function are in dermatology, further research is needed.
Phospholipase C-catalyzed sphingomyelin hydrolysis in a membrane reactor for ceramide production

A membrane reactor for the production of ceramide through sphingomyelin hydrolysis with phospholipase C from Clostridium perfringens was studied for the first time. Ceramide has raised a large interest as an active component in both pharmaceutical and cosmetic industry. The enzymatic hydrolysis of sphingomyelin has been proven to be a feasible method to produce ceramide. In the membrane reactor constructed, the aqueous phase and the organic phase were separated by a membrane containing the immobilized enzyme, while the organic phase was continuously circulated. Among the 10 selected membranes, the enzyme immobilized in membrane RC 70PP had low immobilization efficiency, but retained the highest catalytic activity. Three immobilization methods, i.e. filtration (adsorption/entrapment), covalent binding, and cross-linking, were compared. The enzyme immobilized by filtration had the highest activity even under the low fixation level (9.4%). The optimal flow rate of the organic phase was 5 ml/min. High initial enzyme amount in the immobilization led to the decrease in the fixation level. Both the initial reaction rate and the specific activity of the enzyme increased with increasing enzyme loading, and slightly decreased after the immobilized enzyme amount over 50g in 9.6cm² membrane area. The immobilized enzyme retained 16% of the original activity after five cycles. Finally, the liquid enzyme, the enzyme immobilized on particle carriers, and the enzyme immobilized in the membrane were compared. The study demonstrated the improved enzyme reusability, the fast immobilization process, the straightforward up-scaling and the combination of the hydrolysis with the product separation in the membrane reactor developed.

General information
State: Published
Organisations: Department of Systems Biology, Center for Biological Sequence Analysis, Membrane Technology group, Department of Chemical and Biochemical Engineering
Authors: Zhang, L. (Intern), Liang, S. (Ekstern), Hellgren, L. (Intern), Jonsson, G. E. (Intern), Xu, X. (Intern)
Pages: 895-902
Publication date: 2008
Main Research Area: Technical/natural sciences
Butter-intake decreases ectopic lipid deposition and increase glucose tolerance, compared to highly polyunsaturated oil, in the rat

**General information**

State: Published

Organisations: Department of Systems Biology

Authors: Hellgren, L. (Intern), Pedersen, M. H. (Intern), Vistisen, B. (Intern)

Publication date: 2007

**Publication Information**

Original language: English

Main Research Area: Technical/natural sciences

Source: orbit

Source-ID: 229181

Publication: Research - peer-review › Journal article – Annual report year: 2008

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Enzymatic production of ceramide from sphingomyelin

**General information**

State: Published

Organisations: Center for Biological Sequence Analysis, Department of Systems Biology

Authors: Zhang, L. (Intern), Hellgren, L. (Intern), Xu, X. (Intern)

Publication date: 2007


Main Research Area: Technical/natural sciences

**Links:**

http://www.eurofedlipid.org/meetings/archive/gothenburg/index.htm

Source: orbit

Source-ID: 199178

Publication: Research › Sound/Visual production (digital) – Annual report year: 2007

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Enzymatic Production of Ceramide from Sphingomyelin

Ceramide is the key intermediate in the biosynthesis of all complex sphingolipids. Due to its major role in maintaining the water-retaining properties of the epidermis, ceramide is of great commercial potential in cosmetic and pharmaceuticals such as hair and skin care products. Currently, chemical synthesis of ceramide is a costly and time consuming process, and developments of alternative cost-efficient, high yield production methods are of great interest. In the present, the potential of producing ceramide through the enzymatic hydrolysis of sphingomyelin have been studied. Sphingomyelin, which contains a ceramide moiety, is a ubiquitous component of animal cell membranes, and dairy products or by-products is a rich source of sphingomyelin. It has been verified that enzymatic modification of sphingomyelin is a feasible approach for production of ceramide. The reaction system has been optimized through system evaluation and the optimization of several important factors. Sphingomyelin hydrolysis proved to be more efficient in two-phase (water: organic solvent) system than in one-phase (water-saturated organic solvent) system. Phospholipase C from Clostridium perfringens is the tested enzyme which has the most advantageous properties. For reusing the enzyme, the immobilization of phospholipase C and the properties of immobilized enzyme have been addressed. By screening nine different carriers, we found that the enzyme immobilized on Lewatit VP OC 1600 (Bayer AG) have the highest catalytic activity. After seven recycles, immobilized enzyme retains around 70% of its initial activity. Through kinetic study, it has been found that the hydrolysis reactions catalyzed by both soluble and immobilized enzyme follow the Michaelis-Menten equation. The presentation will describe the research background, introduce the basic reaction system with its optimisation as well as the immobilization study, and release the recent results from the kinetic study.

**General information**

State: Published

Organisations: Department of Systems Biology, Food Production Engineering

Authors: Zhang, L. (Intern), Hellgren, L. (Intern), Xu, X. (Intern)

Publication date: 2007

Immobilization of phospholipase C for the production of ceramide from sphingomyelin hydrolysis

The immobilization of *Clostridium perfringens* phospholipase C was studied for the first time and the catalytic properties of the immobilized enzyme were investigated for the hydrolysis of sphingomyelin to produce ceramide. Ceramide is of great commercial potentials in cosmetic and pharmaceutical industries such as in hair and skin care products, due to its major role in maintaining the water-retaining properties of the epidermis. The feasibility of enzymatic production of ceramide through hydrolysis of sphingomyelin has previously been proven. In order to improve the reusability of the enzyme, the present study was focused on the immobilization of phospholipase C in the production of ceramide from sphingomyelin. By screening nine different carriers, the enzyme immobilized on Lewatit had the highest catalytic activity towards sphingomyelin hydrolysis. Pre-wetting Lewatit with ethanol leaded to higher enzyme fixation on the carrier, but the activity of the enzyme was decreased. Increasing the initial enzyme concentration resulted in more enzyme adsorption on the carrier, where the specific activity was increased. Through optimization of the reaction using the immobilized enzyme, the optimal temperature was around 46 oC and optimal water volume was 3.5 %. The reaction had little dependence on pH. After 7 recycles, immobilized enzyme retained around 70 % of the initial activity. Immobilized enzyme was deactivated irregularly when stored at room temperature, but followed first order deactivation when stored at 40 oC.

**General information**

State: Published
Organisations: Department of Systems Biology, Food Production Engineering
Authors: Zhang, L. (Intern), Hellgren, L. (Intern), Xu, X. (Intern)
Pages: 237-247
Publication date: 2007
Main Research Area: Technical/natural sciences

**Publication information**

Journal: Journal of the American Oil Chemists Society
Volume: 84
ISSN (Print): 0003-021X
Ratings:
- BFI (2018): BFI-level 1
- Web of Science (2018): Indexed yes
- BFI (2017): BFI-level 1
- Web of Science (2017): Indexed Yes
- BFI (2016): BFI-level 1
- Scopus rating (2016): CiteScore 1.64 SJR 0.696 SNIP 0.905
- Web of Science (2016): Indexed yes
- BFI (2015): BFI-level 1
- Scopus rating (2015): SJR 0.682 SNIP 0.997 CiteScore 1.66
- Web of Science (2015): Indexed yes
- BFI (2014): BFI-level 1
- Scopus rating (2014): SJR 0.767 SNIP 1.043 CiteScore 1.68
- BFI (2013): BFI-level 1
- Scopus rating (2013): SJR 0.809 SNIP 1.074 CiteScore 1.71
- ISI indexed (2013): ISI indexed yes
- Web of Science (2013): Indexed yes
- BFI (2012): BFI-level 1
- Scopus rating (2012): SJR 0.871 SNIP 1.236 CiteScore 1.81
- ISI indexed (2012): ISI indexed yes
- Web of Science (2012): Indexed yes
- BFI (2011): BFI-level 1
- Scopus rating (2011): SJR 0.833 SNIP 1.292 CiteScore 1.98
- ISI indexed (2011): ISI indexed yes
- Web of Science (2011): Indexed yes
- BFI (2010): BFI-level 1
- Scopus rating (2010): SJR 0.763 SNIP 1.056
Influence of dietary fatty acids on endocannabinoid and n-acylethanolamine levels in rat brain, small intestine and liver

General information
State: Published
Organisations: Center for Biological Sequence Analysis, Department of Systems Biology
Authors: Artmann, A. (Ekstern), Petersen, G. (Ekstern), Hellgren, L. (Intern), Skonberg, C. (Ekstern), Hansen, S. H. (Ekstern), Hansen, H. S. (Ekstern)
Publication date: 2007
Event: Abstract from ICRS, Saint Sauveur, Canada.
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 193254
Publication: Research - peer-review › Journal article – Annual report year: 2006

Komælk skal være endnu sundere

General information
State: Published
Organisations: Division of Food Production Engineering, National Food Institute, Center for Biological Sequence Analysis, Department of Systems Biology
Authors: Jørgensen, S. B. (ed.) (Intern), Hellgren, L. (Intern)
Publication date: 2007
Main Research Area: Technical/natural sciences

Publication information
Journal: FoodDTU Midt i Ugen
Original language: Danish
Source: orbit
Source-ID: 258525
Publication: Communication › Journal article – Annual report year: 2007
Skin lipids: Presentation of a newly developed method for collection of human stratum corneum for lipid analysis

General information
State: Published
Organisations: Center for Biological Sequence Analysis, Department of Systems Biology
Authors: Jungersted, J. (Ekstern), Hellgren, L. (Intern), Møller, P. (Intern), Jemec, G. (Ekstern), Agner, T. (Ekstern)
Publication date: 2007
Event: Abstract from Stratum Corneum V, Cardiff, Great Britain.
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 199092
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2007

Sphingomyelinase and ceramidase activities in human plasma

General information
State: Published
Organisations: Center for Biological Sequence Analysis, Department of Systems Biology
Authors: Hellgren, L. (Intern), Mathiassen, J. H. (Intern), Miles, E. A. (Ekstern), Calder, P. C. (Ekstern)
Publication date: 2007
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 199091
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2007

The effect of combining weight loss and n-3 PUFA intake on obese and insulin resistant mice

General information
State: Published
Organisations: Center for Biological Sequence Analysis, Department of Systems Biology
Authors: Pedersen, M. H. (Intern), Hellgren, L. (Intern)
Publication date: 2007
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 199090
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2007

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)
Publication date: 2007
Publication information
Original language: English
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 199067
Publication: Research › Sound/Visual production (digital) – Annual report year: 2007

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
The source of dietary fatty acids alter the activity of secretory sphingomyelinase in the rat

General information
State: Published
Organisations: Department of Systems Biology
Authors: Drachmann, T. (Intern), Mathiassen, J. H. (Intern), Pedersen, M. H. (Intern), Hellgren, L. (Intern)
Pages: 1003-1009
Publication date: 2007
Main Research Area: Technical/natural sciences

Publication information
Journal: Lipid Science and Technology
Issue number: 10
ISSN (Print): 1438-7697
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 2.06 SJR 0.71 SNIP 1.024
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.642 SNIP 0.881 CiteScore 1.85
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.737 SNIP 1.051 CiteScore 1.98
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.852 SNIP 1.124 CiteScore 2.16
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.873 SNIP 1.207 CiteScore 2.06
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.732 SNIP 0.945 CiteScore 1.75
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 0.791 SNIP 1.049
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 0.838 SNIP 1.077
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Lipids and stable isotopes in marine food webs in West Greenland: Trophic Relations and health implications

General information
State: Published
Organisations: Enzyme and Protein Chemistry, Department of Systems Biology
Authors: Møller, P. (Intern), Hellgren, L. (Intern)
Number of pages: 210
Publication date: Sep 2006

Publication information
ISBN (Print): 978-87-7772-941-6
Original language: English
Main Research Area: Technical/natural sciences
Electronic versions: phd_PEM.pdf
Source: orbit
Source-ID: 191363
Publication: Research › Ph.D. thesis – Annual report year: 2006

Enzymatic production of ceramide from sphingomyelin
Due to its major role in maintaining the water-retaining properties of the epidermis, ceramide is of great commercial potentials in cosmetic and pharmaceutical industries such as in hair and skin care products. Chemical synthesis of ceramide is a costly process, and developments of alternative cost-efficient production methods are of great interest. Present study was the first attempt to perform a systematic study on the production of ceramide through enzymatic hydrolysis of sphingomyelin. Sphingomyelin hydrolysis proved to be more efficient in two-phase (water:organic solvent) system than in one-phase (water-saturated organic solvent) system. Among the screened phospholipase C, the Clostridium petfringens enzyme had the highest sphingomyetin conversion rate, with very small temperature dependence. Addition of ethanol to the system markedly enhanced the rate of ceramide formation, and a mixture of ethyl acetate: hexane (50:50) was the best organic solvent tested. Other factors such as (NH4)(2)SO4, MCI and CaCl, were also tested but excluded for further consideration. On the basis of the initial experiments, the reaction system was optimized using response surface methodology including five factors (enzyme amount, water amount, ethanol amount, reaction time and the hexane ratio of organic solvent). Water content and enzyme amount was shown to have the most significant influence on the hydrolysis reaction in the fitted quadratic model. The efficiency of sphingomyelin hydrolysis was dramatically improved through system evaluation and optimization, with the optimal conditions at 75 min reaction time, 3 U ml(-1) enzyme amount, 6% water amount, 1.8% ethanol arnount and 46% hexane in ethylacetate. (c) 2005 Elsevier B.V. All rights reserved.

General information
Butter improves glucose tolerance compared with a highly polyunsaturated oil in the rat

Background: In several recent studies, it has been shown that markers of milk-fat intake, are strongly correlated to a low fasting-insulin level, indicating a positive correlation between milk-fat intake and improved glucose-tolerance [1, 2]. This is in contradiction to the general findings in epidemiological studies, where the typical fatty acid composition of milk-fat, i.e. a high level of saturated fatty acids (SFA) and low concentration of polyunsaturated fatty acids (PUFAs), has been correlated to increased insulin-resistance. It is therefore essential to characterize the impact of milk-fat on glucose-tolerance in intervention studies. Methods: 16 rats were divided into two groups and fed a semisynthetic diet containing 31 E-% fat, either as butter or highly polyunsaturated grapeseed oil. After 12 weeks on the diets, glucose-tolerance was assayed with the oral-glucose tolerance test (OGTT). Results and Discussion: The OGTT revealed that the rats on the butter-containing diet, had a substantially higher glucose tolerance than the rats, which were fed grapeseed oil (area under the curve = 195 ± 31 mM*min⁻² vs. 310 ± 13 mM*min⁻², n= 8, p=0.004). There were no differences in serum triacylglycerol (TAG), serum free fatty acid and leptin between the groups. However, the butter-fed rats had a lower content of TAG in the white gastrocnemius muscle (7.7 ± 1.5 vs. 23.1 ± 6.2 mg/g tissue, p<0.01), and a much higher n-3 PUFA content (total n-3 PUFAs 1.43 ± 0.06 vs 0.73 ± 0.02g/mg tissue, p <0.0001) and lower n-6/n-3 PUFA ratio (2.29 ± 0.09 vs 7.09 ± 0.24, p
Enzymatic Modification of Sphingomyelin

Due to its major role in maintaining the water-retaining properties of the epidermis, ceramide is of great commercial potential in cosmetic and pharmaceuticals such as hair and skin care products. Currently, chemical synthesis of ceramide is a costly process, and developments of alternative cost-efficient, high yield production methods are of great interest. In the present study, the potential of producing ceramide through the enzymatic hydrolysis of sphingomyelin have been studied. sphingomyelin is a ubiquitous membrane-lipid and rich in dairy products or by-products. It has been verified that sphingomyelin modification gives a feasible approach to the potential production of ceramide. The reaction system has been improved through system evaluation and the optimization of several important factors, and phospholipase C from Clostridium perfringens shows higher activity towards the hydrolysis reaction. From several particles which the enzyme was immobilized on, Lewatit VP OC 1600 (Bayer AG) is the most desirable as a consequence of the highest retention activity of the immobilized enzyme. The further research focus on the immobilization using this carrier was conducted. This presentation will describe the research background, introduce the basic reaction system with its optimisation, and release the recent results in the immobilization study.

General information
State: Published
Organisations: Food Production Engineering, Department of Systems Biology
Authors: Zhang, L. (Intern), Hellgren, L. (Intern), Xu, X. (Intern)
Publication date: 2006

Exploring Biosynthetic Control in Lipid Metabolism

General information
State: Published
Organisations: Center for Microbial Biotechnology, Department of Systems Biology, King Mongkut's University of Technology Thonburi, Pontificia Universidad Católica
Authors: Jewett, M. C. (Intern), Nookaew, I. (Ekstern), Pizarro, F. A. (Ekstern), Hellgren, L. (Intern), Agosin, E. (Ekstern), Nielsen, J. (Intern)
Publication date: 2006
Event: Abstract from American Institute of Chemical Engineering : Annual Meeting, .
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 199088
The dietary fatty acid source regulates the activity of secretory sphingomyelinase, an enzyme involved in inflammatory signalling and atherogenesis

General information
State: Published
Organisations: Department of Systems Biology
Authors: Hellgren, L. (Intern), Nielsen, T. D. (Ekstern), Mathiassen, J. H. (Ekstern), Pedersen, M. H. (Intern)
Publication date: 2006
Event: Abstract from LMC Conference: Nutrigenomics and Health: From visions to Food, Copenhagen, Denmark.
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 199083
Publication: Research - peer-review » Conference abstract for conference – Annual report year: 2006

The dietary fatty acid source regulates the activity of secretory sphingomyelinase, an enzyme involved in inflammatory signalling and atherogenesis

General information
State: Published
Organisations: Department of Systems Biology
Authors: Hellgren, L. (Intern), Nielsen, T. D. (Ekstern), Mathiassen, J. H. (Ekstern), Pedersen, M. H. (Intern)
Publication date: 2006
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 199085
Publication: Research - peer-review » Conference abstract for conference – Annual report year: 2006

Combinatorial effects of dietary fatty acids and probiotics 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), Straarup, E. M. (Intern), Hellgren, L. (Intern), Frøkiær, H. (Intern)
Publication date: 2005
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 199055
Publication: Research - peer-review » Conference abstract for conference – Annual report year: 2006

Enzymatic modification of sphingomyelin

General information
State: Published
Organisations: Food Production Engineering, Department of Systems Biology
Authors: Zhang, L. (Intern), Hellgren, L. (Intern), Xu, X. (Ekstern)
Pages: S78-S78
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
Web of Science (2017): Indexed yes
Enzymatic Modification of Sphingomyelin

Due to its major role in maintaining the water-retaining properties of the epidermis, ceramide is of great commercial potential in cosmetic and pharmaceuticals such as hair and skin care products. Currently, chemical synthesis of ceramide is a costly process, and developments of alternative cost-efficient, high yield production methods are of great interest. In
the present study, the potential of producing ceramide through enzymatic hydrolysis of sphingomyelin have been studied. Sphingomyelin (SM) is a ubiquitous membrane-lipid and dairy products or by-products is a rich source of sphingomyelin. In present study, we have optimized the production of ceramide from sphingomyelin using Phospholipase C from Clostridium perfringens.

General information
State: Published
Organisations: Food Production Engineering, Department of Systems Biology, Enzyme and Protein Chemistry
Authors: Zhang, L. (Intern), Hellgren, L. (Intern), Xu, X. (Intern)
Publication date: 2005
Event: Poster session presented at 12th European Congress on Biotechnology, Kongens Lyngby, Denmark.
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 184443
Publication: Research › Poster – Annual report year: 2005

Enzymatic Modification of Sphingomyelin
Sphingomyelin (SM) is a ubiquitous component of animal cell membranes, and it is the most abundant sphingolipid. Ceramide, a hydrolysis product from SM, has an important role in cellular signaling, and especially in the regulation of apoptosis, cell differentiation, transformation and proliferation. Due to its major role in the water-retaining properties of the epidermis, ceramide is of great commercial potential in cosmetic and pharmaceuticals such as hair and skin care products. In current, ceramide is not easy to synthesis for industrial application and synthetic ceramide is still expensive. Therefore, it is desirable to develop alternative cost-efficient, high yield production methods. This study optimized the enzymatic production of ceramide from SM. Phospholipase C from Clostridium perfringens was chosen to catalyze the reaction. Several important factors were considered in optimization.

General information
State: Published
Organisations: Food Production Engineering, Department of Systems Biology, Enzyme and Protein Chemistry
Authors: Zhang, L. (Intern), Hellgren, L. (Intern), Xu, X. (Intern)
Publication date: 2005
Event: Poster session presented at LipidForum : ENZYMES IN LIPID TECHNOLOGY, Copenhagen, Denmark, .
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 184441
Publication: Research › Poster – Annual report year: 2005

Milk-derived GM(3) and GD(3) 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: Department of Systems Biology
Authors: Bronnum, H. (Ekstern), Seested, T. (Ekstern), Hellgren, L. (Intern), Pedersen, S. B. (Intern), Frokiaer, H. (Ekstern)
Pages: 551-557
Publication date: 2005
Main Research Area: Technical/natural sciences
Publication information
Journal: Scandinavian Journal of Immunology
Volume: 61
Issue number: 6
ISSN (Print): 0300-9475
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
Main Research Area: Technical/natural sciences

Publication information
Journal: Scandinavian Journal of Immunology
Volume: 61
Issue number: 551-557
ISSN (Print): 0300-9475
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 2.03 SJR 0.951 SNIP 0.646
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.93 SNIP 0.684 CiteScore 1.97
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.898 SNIP 0.666 CiteScore 1.91
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.86 SNIP 0.712 CiteScore 2.05
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.88 SNIP 0.749 CiteScore 2.16
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.854 SNIP 0.66 CiteScore 2.06
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 0.844 SNIP 0.622
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 0.962 SNIP 0.662
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 0.236 SNIP 0.078
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 0.286 SNIP 0.141
Scopus rating (2006): SJR 0.421 SNIP 0.125
Scopus rating (2005): SJR 0.999 SNIP 0.642

General information
State: Published
Organisations: Department of Biochemistry and Nutrition, Department of Systems Biology
Authors: Fledelius, C. (Intern), Larsen, H. R. (Ekstern), Vinterby, A. (Ekstern), Damgaard, J. (Ekstern), Hellgren, L. (Intern), Gottfredsen, C. F. (Ekstern), Daugaard, J. R. (Ekstern)
Publication date: 2005
Event: Abstract from American Diabetic Society: 65th Scientific Session
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 199084
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2005

Sphingolipids in signal transduction and pathophysiology

General information
State: Published
Organisations: Department of Systems Biology
Authors: Hellgren, L. (Intern)
Publication date: 2005

Publication information
Original language: English
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 199087
Publication: Research › Sound/Visual production (digital) – Annual report year: 2005

A solid dietary fat containing fish oil redistributes lipoprotein subclasses without increasing oxidative stress in men

There is a demand and need for healthy solid dietary fats. However, synthetic fats can be tailored to contain specific physiologic properties. Our goal was to design dietary solid test fats that would be both beneficial to the atherogenic lipid profile and stable against lipid peroxidation. Sixteen men (age 35-75 y) substituted 80 g of their normal dietary fat intake with test fat for two periods of 21 d each in a double-blind, randomized, crossover study. Although solid, both test fats were low in cholesterol-raising SFA. Test fat "F" contained 5 g/100 g long chain (n-3) fatty acids matched by oleic acid in test fat "O." Plasma total triacylglycerol (TAG), VLDL TAG, cholesterol in VLDL, and intermediate density lipoproteins (IDL) were lower (P <0.05), whereas apolipoprotein (apo) B of the large LDL-2 (d = 1031-1042 g/L) subclass, and cholesterol of HDL2b subclass, were higher after intake of F than O fat (P <0.05). There was no difference in the effect on in vivo oxidation measured as the ratio of plasma isoprostanes F-2 to arachidonic acid and urinary isoprostanes, whereas the vitamin E activity/plasma total lipids ratio was higher after intake of F than O (P = 0.008). In conclusion, a solid dietary fat containing (n-3) PUFA decreased plasma TAG, VLDL, and IDL cholesterol, and redistributed lipoprotein subclasses in LDL and HDL, with a higher concentration of the larger and less atherogenic subfractions. These changes took place without an increase in oxidative stress as measured by in vivo markers.
Intake of phytosterols (and -stanols) has been shown to decrease the level of low-density lipoprotein cholesterol and thus protect against development of cardiovascular diseases. Therefore, studies on the cultivar and year-to-year variation in phytosterol content in rye grains have been performed. The phytosterol content and composition of different rye cultivars, grown under identical conditions on the same field in three consecutive years, were analyzed. Both cultivar and year-to-year variation in sterol content were statistically significant ($p < 0.0001$). The total sterol content varied from 1007 +/- 21 mg/kg in the highest yielding cultivar, Tsulpan 3, to 761 +/- 10 mg/kg in the lowest yielding cultivar (Amando in the 1999 harvest). Because the meteorological conditions varied substantially between the different years, it was possible to deduce the impact of varying weather conditions on phytosterol content in the different cultivars. The studied cultivars had all the lowest phytosterol contents in the dry and warm harvest season of 1999. Although there were statistically significant cultivar and year-to-year variations in the sterol composition ($p < 0.0001$), these were only between 2 and 4% of the total sterol content.

**General information**

State: Published
Organisations: Enzyme and Protein Chemistry, Department of Systems Biology
Authors: Zangenberg, M. (Ekstern), Hansen, H. (Ekstern), Jørgensen, J. (Ekstern), Hellgren, L. (Intern)
Pages: 2593-2597
Publication date: 2004
Main Research Area: Technical/natural sciences

**Publication information**

Journal: Journal of Agricultural and Food Chemistry
Volume: 52
ISSN (Print): 0021-8561
Ratings:
- BFI (2018): BFI-level 2
- Web of Science (2018): Indexed yes
- BFI (2017): BFI-level 2
- Web of Science (2017): Indexed yes
- BFI (2016): BFI-level 2
- Scopus rating (2016): CiteScore 3.45 SJR 1.291 SNIP 1.344
- Web of Science (2016): Indexed yes
- BFI (2015): BFI-level 2
- Scopus rating (2015): SJR 1.236 SNIP 1.253 CiteScore 3.23
- Web of Science (2015): Indexed yes
- BFI (2014): BFI-level 2
- Scopus rating (2014): SJR 1.278 SNIP 1.421 CiteScore 3.25
- Web of Science (2014): Indexed yes
- BFI (2013): BFI-level 2
- Scopus rating (2013): SJR 1.423 SNIP 1.479 CiteScore 3.44
- ISI indexed (2013): ISI indexed yes
- Web of Science (2013): Indexed yes
- BFI (2012): BFI-level 2
- Scopus rating (2012): SJR 1.43 SNIP 1.471 CiteScore 3.2
- ISI indexed (2012): ISI indexed yes
- Web of Science (2012): Indexed yes
- BFI (2011): BFI-level 2
Effects of Dietary fatty acid modification in solid fats on blood lipids, lipoprotein subclasses, and oxidative stress in men

General information
State: Published
Organisations: Department of Systems Biology, Royal Veterinary and Agricultural University, Uppsala University, Copenhagen University Hospital
Authors: Tholstrup, T. (Ekstern), Hellgren, L. I. (Intern), Petersen, M. (Ekstern), Basu, S. (Ekstern), Straarup, E. M. (Intern), Schnor, P. (Ekstern), Sandstrøm, B. (Ekstern)
Pages: 1051-1057
Publication date: 2004
Main Research Area: Technical/natural sciences

Publication information
Journal: Journal of Nutrition
Volume: 134
ISSN (Print): 0022-3166
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 3.93 SJR 1.956 SNIP 1.356
Lipids rich in phosphatidylethanolamine from natural gas-utilizing bacteria reduce plasma cholesterol and classes of phospholipids: A comparison with soybean oil

We compared the effects of three different high-lipid diets on plasma lipoproteins and phospholipids in mink (Mustela vison). The 18 mink studied were fed one of the three diets during a 25-d period in a parallel group design. The compared diets had 0, 17, and 67% extracted lipids from natural gas-utilizing bacteria (LNGB), which were rich in PE. The group with 0% LNGB was fed a diet for which the lipid content was 100% soybean oil. The total cholesterol, LDL cholesterol, and HDL cholesterol of animals consuming a diet with 67% LNGB (67LNGB-diet), were significantly lowered by 35, 49, and 29%, respectively, and unesterified cholesterol increased by 17% compared with the animals fed a diet of 100% lipids from soybean oil (SB-diet). In addition, the ratio of LDL cholesterol to HDL cholesterol was 27% lower in mink fed the 67LNGB-diet than those fed the S13-cliet. When the mink were fed the 67LNGB-diet, plasma PC, total phospholipids,
lysoPC, and PI were lowered significantly compared with the mink fed a SB-diet. Plasma total cholesterol was correlated
with total phospholipids as well as with PC (R = 0.8, P <0.001). A significantly higher fecal excretion of unesterified
cholesterol, cholesteryl ester, PC, lysoPC, and PE was observed in the 67LNGB-fed mink compared with the SB-fed mink.
We conclude that phospholipids from the 67LNGB-diet decreased plasma lipoprotein levels, the LDL-HDL cholesterol
ratio, and plasma phospholipid levels, especially lysoPC and PC, compared with the highly unsaturated soybean oil. Our
findings indicate that the decrease of plasma cholesterol is mainly caused by a specific mixture of phospholipids
containing a high level of PE, and not by the dietary FA composition. The lack of significant differences in the level of
plasma PE due to the diets indicates that most of the PE from LNGB has been converted to PC in the liver. Thus, plasma
cholesterol may at least be partly regulated by phospholipid methylation from PE to PC in the liver.

General information
State: Published
Organisations: Center for Biological Sequence Analysis, Department of Systems Biology
Authors: Müller, H. (Ekstern), Hellgren, L. (Intern), Olsen, E. (Ekstern), Skrede, A. (Ekstern)
Pages: 833-841
Publication date: 2004
Main Research Area: Technical/natural sciences

Publication information
Journal: Lipids
Volume: 39
Issue number: 9
ISSN (Print): 0024-4201
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 0.693 SNIP 0.77 CiteScore 1.94
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.782 SNIP 0.744 CiteScore 1.96
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.792 SNIP 0.876 CiteScore 2.07
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.903 SNIP 0.976 CiteScore 2.59
ISI indexed (2013): ISI indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.888 SNIP 1.048 CiteScore 2.5
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.765 SNIP 0.931 CiteScore 2.3
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 0.798 SNIP 0.898
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 0.694 SNIP 0.892
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 0.707 SNIP 0.841
Scopus rating (2007): SJR 0.741 SNIP 0.904
Scopus rating (2006): SJR 0.83 SNIP 0.788
Web of Science (2006): Indexed yes
Scopus rating (2005): SJR 0.673 SNIP 0.801
Web of Science (2005): Indexed yes
Scopus rating (2004): SJR 0.75 SNIP 0.876
Web of Science (2004): Indexed yes
Sphingolipids in the human diet - occurrence and physiological effects

General information
State: Published
Organisations: Department of Systems Biology
Authors: Hellgren, L. (Intern)
Pages: 129-133
Publication date: 2002
Main Research Area: Technical/natural sciences

Publication information
Journal: Lipid Technology
Volume: 14
Ratings:
Scopus rating (2016): SJR 0.224 SNIP 0.29 CiteScore 0.53
Scopus rating (2015): SJR 0.227 SNIP 0.278 CiteScore 0.64
Scopus rating (2014): SJR 0.287 SNIP 0.353 CiteScore 0.66
Scopus rating (2013): SJR 0.264 SNIP 0.311 CiteScore 0.43
ISI indexed (2013): ISI indexed no
Scopus rating (2012): SJR 0.323 SNIP 0.499 CiteScore 0.4
ISI indexed (2012): ISI indexed no
Scopus rating (2011): SJR 0.323 SNIP 0.368 CiteScore 0.39
ISI indexed (2011): ISI indexed no
Scopus rating (2010): SJR 0.197 SNIP 0.258
Web of Science (2002): Indexed yes
Original language: English
Source: orbit
Source-ID: 155196
Publication: Research - peer-review › Journal article – Annual report year: 2004

Age-dependent variation in membrane lipid synthesis in leaves of garden pea (Pisum sativum L.)
To study membrane lipid synthesis during the lifespan of a dicotyledon leaf, the second oldest leaf of 10-40-d-old plants of garden pea (Pisum sativum L.) was labelled with [1-C-14]acetate and the distribution of radioactivity between the major membrane lipids was followed for 3 d. In the expanding second oldest leaf of 10-d-old plants, acetate was primarily allocated into phosphatidylcholine (PC) during the first 4 h of labelling. During the following 3 d, labelling of PC decreased and monogalactosyldiacylglycerol (MGDG) became the most radioactive lipid. In the fully expanded second oldest leaf of older plants, acetate was predominantly allocated into phosphatidylglycerol (PG), which remained the major radiolabelled lipid during the 3 d studied. The proportion of radioactivity recovered in MGDG decreased with increasing plant age up to 20 d, suggesting that, in expanded leaves, MGDG is more stable and requires renewal to a lower extent than PG. When the second oldest leaf approached senescence, labelling of MGDG again increased, indicating an increased need for thylakoid repair. The proportion of acetate allocated into phosphatidylethanolamine and free sterols was largest in leaves of 18-26-d-old plants and in the youngest leaves, respectively. Thus, these results demonstrate that the distribution of newly synthesized fatty acids between acyl lipid synthesis in the chloroplast and extraplastidial membranes strongly varies with leaf age, as do the proportion utilized for sterol synthesis. The findings emphasize the importance of defining the developmental stage of the leaf material used when performing studies on leaf lipid metabolism.
Effects of moderately enhanced levels of ozone on the acyl lipid composition and dynamical properties of plasma membranes isolated from garden pea (Pisum sativum)

Plasma membranes were isolated from leaves of 16-day-old garden pea, Pisum sativum L., that had been grown in the absence or presence of 65 nl l(-1) ozone for 4 days prior to membrane isolation. Plasma membranes from ozone-fumigated plants contained significantly more acyl lipids per protein than those from leaves of plants grown in filtered air on a molar/weight ratio. The ratio between the major acyl lipids, phosphatidylethanolamine (PE) and phosphatidylcholine (PC), also increased due to the ozone fumigation, while the fatty acid unsaturation level was unaltered in total plasma membrane acyl lipids, as well as in PC and PE. The amount of free sterols per protein was unaltered, but the percentage of campesterol increased, concomitant with a decrease in stigmasterol. The dynamical properties of the isolated plasma membranes were assessed using Laurdan fluorescence spectroscopy, which monitors water penetration and mobility at the hydrophilic-hydrophobic interface of the membrane. At 0 degreesC, the molecular mobility was slightly lower in plasma membranes from ozone-fumigated plants than in plasma membranes from control plants, possibly reflecting the increased PE/PC, campesterol/stigmasterol and lipid/protein ratios, and suggesting that ozone-fumigated pea plants may be more susceptible to freezing injuries.
Fat Digestion and Absorption

General information
State: Published
Organisations: Department of Systems Biology
Authors: Hellgren, L. (Intern)
Publication date: 2001
Main Research Area: Technical/natural sciences

Publication information
Journal: Journal of the Science of Food and Agriculture
Volume: 81
Issue number: 15
ISSN (Print): 0022-5142
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 2.48 SJR 0.87 SNIP 1.222
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.813 SNIP 1.088 CiteScore 2.11
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.819 SNIP 1.153 CiteScore 2.1
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.846 SNIP 1.224 CiteScore 2.22
Occurrence of bioactive sphingolipids in meat and fish products

Recent research has revealed that the degradation products of dietary sphingolipids are biologically highly active and have the capacity to inhibit the development of colon cancer in mice. Nevertheless, the content of sphingolipids in common foodstuff has never been systematically analyzed. Therefore we investigated the contents of sphingomyelin and neutral glycosphingolipids in commonly consumed meat and fish products. Sphingomyelin and glycosphingolipids were found in all foodstuffs studied. The total amount varied between 118 +/- 17 nmol/g (cod) to 589 +/- 39 nmol/g (chicken leg). Generally, lower amounts of sphingolipids were determined in fish meat than in red meat and poultry, while poultry was the richest source of this class of lipids. However, fish meat contained a relatively high content of neutral glycolipids compared with other types of meat. Thus, in fish the ratio sphingomyelin/neutral glycolipids varied from 1 to 2.9, while in poultry this ratio varied between 5.2 to 19.2 and in red meat it varied from 1.6 to 8.3. The fatty acid composition of sphingomyelin in fish was dominated by C24:1 (Delta (9)) or C22:1 (Delta (9)), while C16:0 and C18:0 were the dominating sphingomyelin species in poultry and C18:0 in the meat of mammal origin.

General information

State: Published
Organisations: Enzyme and Protein Chemistry, Department of Systems Biology
Authors: Hellgren, L. (Intern)
Pages: 661-667
The impact of different phytosterols on the molecular dynamics in the hydrophobic/hydrophilic interface phosphatidylcholine- liposomes

Plant sterols differ from cholesterol in having an alkyl group at Delta -24, and, in the case of stigmasterol, also a Delta -22 double bond. The effects of 10 mol% of three plant sterols (campesterol, fl-sitosterol, stigmasterol) and cholesterol on the molecular dynamics and phase behavior in multilamellar liposomes made from different phosphatidylcholine (PC) molecular species have been compared, utilizing the fluorescent probe Laurdan (2-dimethyl-amino-6-laurylnaphthalene). Laurdan reports the molecular mobility in the hydrophilic/hydrophobic interface of the membrane by determining the rate of dipolar relaxation of water molecules close to the glycerol backbone of PC. Our results showed that the Delta -24 alkyl group of plant sterols did not affect their ability to reduce molecular mobility in this region of the PC membranes. However, the plant sterols had a decreased capacity compared to cholesterol to inhibit formation of co-existing domains of gel and liquid-crystalline phases in membranes composed of equimolar dilauroyl-PC and dipalmitoyl-PC. The Delta -22 double bond present in stigmasterol decreased the ability of this sterol, compared to the other phytosterols, to reduce the molecular mobility at the hydrophobic/hydrophilic interface in membranes made of a saturated PC molecular species. However, in membranes made from 16:0/18:2-PC, a lipid species common in plant plasma membranes, stigmasterol was as efficient as other sterols in affecting the polarity and molecular mobility at the hydrophilic/hydrophobic interface of the membrane at 25 degreesC, but was, in contrast to the other sterols, without effect at 0 degreesC. Our results thus confirm as well as contradict the results of previous studies of the interactions between saturated PC and sterols, where other membrane regions were probed. The physiological relevance of the findings is discussed.

General information
State: Published
Organisations: Department of Systems Biology
Authors: Hellgren, L. (Intern), Sandelius, A. (Ekstern)
Pages: 23-32
Publication date: 2001
Main Research Area: Technical/natural sciences

Publications information
Journal: Physiologia Plantarum
Volume: 113
Issue number: 1
ISSN (Print): 0031-9317
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 1.437 SNIP 1.092 CiteScore 3.52
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.54 SNIP 1.186 CiteScore 3.55
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.373 SNIP 1.142 CiteScore 3.23
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.46 SNIP 1.31 CiteScore 3.64
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 1.622 SNIP 1.348 CiteScore 3.61
ISI indexed (2012): ISI indexed yes
Expression of barley serpin genes, cloning of wheat serpins, and a loop deletion in Arabidopsis thaliana serpin sequences

General information
State: Published
Organisations: Department of Biochemistry and Nutrition, Department of Systems Biology
Authors: Rasmussen, S. K. (Ekstern), Roberts, T. H. (Intern), Jensen, H. Ø. (Intern), Hellgren, L. (Intern), Hejgaard, J. (Intern)
Number of pages: 462
Publication date: 1999

Host publication information
Title of host publication: 2nd International Symposium on the structure and biology of Serpins
Place of publication: Queens College, Cambridge
Main Research Area: Technical/natural sciences
Conference: 2nd International Symposium on the structure and biology of Serpins, Queens College, Cambridge, 01/01/1999
Source: orbit
Source-ID: 199094
Publication: Research › Article in proceedings – Annual report year: 1999

A novel method in studies of dynamical properties in plant membrane: Laurdan fluorescence spectroscopy
A new method to study dynamical properties of biological membranes, excitation generalized polarization (excitation GP) of Laurdan (6-lauroyl-2-dimethylaminonaphthalene) fluorescence, has for the first time been used in plant science. This method allows the determination of the molecular dynamics in biological membranes, using simple steady-state fluorescence measurements. Laurdan spectroscopy also determines the phase state of the membranes, and separation into co-existing gel- and liquid-crystalline phases can be revealed. A protocol for labelling wheat (Triticum aestivum L.) plasma membranes with Laurdan have been established. The method has been used to probe the dynamical alterations
that occur in wheat plasma membranes at changed temperatures. The method detects changes in plasma membrane
dynamics induced by alterations in temperature of 2 degrees C. The results for plasma membranes are similar to those
obtained for animal cell membranes, and show that isolated wheat plasma membranes occur in a homogenous liquid-
crystalline phase at all temperatures tested, from 4 degrees C to 28 degrees C. Laurdan fluorescence spectroscopy is a
promising tool in plant membrane research, acid it is suggested that the temperature dependence of excitation GP is a
suitable parameter to use in determing the effect on membrane dynamics by altered membrane lipid composition.
Plant membrane lipids: the impact of ozone on lipid composition, lipid metabolism and the dynamical properties of plasma membranes

General information
State: Published
Organisations: University of Gothenburg
Authors: Hellgren, L. (Intern)
Publication date: 1996

Publications information
Original language: English
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 191836
Publication: Research Ph.D. thesis – Annual report year: 1996

In situ leaf lipid metabolism in garden pea (Pisum sativum L.) exposed to moderately enhanced levels of ozone

General information
State: Published
Organisations: University of Gothenburg
Authors: Hellgren, L. (Intern), Carlsson, A. S. (Ekstern), Selldén, G. (Ekstern), Sandelius, A. S. (Ekstern)
Pages: 221-230
Publication date: 1995
Main Research Area: Technical/natural sciences

Publications information
Journal: Journal of Experimental Botany
Volume: 46
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 6.02 SJR 2.78 SNIP 1.728
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 2.761 SNIP 1.822 CiteScore 5.97
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 2.781 SNIP 2.046 CiteScore 5.93
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 2.626 SNIP 1.973 CiteScore 6
ISI indexed (2013): ISI indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 2.612 SNIP 1.936 CiteScore 5.47
ISI indexed (2012): ISI indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 2.596 SNIP 1.865 CiteScore 5.19
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
The leaf acyl composition of plants exposed to moderately enhanced levels of ozone: Species, age and dose dependence

General information
State: Published
Organisations: Swedish Environmental Research Institute, University of Gothenburg
Authors: Sandelius, A. S. (Ekstern), Carlsson, A. S. (Ekstern), Pleijel, H. (Ekstern), Hellgren, L. (Intern), Wallin, G. (Ekstern), Selldén, G. (Ekstern)
Pages: 459-461
Publication date: 1995

Host publication information
Title of host publication: Plant Lipid Metabolism
Place of publication: Dordrecht
Publisher: Kluwer Academic Publishers
Editors: Kader, J., Mazliak, P.
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 191833
Publication: Education › Book chapter – Annual report year: 1995

Effects of moderately enhanced levels of ozone on the acyl lipid composition of leaves of garden pea (Pisum sativum)
Plants of garden pea (Pisum sativum L.) were exposed to charcoal-filtered air with or without addition of 65 +/- 5 nl l(-1) ozone. Plants were harvested daily for 9 days and lipids were extracted from the second-oldest leaf. Visible injury of this leaf was evident from day 5 on, while the differences in lipids between ozone and control treatments were observed earlier. Ozone caused large decreases in the contents of monogalactosyldiacylglycerol (MGDG), digalactosyldiacylglycerol (DGDG) and sulfoquinovosyldiacylglycerol (SQDG), a slower decrease in the content of phosphatidylcholine (PC) but an increase in the content of phosphatidylethanolamine (PE) per leaf area, compared with exposure to charcoal-filtered air. The content of phosphatidylglycerol (PG) was unaffected by ozone. Compared with charcoal-filtered air, fumigation with ozone resulted in a decrease in the proportion of linolenic acid (18:3) of the total lipid extract, with a concomitant increase in the proportion of linoleic acid (18:2). For individual lipids, ozone caused a similar pattern of decreased 18:3 and increased 18:2 in MGDG, SQDG, PC and PE, while the fatty acid composition of DGDG was unaffected. In PG, ozone decreased the proportions of 18:3 and trans-Delta(3)-decenoic acid (16:1(trans)), balanced by increased proportions of palmitic and oleic acids. The contents of chlorophylls and carotenoids were unaffected by ozone. Out results show that moderately elevated levels of ozone cause significant changes in the polar lipid composition of garden pea leaves and in the level of unsaturation of the lipid acyl groups and, furthermore, that ozone has different effects, which could be direct or indirect, on chloroplast Lipids (MGDG, DGDG, SQDG, PG acylated with 16:1(trans)) and cytosolic membrane lipids.
Isolation of a putative vesicular intermediate in the cell-free transfer of membrane from transitional endoplasmic reticulum to the Golgi apparatus of etiolated seedlings of garden pea

**General information**

State: Published
Organisations: Purdue University, University of Gothenburg
Authors: Hellgren, L. (Intern), Morré, D. J. (Ekstern), Selldén, G. (Ekstern), Sandelius, A. S. (Ekstern)
Pages: 197-205
Publication date: 1993
Main Research Area: Technical/natural sciences

**Publication information**

Journal: Journal of Experimental Botany
Volume: 44
Ratings:

**BFI (2018):** BFI-level 2

**Web of Science (2018):** Indexed yes

**BFI (2017):** BFI-level 2

**Web of Science (2017):** Indexed Yes

**BFI (2016):** BFI-level 2

**Scopus rating (2016):** CiteScore 6.02 SJR 2.78 SNIP 1.728

**Web of Science (2016):** Indexed yes

**BFI (2015):** BFI-level 2

**Scopus rating (2015):** SJR 2.761 SNIP 1.822 CiteScore 5.97

**Web of Science (2015):** Indexed yes

**BFI (2014):** BFI-level 2

**Scopus rating (2014):** SJR 2.781 SNIP 2.046 CiteScore 5.93

**Web of Science (2014):** Indexed yes

**BFI (2013):** BFI-level 2

**Scopus rating (2013):** SJR 2.626 SNIP 1.973 CiteScore 6

**ISI indexed (2013):** ISI indexed yes

**BFI (2012):** BFI-level 2

**Scopus rating (2012):** SJR 2.612 SNIP 1.936 CiteScore 5.47

**ISI indexed (2012):** ISI indexed yes

**BFI (2011):** BFI-level 2

**Scopus rating (2011):** SJR 2.596 SNIP 1.865 CiteScore 5.19

**ISI indexed (2011):** ISI indexed yes

**Web of Science (2011):** Indexed yes

**BFI (2010):** BFI-level 2

**Scopus rating (2010):** SJR 2.336 SNIP 1.8

**BFI (2009):** BFI-level 2

**Scopus rating (2009):** SJR 2.344 SNIP 1.698

**Web of Science (2009):** Indexed yes

**BFI (2008):** BFI-level 2

**Scopus rating (2008):** SJR 2.197 SNIP 1.528

**Web of Science (2007):** Indexed yes

**Scopus rating (2006):** SJR 1.822 SNIP 1.384

**Scopus rating (2005):** SJR 1.715 SNIP 1.614
ATP-dependent cell-free transfer of membrane lipids from nuclei to Golgi apparatus of germinating axes of garden pea

ATP-dependent cell-free transfer of membrane constituents radiolabeled with [C-14]acetate, primarily lipids, was demonstrated between isolated nuclei in suspension and purified Golgi apparatus immobilized on nitrocellulose strips prepared from garden pea (Pisum sativum) in the presence of pea cytosol. The ATP-dependent transfer correlated with the ability of the nuclear envelope to form 50-70 nm vesicles and blebs in an ATP-dependent manner. Specific transfer, transfer at 23-degrees-C minus transfer at 4-degrees-C, was approximately doubled by addition of ATP and was greater for peas germinated for 2 days than for peas germinated for 3 days. ATP plus cytosol-dependent transfer could not be demonstrated using radiolabeled pea nuclei as donor with purified endoplasmic reticulum, plasma membrane, nuclei, mitochondria or amyloplasts as acceptors. The results provide a second example, in addition to transfer between endoplasmic reticulum and Golgi apparatus, where ATP-and temperature-dependent transfer via 50-70 nm transition vesicles can be demonstrated in a cell-free system.

General information
State: Published
Organisations: University of Gothenburg
Authors: Morré, D. J. (Ekstern), Penel, C. (Ekstern), Morré, D. (Ekstern), Hellgren, L. (Intern), Sandelius, A. S. (Ekstern), Greppin, H. (Ekstern)
Pages: 1-9
Publication date: 1992
Main Research Area: Technical/natural sciences

Publication information
Journal: Protoplasma
Volume: 170
Issue number: 1-2
ISSN (Print): 0033-183X
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 0.822 SNIP 0.962 CiteScore 2.34
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.952 SNIP 0.948 CiteScore 2.26
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.1 SNIP 1.018 CiteScore 2.69
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.34 SNIP 1.113 CiteScore 2.94
ISI indexed (2013): ISI indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 1.021 SNIP 1.052 CiteScore 2.29
ISI indexed (2012): ISI indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.646 SNIP 0.626 CiteScore 1.48
ATP-induced budding of nuclear envelope in vitro

Fractions enriched in intact nuclei and nuclear fragments isolated from etiolated hypocotyls of soybean responded in vitro to ATP plus a concentrated fraction of cytoplasmic proteins by formation of ca. 50-70 nm buds and vesicles resembling those observed to bud from the outer membrane of the nuclear envelope in situ at regions of nuclear envelope-Golgi apparatus interface. Similar vesicles are normally considered to function in the transfer of materials from the outer membrane of the nuclear envelope to cis elements of the Golgi apparatus.

General information
State: Published
Organisations: University of Gothenburg
Authors: Hellgren, L. (Intern), Morré, D. J. (Ekstern)
Pages: 238-242
Publication date: 1992
Main Research Area: Technical/natural sciences

Publication information
Journal: Protoplasma
Volume: 167
Issue number: 3-4
ISSN (Print): 0033-183X
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 0.822 SNIP 0.962 CiteScore 2.34
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.952 SNIP 0.948 CiteScore 2.26
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.1 SNIP 1.018 CiteScore 2.69
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.34 SNIP 1.113 CiteScore 2.94
ISI indexed (2013): ISI indexed yes
BFI (2012): BFI-level 1
Metabolism and in vivo transport of phosphatidylinositol in hypocotyls of dark-grown soybean

General information
State: Published
Organisations: Unknown
Authors: Sandelius, A. S. (Ekstern), Hellgren, L. (Intern)
Pages: 257-259
Publication date: 1990

Host publication information
Title of host publication: Plant-lipid biochemistry, structure & utilization
Place of publication: London
Publisher: Portland Press Ltd.
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 191830
Publication: Education › Book chapter – Annual report year: 1990

Projects:

Biomarkers and their use in age-related disease prediction - exploring the relationship between obesity and type II diabetes

Department of Systems Biology
Period: 01/07/2013 → 15/02/2017
Number of participants: 8
Phd Student:
Møller, Katrine Dragsbæk (Intern)
Supervisor:
Beck-Nielsen, Henning (Ekstern)
Henriksen, Kim (Ekstern)
Deciphering complex regulatory traits relating to host metabolism and immunity

Department of Systems Biology
Period: 15/12/2012 → 15/02/2017
Number of participants: 7
PhD Student:
Laursen, Janne Marie (Intern)
Supervisor:
Hellgren, Lars (Intern)
Workman, Christopher (Intern)
Main Supervisor:
Pedersen, Susanne Brix (Intern)
Examiner:
Licht, Tine Rask (Intern)
Clavel, Thomas (Ekstern)
Palandan, Søren Riis (Ekstern)

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

Relations
Publications:
Regulation of host metabolism and immunity by the gut microbiome
Project: PhD

Revealing the pathophysiology of multiple chemical sensitivity; Immunologic response and gene expression profiling of individuals suffering from chemical sensitivity after a controlled chemical exposure

Department of Systems Biology
Period: 15/12/2012 → 15/12/2015
Number of participants: 7
PhD Student:
Dantoft, Thomas Meinertz (Intern)
Supervisor:
Engkilde, Kåre (Ekstern)
Skovbjerg, Sine (Ekstern)
Main Supervisor:
Hellgren, Lars (Intern)
Examiner:
Madsen, Charlotte Bernhard (Intern)
Poulsen, Lars Kærgaard (Intern)
Sainio, Markku Alarik (Ekstern)

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

Can the use of dairy phospholipids as emulgators protect against a pro-obesogenic intestinal microbiota?
The results from a pilot-study in our labs, indicates that it possible to modulate the composition of the intestinal microbiota by emulsifying fat in milk phospholipids (MPL), instead of using soy-lecithin that is normally used f ex. in infant formulas. In the study, we mimicked the intestinal colonization occurring at birth, by transferring germ-free mice out of the sterile environment and into cages containing faeces from a normal mouse, while they were given the emulsions for three week. The results show that the numbers of bacteria from the phylum Firmicutes decreased in the colon lumen in mice that were given the MPL-based emulsions (fig. 1 below) while Bacteriodetes was not affected. Since obesity-development have been linked to increased ratio between Firmicutes and Bacteriodetes in the colon, the result indicates that it could be possible to reduce the risk of developing obesity later in life by exchanging soy-lecithin with MPL in infant formulas. To elucidate this possibility, we want to perform three studies in which we will validate the results from the pilot-study in a bigger study, determine the mechanism that is explaining the effect on microbial composition and determine whether this effect is persistent also after intake of the emulsion have stopped and whether it actually reduce the risk of developing obesity and metabolic diseases later in life.

National Food Institute
Division of Food Microbiology
Department of Systems Biology
Center for Biological Sequence Analysis
Period: 02/01/2012 → 31/12/2015
Number of participants: 3
Project participant:
Licht, Tine Rask (Intern)
Bennike, Rikke Mette Guldhammer (Intern)
Project Manager, organisational:
Hellgren, Lars (Intern)

Financing sources
Source: Public research council
Name of research programme: Mejerbrugets ForskningsFond
Amount: 360,000.00 Danish Kroner
**Effects of emulgating dietary fat with dairy phospholipids on establishment of the gut microbiota**

Department of Systems Biology  
Period: 01/12/2011 → 02/09/2015  
Number of participants: 6  
Phd Student: Bennike, Rikke Mette Guldhammer (Intern)  
Supervisor: Licht, Tine Rask (Intern)  
Main Supervisor: Hellgren, Lars (Intern)  
Examiner: Jacobsen, Charlotte (Intern)  
Ahrné, Siv (Ekstern)  
Lauridsen, Charlotte (Ekstern)  

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

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**The role of fetal exposures to endotoxins in fetal programming of metabolic syndrome**

Department of Systems Biology  
Period: 01/06/2010 → 27/11/2013  
Number of participants: 6  
Phd Student: Ingvorsen, Camilla (Intern)  
Supervisor: Pedersen, Susanne Brix (Intern)  
Main Supervisor: Hellgren, Lars (Intern)  
Examiner: Nellemann, Christine (Intern)  
Vaag, Allan (Ekstern)  
Zeyda, Maximilian (Ekstern)  

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

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**Innovative Applications of marine phospholipids for development of healthy foods**

National Food Institute  
Period: 15/10/2009 → 24/04/2013  
Number of participants: 7  
Phd Student: Lu, Henna Fung Sieng (Intern)  
Supervisor: Baron, Caroline P. (Intern)  
Nielsen, Nina Skall (Intern)  
Main Supervisor: Jacobsen, Charlotte (Intern)  
Examiner: Hellgren, Lars (Intern)  
Levaas, Erik (Ekstern)  
Olsen, Karsten (Ekstern)
Improved nutritional Properties of dairy fat from cows feed green plant material - the role of peroxime Proliferator-activator receptor agonists

Department of Systems Biology
Period: 01/04/2008 → 18/04/2012
Number of participants: 6
Phd Student:
Drachmann, Tue (Intern)
Supervisor:
Pedersen, Susanne Brix (Intern)
Main Supervisor:
Hellgren, Lars (Intern)
Examiner:
Lundegaard, Claus (Intern)
Jensen, Merete Myrup (Intern)
Madsen, Lise (Ekstern)

Omega-3 food emulsions: Control and Investigation of Molecular Structure in Relation to Lipid Oxidation

National Food Institute
Period: 01/04/2008 → 28/03/2012
Number of participants: 7
Phd Student:
Horn, Anna Frisenfeldt (Intern)
Supervisor:
Nielsen, Nina Skall (Intern)
Szabo, Peter (Intern)
Main Supervisor:
Jacobsen, Charlotte (Intern)
Examiner:
Hellgren, Lars (Intern)
Andersen, Mogens Larsen (Ekstern)
Genot, Claude (Ekstern)

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:
Frøkiær, 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

The Influence of the Physical Properties of Lipid-Formulations on the Developing Immune System in Early Life

Department of Systems Biology
Period: 01/09/2007 → 09/07/2013
Number of participants: 3
Phd Student:
Mathiassen, Jakob Hovalt (Intern)
Supervisor:
Frøkiær, Hanne (Intern)
Main Supervisor:
Hellgren, Lars (Intern)

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

Nutritional Immunology
This project runs under the FoodDTU umbrella, and one of its purposes is to create new collaborations between different DTU institutes with ongoing research related to food science. The participating institutes are DTU-Food, DTU-Biosys and DTU-Aqua. The purpose is to elucidate the impact of specific dietary components including e.g. fish oil on the intestinal microbiota and thereby on the development of the immune system in early life. The results are expected to create a basis for better nutritional advice for pregnant women.

National Food Institute
Department of Systems Biology
University of Copenhagen
Number of participants: 14
Project participant:
Kristensen, Matilde Bylov (Intern)
Wilcks, Andrea (Intern)
Bergström, Anders (Intern)
Nellemann, Christine (Intern)
Kaln, Charlotte (Intern)
Jacobsen, Charlotte (Intern)
Nielsen, Nina Skall (Intern)
Horn, Anna Frisenfeldt (Intern)
Mathiassen, Jakob Hovalt (Intern)
Hellgren, Lars (Intern)
Fink, Lisbeth Nielsen (Intern)
Frekjaer, Hanne (Ekstern)
Broeng Metzdorff, Stine (Ekstern)
Project Manager, organisational:
Licht, Tine Rask (Intern)
Project
Nutritional Immunology
This project runs under the FoodDTU umbrella, and one of its purposes is to create new collaborations between different DTU institutes with ongoing research related to food science. The participating institutes are DTU-Food, DTU-Biosys and DTU-Aqua. The purpose is to elucidate the impact of specific dietary components including e.g. fish oil on the intestinal microbiota and thereby on the development of the immune system in early life. The results are expected to create a basis for better nutritional advice for pregnant women.

National Food Institute

Nutrigenomic Studies of Interactions between gut Microbiota, Enterocytes and the Immune System

Milk Bioactives to Prevent Gut Inflammation
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

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)
Freskær, 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

Enchanging Production of Nutraceuticals in Genetically Engineered Saccharomyces Cerevisiae
Department of Systems Biology
Period: 01/01/2007 → 28/09/2011
Number of participants: 6
Phd Student:
de Andrade Pereira Tavares, Sabina (Intern)
Supervisor:
Gunnarsson, Nina (Intern)
Main Supervisor:
Frisvad, Jens Christian (Intern)
Examiner:
Hellgren, Lars (Intern)
Piskur, Jure (Intern)
vand den Brink, Hans (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: ErhvervsPhD-ordningen VTU
Project: PhD
Isolation of human leukocytes and their chromosomes (part of the total chromosomal analysis system)

Department of Micro- and Nanotechnology
Period: 01/11/2006 → 26/05/2010
Number of participants: 6
PhD Student:
Moresco, Jacob Lange (Intern)
Supervisor:
Dufva, Martin (Intern)
Main Supervisor:
Svendsen, Winnie Edith (Intern)
Examiner:
Hellgren, Lars (Intern)
Pastorekova, Silvia (Ekstern)
Vellekoop, Michael Johannes (Ekstern)

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

Glycoglycerolipids Enzymatic Synthesis and Food Applications

Department of Systems Biology
Period: 01/10/2006 → 30/09/2008
Number of participants: 4
PhD Student:
Acharya, Ashishkumar Hitendrakumar (Intern)
Supervisor:
Sparsø, Flemming Vang (Ekstern)
Xu, Xuebing (Intern)
Main Supervisor:
Hellgren, Lars (Intern)

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

Improvement of Oxidative Stability of Fish Oil Enriched Foods - Ingredients Interactions and Antioxidant Effects

National Food Institute
Period: 01/08/2006 → 23/06/2010
Number of participants: 6
PhD Student:
Sørensen, Ann-Dorit Moltke (Intern)
Supervisor:
Nielsen, Nina Skall (Intern)
Main Supervisor:
Jacobsen, Charlotte (Intern)
Examiner:
Hellgren, Lars (Intern)
Olsen, Karsten (Ekstern)
Villeneuve, Pierre (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: Ansat eksternt
Project: PhD
**Nutritious and Tasty n-3 PUFA rich products for a slim and healthy population : Weight reducing and Metabolic Syndrome Effects of n-3 LCPUFA and LCF**

The aim with the project is to increase our understanding on how long-chained n-3 polyunsaturated fatty acids can be used to increase weight-loss and/or improve the positive health impact of weight-loss in obese persons.

**Administration**

Department of Systems Biology  
Period: 01/08/2006 → 31/07/2010  
Number of participants: 1  
Acronym: Nu3health  
Project ID: 45912  
Project participant: Hellgren, Lars (Intern)

**Financing sources**

Source: Forskningsrådene - Andre  
Name of research programme: Forskningsrådene - Andre  
Amount: 1,164,600.00 Danish Kroner

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**Enzymatic production of ceramide from sphingomyelin**

Ceramide and ceramide derivatives have raised a large interest as active components in both pharmaceutical and cosmetic industry. This interest is based on the fact that ceramide is a highly potent intracellular signalling lipid, involved in the regulation of apoptosis, cell differentiation, transformation and proliferation as well as metabolic regulation. Ceramide is also the main component of the stratum corneum intercellular lipids in the skin and is essential for its water-barrier function. Furthermore, liposomes containing high concentrations of natural ceramides have antitumor activity in vivo and recent results indicate that these liposomes can be used as an effective strategy for diminishing breast and lung cancer tumors. Studies also show that topical mixtures of stratum corneum lipids, dominated by ceramide, are highly efficient in repairing water-barrier function in children suffering from childhood atopic dermatitis. In the cosmetic industry, formulations using ceramide, as a moisture-retaining ingredient is a rapidly growing segment. It is claimed that these products dramatically increase skin's hydration level, repair the cutaneous barrier and prevent vital moisture loss, and contribute to reducing dry flaky skin and aged appearance. Hence, there is a growing market for ceramide and this market is founded on high-value products. Chemical synthesis of ceramide is complex and expensive. Therefore, there is a large interest in obtaining ceramide from other sources, for example through hydrolysis of sphingomyelin (SM). SM is one of the dominating phospholipids in bovine milk and in dairy by-products. The phospholipid fraction in whey contains about 30% SM. Since SM contains a ceramide moiety, whey phospholipids could be a safe and convenient source of ceramide. Hence, enzymatic production of ceramide from dairy phospholipids represents a promising system for a safe production of ceramide. However, this requires the development of efficient and scalable enzyme-based processes for hydrolysis of the phosphodiester bond between ceramide and phosphorylcholine, as well as cost-effective purification of ceramide from the other components of the starting fraction. The modification site for production of ceramide from SM is the bond between the primary hydroxy group of ceramide and phosphorylcholine. Since this bond cannot be specifically broken using chemical hydrolysis, an enzyme-based method must be used. Potential enzymes for cleaving the phosphodiester bond are Sphingomyelinase (SMase) and phospholipase C (PLC). Establishing a profitable enzymatic production of ceramide from sphingomyelin probably requires an enzyme with a high catalytic activity on SM, but relatively low activity on other phospholipids. No previous work has been made concerning this development.

**Administration**

Technical Information Center of Denmark  
Period: 01/03/2005 → 28/02/2008  
Number of participants: 2  
Project ID: 45756  
Project participant:  
Zhang, Long (Intern)  
Hellgren, Lars (Intern)

**Financing sources**

Source: Ph.d. Institut finansieret  
Name of research programme: Ph.d. Institut finansieret  
Amount: 1,400,000.00 Danish Kroner
Enzymatic Production of Ceramide from Sphingomyelin

Ceramide and ceramide derivatives have raised a large interest in being used as active components in both the pharmaceutical and cosmetic industry. The aim of the project is to develop an efficient process and to define the optimal conditions for the enzyme based ceramide production from the hydrolysis of sphingomyelin.

Department of Systems Biology
Period: 01/03/2005 → 31/07/2008
Number of participants: 2
Project ID: 183689
Contact person:
Xu, Xuebing (Intern)
Hellgren, Lars (Intern)

Financing sources
Source: Ph.d. Institut finansieret
Name of research programme: Ph.d. Institut finansieret
Project

Enzymatic Production of Ceramide from Sphingomyelin

Department of Systems Biology
Period: 01/03/2005 → 01/04/2009
Number of participants: 6
Phd Student:
Zhang, Long (Intern)
Supervisor:
Xu, Xuebing (Intern)
Main Supervisor:
Hellgren, Lars (Intern)
Examiner:
Mu, Huiling (Intern)
Adlercreutz, Patrick (Ekstern)
Villeneuve, Pierre (Ekstern)

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

Production and Nutritional Aspects of Butter Enriched with Diacylglycerols

Department of Systems Biology
Period: 15/10/2002 → 27/03/2006
Number of participants: 8
Phd Student:
Kristensen, Janni Brogaard (Intern)
Supervisor:
Jacobsen, Charlotte (Intern)
Nielsen, Nina Skall (Intern)
Xu, Xuebing (Intern)
Main Supervisor:
Mu, Huiling (Intern)
Examiner:
Hellgren, Lars (Intern)
Adlercreutz, Patrick (Ekstern)
Jensen, Merete Myrup (Intern)

Financing sources
Source: Internal funding (public)
Name of research programme: Offentlig finansiering
Marint født 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

Production of magarine fats by lipase-catalysed interesterification a process, quality, and nutritional study for industrial application

Department of Systems Biology
Period: 01/10/2001 → …
Number of participants: 8
Phd Student:
Zhang, Hong (Intern)
Supervisor:
Jacobsen, Charlotte (Intern)
Nilsson, Jörgen (Ekstern)
Pedersen, Lars Saaby (Ekstern)
Main Supervisor:
Adler-Nissen, Jens (Intern)
Examiner:
Hellgren, Lars (Intern)
Adlercreutz, Patrick (Ekstern)
Mortensen, Børge (Ekstern)

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

The importance of sphingolipid metabolism on cholesterol uptake.
The receptor facilitating cholesterol uptake in the small intestine is localized in sphingolipid enriched membrane domains. These domains are implicated as carriers of proteins from the Golgi complex to the plasma membrane, and activities of other proteins localized in these domains are dependent on the rate of sphingolipid synthesis. Therefore, we will determine if it is possible to alter the cholesterol uptake, and thereby the blood-cholesterol level, by altering sphingolipid synthesis either through altered dietary habits or pharmacologically.

Department of Biochemistry and Nutrition
Period: 01/01/2000 → 31/12/2000
Number of participants: 2
Project participant:
Bukhave, Klaus (Intern)
Nutritional importance of dietary sphingolipids

Sphingolipids is a group of lipids which recently have been showed to have large biological activity. Therefore, we determine the content of sphingolipids in danish foodstuff, and study the physiological effects of intake of sphingolipids.

Department of Biochemistry and Nutrition
Period: 01/10/1998 → ...
Number of participants: 1

Absorption og metabolisme af omestrede triglycerider

Department of Systems Biology
Period: 01/08/1998 → 21/02/2003
Number of participants: 6
Phd Student:
Vistisen, Bodil (Intern)
Supervisor:
Mu, Huiling (Intern)
Main Supervisor:
Høy, Carl-Erik (Intern)
Examiner:
Hellgren, Lars (Intern)
Christensen, Michael Søberg (Intern)
Müllertz, Anette (Ekstern)

Emæringsmæssige effekter af mælkefodstoffers fysiske tilstand

Department of Systems Biology
Period: 01/04/1997 → 07/10/2002
Number of participants: 5
Phd Student:
Fruekilde, Maj-Britt (Intern)
Main Supervisor:
Høy, Carl-Erik (Intern)
Examiner:
Hellgren, Lars (Intern)
Jensen, Merete Myrup (Intern)
Müllertz, Anette (Ekstern)
Name of research programme: Sektorministerium, Stip-SU
Project: PhD