

Anderson RC, C. A., McNabb WC, Park ZA, McCann MJ, Kelly WJ, Roy NC (2010). "Lactobacillus plantarum MB452 enhances the function of the intestinal barrier by increasing the expression levels of genes involved in tight junction formation." BMC Microbiology 10: 316.


We evaluated the potential of apple to reduce inflammation. Phenolic compounds and triterpenes were analysed in 109 apple cultivars. Total phenolics ranged from 29 to 7882 µg g−1 of fresh weight (FW) in the flesh and from 733 to 4868 µg g−1 FW in the skin, with flavonols including epicatechin and procyanidins as major components. Ursolic (44.7 to 3522 µg g−1 FW) and oleanolic (47.2 to 838 µg g−1 FW) acids dominated the skin triterpene profile. Five chemically contrasting cultivars were fractionated and their immune-modulating activity measured using two cell-based assays targeting key points in the inflammation process. Cultivars exhibiting high contents of procyanidins were the most potent at inhibiting NF-κB while triterpene-rich fractions reduced the promoter activity of the gene of TNFα. This study provides new insights into how apple genetic diversity could be used to alleviate inflammation.


Three triterpene-caffeates have been isolated from skins of a russeted apple cv. Merton Russet and identified by LC-MS and NMR as betulinic acid-3- cis-caffeate, betulinic acid-3-trans-caffeate, and oleanolic acid-3-trans-caffeate. Betulinic acid-3-trans-caffeate and oleanolic acid-3-trans-caffeate were also found in russeted pear skins. These compounds have not been previously reported in apples or pears, or in any other foods. Their presence was related to suberized tissue as they were only found in russet portions of the partially russeted apple cv. Cox’s Orange Pippin and were not detected in the waxy apple cv. Royal Gala. High concn. of betulinic acid-3-trans-caffeate were found in the bark of both Merton Russet and Royal Gala trees. The 3 triterpene-caffeates showed anti-inflammatory activity in vitro, inhibiting NF-kappaB activation with IC 50’s of 6-9µM. Betulinic acid-3-trans-caffeate, the predominant compound in the apples, was immuno-modulatory at around
10μM in the in vitro and ex vivo bioassays, boosting production of the pro-inflammatory cytokine TNFalpha in cells stimulated with bacterial lipopolysaccharides.


Epigenetic changes in chromatin structure can influence gene expression without affecting the DNA sequence. The most commonly studied epigenetic modification, DNA methylation, has been implicated in normal tissue development and disease progression, and can be influenced by diet and other environmental factors. Current H PLC methods of determining DNA methylation may require relatively large amounts of DNA (50 μg); as many tissues have low DNA yields, this can be hard to achieve. We isolated DNA from mouse colon and liver in a study investigating post-natal supplementation with selenium and folic acid. After optimizing the methods to account for lower initial DNA amounts, we digested 3 μg of DNA to deoxynucleotide monophosphates, then purified and quantified it. Samples were analyzed by reversed-phase H PLC to determine global DNA methylation levels using commercial nucleotide standards. The H PLC column was cooled to 6 degrees C (reducing run time), and detection was at 280 nm (UV). We showed that methylated cytosine can be accurately and reproducibly measured in as little as 3 μg of DNA using this HPLC analysis method (within-assay CV <2%). We also used this method to detect reduced DNA methylation in liver (P = 0.009) in response to post-natal supplementation with selenium and folate.


The mucus layer covering the epithelial surface of the gastrointestinal tract serves as the front line of protection against the luminal contents and plays a key role in the establishment and activity of the commensal microbiota. The composition and complexity of the bacterial community within this environment is altered by the introduction of fermentable dietary components. These dietary components can change the metabolic end products of bacterial fermentation, which in turn are able to modify the expression of mucin genes and proteins leading to an increase in the mucus layer thickness. This review introduces some of the key interactions between fermentable carbohydrates, commensal bacteria, and intestinal cells which influence mucin production.


Animal models are an important tool to understand the complex pathogenesis of inflammatory bowel diseases (IBDs). This study tested the anti-inflammatory potential of a green tea extract rich in polyphenols (GrTP) in the colon of the multidrug resistance targeted mutation (Mdr1a(-/-)) mouse model of IBD. Insights into mechanisms responsible for this
reduction in inflammation were gained using transcriptome and proteome analyses. Mice were randomly assigned to an AIN-76A (control) or GrTP-enriched diet. At 21 or 24 weeks of age, a colonic histological injury score was determined for each mouse, colon mRNA transcript levels were assessed using microarrays, and colon protein expression was measured using two-dimensional gel electrophoresis and liquid chromatography-mass spectrometry protein identification. Mean colonic histological injury score of GrTP-fed Mdr1a(-/-) mice was significantly lower compared to those fed the control diet. Microarray and proteomics analyses showed reduced abundance of transcripts and proteins associated with immune and inflammatory response and fibrinogenesis pathways, and increased abundance of those associated with xenobiotic metabolism pathways in response to GrTP, suggesting that its anti-inflammatory activity is mediated by multiple molecular pathways. Peroxisome proliferator-activated receptor-alpha and signal transducer and activator of transcription 1 appear to be two key molecules which regulate these effects. These results support the view that dietary intake of polyphenols derived from green tea can ameliorate intestinal inflammation in the colon of a mouse model of IBD, and are in agreement with studies suggesting that consumption of green tea may reduce IBD symptoms and therefore play a part in an overall IBD treatment regimen. Copyright 2013 Elsevier Inc. All rights reserved.


Nutrigenomics studies the response of the human genome to diet and the impact of that interaction on health and performance. As such it is a multidisciplinary or "systems biology" approach that utilises the many tools of functional genomics, including genetics, transcriptomics (micro-arrays), proteomics and metabolomics. The goal of nutrigenomics is to develop foods that can be matched to individual human genotypes to benefit the health of those individuals and enhance normal physiological processes. This will lead to the development of personalised nutrition and new foods for individualised health and nutritional benefit. Nutrigenomics New Zealand (NuNZ) is largely funded by the Foundation for Research, Science and Technology (FoRST). Using the combined expertise of scientists within The University of Auckland, AgResearch Limited, HortResearch, and Crop & Food Research, NuNZ is addressing the goals of nutrigenomics with respect to Crohn's Disease. This is one of the Inflammatory Bowel Diseases, and is an ideal first target that will enable us to establish a nutrigenomics capability within New Zealand. Fractions derived from a diverse range of foods that includes fruit, vegetables, cereals, herbs, spices, seafood, meat and milk are being tested for anti-inflammatory efficacy using both cell-based assays and animal models, and those that show promise will eventually be matched to the genotype of patients within New Zealand with Crohn's Disease. Developing an understanding of the link between genotype and diet for Crohn's Disease will lead to improved health and quality of
life for those individuals. The organisational structure and scientific approach of NuNZ will be presented, along with results to date.


Background: Consumption of high-fat diets has negative impacts on health and well-being, some of which may be epigenetically regulated. Selenium and folate are two compounds which influence epigenetic mechanisms. We investigated the hypothesis that post-weaning supplementation with adequate levels of selenium and folate in offspring of female mice fed a high-fat, low selenium and folate diet during gestation and lactation will lead to epigenetic changes of potential importance for long-term health. Methods: Female offspring of mothers fed the experimental diet were either maintained on this diet (HF-low-low), or weaned onto a high-fat diet with sufficient levels of selenium and folate (HF-low-suf), for 8 weeks. Gene and protein expression, DNA methylation, and histone modifications were measured in colon and liver of female offspring. Results: Adequate levels of selenium and folate post-weaning affected gene expression in colon and liver of offspring, including decreasing Slc2a4 gene expression. Protein expression was only altered in the liver. There was no effect of adequate levels of selenium and folate on global histone modifications in the liver. Global liver DNA methylation was decreased in mice switched to adequate levels of selenium and folate, but there was no effect on methylation of specific CpG sites within the Slc2a4 gene in liver. Conclusions: Post-weaning supplementation with adequate levels of selenium and folate in female offspring of mice fed high-fat diets inadequate in selenium and folate during gestation and lactation can alter global DNA methylation in liver. This may be one factor through which the negative effects of a poor diet during early life can be ameliorated. Further research is required to establish what role epigenetic changes play in mediating observed changes in gene and protein expression, and the relevance of these changes to health.


The effects of wet (canned) or dry (kibbled) diets on faecal bacterial populations in the cat were investigated in eight domestic short-haired cats (four males and four females; averaging 6 years of age and 3.4 kg) in a nested design. The cats were fed ad libitum a commercially available wet diet (moisture 82.0 %, crude protein 51.7 %, fat 28.9 %, carbohydrate (CHO) 8.9% and ash 10.6% DM) for 5 weeks. On the fifth week, individual feed intakes and faecal outputs were determined. Fresh faecal samples were collected twice daily, mixed for homogeneity, subsampled and stored at -85 degrees C until analysis. The cats were then switched to a commercially available dry diet (moisture 8.5%, crude protein 33.0 %, fat 11.0 %, CHO 49.4% and ash 6.6% DM) for 5 weeks, and fresh faeces were sampled as described previously. Energy intake tended to be higher in cats fed dry diets (P<0.10), but body weight was similar between the two feeding periods (P>0.05). Denaturing gradient gel electrophoresis (DGGE) of bacterial 16S rRNA genes amplified from DNA extracted from faeces was performed. The unweighted pair group method with arithmetic
mean cluster analysis of bacterial community profiles using Pearson's correlation revealed diet-specific clustering when the same cats were fed on either a dry or a wet diet (dissimilarity between the groups, 88.6 %; P<0.001). Subsequent cloning and sequencing of five selected distinct DGGE bands indicated that members of the Pelomonas and Fusobacteriaceae were influenced by a short-term change in diet format. This suggests that 5-week dietary exposure is sufficient to alter gastrointestinal microflora.


Smart Foods, or foods with functions that confer health benefits, are the future of the food and nutrition sectors. Pastoral products such as milk and meat are easily manipulated to improve the health benefits of these products. Therefore, there is the potential for farmers to add value to their current products. Additionally, the identification of key nutrients for health and the prevention of disease using nutrigenomic and nutritional epigenetic approaches may identify new ways to manipulate milk and meat products. However, consumer perceptions of product efficacy and the marketing of foods with health claims will be drivers behind the uptake of Smart Foods in the future.


The field of personalized medicine is currently broadening in scope in at least three crucial dimensions. First, while genetics/genomics individual variability is an important aspect of personalized medicine, it is clear that environmental, nutritional, lifestyle and social risk factors play a crucial role for suboptimal therapeutics or disease susceptibility. Second, personalized medicine can inform not only drug therapy but also preventative medicine such that public health interventions that mitigate or prevent disease risks are also customized at an individual and subpopulation level. Third, personalized medicine is now truly global in scope demanding scholarship and innovation analysis beyond the developed countries. In this paper, we critically bring together these three emerging and broader strands of personalized medicine by focusing on prevention of prostate cancer in the developing world. Although prostate cancer prevalence used to be lower in developing countries in the past, this situation is beginning to change rapidly as people living in the developing world transition to a lifestyle more similar to that found in affluent countries. This transition to decreased physical activity, burgeoning overweight/obesity levels, changing nutritional habits, and greater consumption of tobacco, leads to an increased prevalence of non-communicable diseases. There are indications that these changes may also lead to an increase in prostate cancer in low and middle income countries (LMICs). We outline the risk factors associated with prostate cancer, some of the changes that are taking place in LMICs, the reasons behind these changes and the need for personalized or rationally targeted preventative interventions against prostate cancer in LMICs and globally. © 2012 Bentham Science Publishers.


Background: Variants in the DLG5 gene have been associated with inflammatory bowel disease (IBD) in samples from some, but not all populations. In particular, 2 nonsynonymous single-nucleotide polymorphisms (SNPs), R30Q (rs1248696) and P1371Q (rs2289310), have been associated with an increased risk of IBD, and a common haplotype (called haplotype "A") has been associated with reduced risk. Methods: We genotyped R30Q, P1371Q, and a haplotype A tagging SNP (rs2289311) in a New Zealand Caucasian cohort of 389 Crohn's disease (CD) patients, 406 ulcerative colitis (UC) patients, and 416 population controls. Each SNP was tested for association with disease susceptibility and clinical phenotypes. We also performed a meta-analysis of R30Q data from published association studies. Results: The haplotype A tagging SNP was associated with reduced risk of IBD at the 0.05 significance level (P = 0.036) with an allelic odds ratio of 0.83 (95% confidence interval [CI]: 0.69-0.99). Association with haplotype A was strongest (odds ratio ~0.57) in UC patients with familial IBD or extraintestinal manifestations. The R30Q and P1371Q polymorphisms were not significantly associated with UC, CD, or IBD. Analysis of male and female data did not find any gender-specific associations. Meta-analysis gave no evidence of association of R30Q with IBD. Conclusions: Meta-analysis demonstrates that the minor allele of R30Q is not a risk factor for IBD across populations. This study provides some evidence that DLG5 haplotype A is associated with reduced risk of IBD in the New Zealand Caucasian population, but this association will need to be replicated in an independent sample.


Whole-genome association studies present many new statistical and computational challenges due to the large quantity of data obtained. One of these challenges is haplotype inference; methods for haplotype inference designed for small data sets from candidate-gene studies do not scale well to the large number of individuals genotyped in whole-genome association studies. We present a new method and software for inference of
haplotype phase and missing data that can accurately phase data from whole-genome association studies, and we present the first comparison of haplotype-inference methods for real and simulated data sets with thousands of genotyped individuals. We find that our method outperforms existing methods in terms of both speed and accuracy for large data sets with thousands of individuals and densely spaced genetic markers, and we use our method to phase a real data set of 3,002 individuals genotyped for 490,032 markers in 3.1 days of computing time, with 99% of masked alleles imputed correctly. Our method is implemented in the Beagle software package, which is freely available.


High-throughput technologies in the era of post-genomics provide new opportunities to investigate complex biological systems. Data can be collected for a system of interest at the level of gene expression, protein expression and metabolite concentration changes and then used for the assessment of interactions of molecules. However, the vast amount of information also poses challenges for data management, analysis and interpretation. This paper aims to outline the technical complexity and sources of variation in the technologies involved in molecular systems biology and computational strategies for data integration.


Background: The polyphenolic products of the phenylpropanoid pathway, including proanthocyanidins, anthocyanins and flavonols, possess antioxidant properties that may provide health benefits. To investigate the genetic architecture of control of their biosynthesis in apple fruit, various polyphenolic compounds were quantified in progeny from a 'Royal Gala'x'Braeburn' apple population segregating for antioxidant content, using ultra high performance liquid chromatography of extracts derived from fruit cortex and skin. Results: Construction of genetic maps for 'Royal Gala' and 'Braeburn' enabled detection of 79 quantitative trait loci (QTL) for content of 17 fruit polyphenolic compounds. Seven QTL clusters were stable across two years of harvest and included QTLs for content of flavanols, flavonols, anthocyanins and hydroxycinnamic acids. Alignment of the parental genetic maps with the apple whole genome sequence in silico enabled screening for co-segregation with the QTLs of a range of candidate genes coding for enzymes in the polyphenolic biosynthetic pathway. This co-location was confirmed by genetic mapping of markers derived from the gene sequences. Leucoanthocyanidin reductase (LAR1) co-located with a QTL cluster for the fruit flavanols catechin, epicatechin, procyanidin dimer and five unknown procyanidin oligomers identified near the top of linkage group (LG) 16, while hydroxy cinnamate/quinate transferase (HCT/HQT) co-located with a QTL for chlorogenic acid concentration mapping near the bottom of LG 17. Conclusion: We conclude that LAR1 and HCT/HQT are likely to
influence the concentration of these compounds in apple fruit and provide useful allele-specific markers for marker assisted selection of trees bearing fruit with healthy attributes.


The aim of this study was to apply flow cytometric (FCM) analysis to assess the use of sucrose and lecithin vesicles for the protection of probiotic lactic acid bacteria in response to the challenge of gastric acidity and bile salts. FCM analysis in combination with fluorescent probes carboxyfluorescein (cF) and propidium iodide was used to reveal the physiological heterogeneity in the stressed bacteria population. Three subpopulations (intact, stressed, and damaged) were differentiated by FCM in all six examined strains. Significant changes were observed in the presence of the selected protectants. The addition of 20 mM sucrose in the simulated gastric fluid substantially increased the number of intact cells over 20 folds and reduced the damaged subpopulation by half. The presence of 2 % (w/v) lecithin vesicles was shown to protect 50 % more intact cells from the challenge of bile salts. The improved survival as evaluated by FCM analysis was further assessed for the proliferation capacity by sorting a number of cells from each subpopulation on nutrient agar plate. The result confirmed conformity between the proliferation-based cultivability and the probe-indicated viability in the samples of the intact and the damaged subpopulations. However, it also revealed the complexities of the stressed (injured) subpopulation. In conclusion, FCM analysis confirmed that the selected protectants could improve the survival of the probiotic strains in the simulated GI environments. The FCM analysis also proved to be a useful analytical tool for the probiotics research.


Probiotic bacteria were previously encapsulated in sub-100 µm Ca(2+) alginate microcapsules for enhanced survival in human gastrointestinal tract. The aim of this study is to evaluate the altered mucoadhesive property of the probiotic delivery system by coating it with mucoadhesive chitosan or thiolated chitosan, for prolonged retention in human colon. The results confirmed that cross-linking with calcium ions reduced the mucoadhesive property of alginate hydrogel, thus questioning the intrinsic mucoadhesiveness of uncoated systems. In contrast, chitosan and thiolated chitosan were found to be adsorbed on sub-100 µm Ca(2+) alginate microcapsules, and substantially improved the mucoadhesion performance of the system. The adhesion performance was correlated to the amount of mucoadhesive coating polymer adsorbed on the surface of the system. The coated system was demonstrated on HT29-MTX colonic epithelial monolayer to deliver markedly higher amount of probiotic bacteria to the in vitro model of colonic mucosa. Additionally, the coatings were also found to exert significantly stronger mucoadhesion to colonic mucosa tissue at slight acid neutral pH with less ambient water, which conforms to the physiological environment of the colon, thus supporting prolonged retention in this region.

The aim of this study was to evaluate whether immobilizing a probiotic strain Lactobacillus reuteri DPC16 in chitosan-coated alginate microcapsules affected their inhibitory performance against food-borne pathogens. The probiotic strain was encapsulated in sub-100 μm alginate microspheres which were further coated with chitosan. This type of probiotic microcapsules was investigated in a co-culture model for its effect against two food-borne pathogenic bacteria. The results confirmed the comparable inhibitory performances between the planktonic and the microencapsulated DPC16 in terms of the medium acidification and the reuterin production in the presence of sufficient nutrients. However, if an infertile condition was present, in which energy source was limited, the planktonic DPC16 tended to instantly accumulate a higher concentration of reuterin but at the cost of substantial viability loss, whereas immobilization in the chitosan-coated alginate microcapsules extended the survival of DPC16, albeit with a significantly lower reuterin production. In conclusion, no attenuated antimicrobial effect was observed for the immobilized DPC16 in the co-culture model. Microencapsulation rendered an enhanced protection on the embedded probiotics, but it may also induce an altered availability of substrates to those microorganisms. © 2012 Springer Science+Business Media B.V.


In this study, we applied flow cytometric (FCM) analyses to characterize the resistance of a probiotic strain Lactobacillus reuteri DPC16 (DPC16) against diverse stresses. Two fluorescent probes, propidium iodide (PI) and carboxyfluorescein diacetate (cFDA), were combined to the FCM method to reveal multiple cellular statuses of DPC16. The FCM results confirmed that the DPC16 strain had probiotic potential in respect of acid tolerance and bile resistance, whereby more than 60% of DPC16 bacteria remained intact after 1 h exposure to pH 2.0, and over half of DPC16 bacteria were unaffected by the presence of bile salts at a concentration of 0.2 g/100 mL for 1 h even without nutrient supply. In addition, the comparison among a number of lyo-preservatives for the DPC16 strain confirmed that lactose was able to maintain over 60% viable DPC16 bacteria after the lyophilization and subsequent storage period, outperforming all the other selected sugars. To conclude, the superior stress resistance of the novel DPC16 strain was confirmed by the FCM analyses in this study. The FCM technique also proved to be readily incorporated into probiotics research, and capable of providing insightful information. © 2011 Elsevier Ltd.


The establishment of the health-promoting benefits of probiotics is challenged by the antimicrobial bio-barriers throughout the host's gastrointestinal (GI) tract after oral administration. Although microencapsulation has been frequently utilised to enhance the delivery of probiotics, microcapsules of sub-100 μm were found to be ineffective and therefore questioned as an effective delivery vehicle for viable probiotics despite the sensory advantage. In this study, four probiotics strains were encapsulated in chitosan-coated alginate microcapsules of sub-100 μm. Only a minor protective effect was observed from this original type of microcapsule. In order to enhance the survival of these probiotics, sucrose, a metabolisable sugar, and lecithin vesicles were added to the wall material. Both of the ingredients could be readily encapsulated with the probiotics, and protected them from stresses in the simulated GI fluids. The metabolisable sugar effectively increased the survival
of the probiotics in gastric acid, mainly through energizing the membrane-bound F(1)F(0)-
ATPases. The lecithin vesicles proved to alleviate the bile salt stress, and hence notably
reduced the viability loss at the elevated bile salt concentrations. Overall, three out of the
total four probiotics in the reinforced sub-100 μm microcapsules could significantly
survive through an 8-h sequential treatment of the simulated GI fluids, giving less than 1-log
drop in viable count. The most vulnerable strain of bifidobacteria also yielded a viability
increase of 3-logs from this protection. In conclusion, the sub-100 μm microcapsules can be
a useful vehicle for the delivery of probiotics, as long as suitable protectants are
incorporated in the wall matrix.

aspartic proteinase inhibitor SQAPI, is widely present in the Cucurbitales, comprises a small
multigene family and is a member of the phytocystatin family  " Journal of Molecular Evolution


Evidence that establishes the mechanism of the classes of plant proteinase inhibitors (PIs) is
evaluated. Of the eight classes of PIs, six are unique to plants. Except for plant serpins, there
is evidence that PIs from all other classes form tight binding complexes with their target
proteinases, and that they follow the standard mechanism of inhibition.


Background: There is a probable association between consumption of fruit and vegetables
and reduced risk of cancer, particularly cancer of the digestive tract. This anti-cancer activity
has been attributed in part to anti-oxidants present in these foods. Raspberries in particular
are a rich source of the anti-oxidant compounds, such as polyphenols, anthocyanins and
ellagitannins. Methods: A "colon-available" raspberry extract (CARE) was prepared that
contained phytochemicals surviving a digestion procedure that mimicked the
physiochemical conditions of the upper gastrointestinal tract. The polyphenolic-rich extract
was assessed for anti-cancer properties in a series of in vitro systems that model important
stages of colon carcinogenesis, initiation, promotion and invasion. Results: The
phytochemical composition of CARE was monitored using liquid chromatography mass
spectrometry. The colon-available raspberry extract was reduced in anthocyanins and
ellagitannins compared to the original raspberry juice but enriched in other polyphenols and
polyphenol breakdown products that were more stable to gastrointestinal digestion.
Initiation - CARE caused significant protective effects against DNA damage induced by
hydrogen peroxide in HT29 colon cancer cells measured using single cell
microgelelectrophoresis. Promotion - CARE significantly decreased the population of HT29
cells in the G 1 phase of the cell cycle, effectively reducing the number of cells entering the
cell cycle. However, CARE had no effect on epithelial integrity (barrier function) assessed by
recording the trans-epithelial resistance (TER) of CACO-2 cell monolayers. Invasion - CARE
caused significant inhibition of HT115 colon cancer cell invasion using the matrigel invasion
assay. Conclusion: The results indicate that raspberry phytochemicals likely to reach the
colon are capable of inhibiting several important stages in colon carcinogenesis in vitro.


The dihydrochalcones phloretin and phloridzin are major phenolic constituents of apple fruit. Phloretin-d4, deuterated at both the α and β positions, was prepared by hydrogenolysis of naringenin and by deuterium exchange from unlabelled phloretin using Pd/C and sodium formate with methanol-d1 as the source of deuterium. Deuterated derivatives of the glycosides, phloridzin and naringin dihydrochalcone, were similarly prepared.


Inflammatory bowel disease (IBD) is characterized by intestinal inflammation and is believed to involve complex interactions between genetic, immunological, and environmental factors. We measured changes in the proteome associated with bacterially induced intestinal inflammation in the interleukin 10 gene-deficient (Il10(-/-)) mouse model of IBD, established effects of the dietary polyunsaturated fatty acids (PUFAs) n-3 eicosapentaenoic acid (EPA) and n-6 arachidonic acid (AA) on protein expression (using oleic acid as a control fatty acid), and compared these changes with previously observed transcriptome changes in the same model. Ingenuity pathways analysis of proteomics data showed bacterially induced inflammation was associated with reduced expression of proteins from pathways of metabolism and digestion/absorption/excretion of nutrients/ions, and increased expression of cellular stress and immune response proteins. Both PUFA treatments showed anti-inflammatory activity; EPA appeared to act via the PPARalpha pathway, whereas AA appeared to increase energy metabolism and cytoskeletal organization and reduce cellular stress responses, possibly enabling a more robust response to inflammation. While there was agreement between proteomic and transcriptomic data with respect to pathways, there was limited concordance between individual gene and protein data, reflecting the importance of having both gene and protein data to better understand complex diseases such as IBD.


Multidrug resistance targeted mutation (mdr1a (-/-)) mice spontaneously develop intestinal inflammation. The aim of this study was to further characterize the intestinal inflammation in mdr1a (-/-) mice. Intestinal samples were collected to measure inflammation and gene expression changes over time. The first signs of inflammation occurred around 16 weeks of age and most mdr1a (-/-) mice developed inflammation between 16 and 27 weeks of age. The total histological injury score was the highest in the colon. The inflammatory lesions were transmural and discontinuous, revealing similarities to human inflammatory bowel diseases (IBD). Genes involved in inflammatory response pathways were up-regulated whereas genes involved in biotransformation and transport were down-regulated in colonic epithelial cell scrapings of inflamed mdra1 (-/-) mice at 25 weeks of age compared to non-inflamed FVB mice. These results show overlap to human IBD and strengthen the use of this in vivo model to study human IBD. The anti-inflammatory regenerating islet-derived genes were expressed at a lower level during inflammation initiation in non-inflamed colonic epithelial cell scrapings of mdr1a (-/-) mice at 12 weeks of age. This result suggests that an insufficiently suppressed immune response could be crucial to the initiation and development of intestinal inflammation in mdr1a (-/-) mice.


Inflammatory bowel disease (IBD) is a collective term for conditions characterised by chronic inflammation of the gastrointestinal tract involving an inappropriate immune response to commensal microorganisms in a genetically susceptible host. In this study, we examined the effects of aqueous and ethyl acetate extracts of gold kiwifruit (Actinidia chinensis) or green kiwifruit (Actinidia deliciosa) using in vitro models of IBD. These models comprised primary macrophages and intestinal epithelial cells isolated from IL10 gene deficient (Il10 −/-) and C57BL/6J mice. Whole-genome gene and protein expression level profiling indicated that KFE influenced immune signalling pathways and metabolic processes within the colonic tissue; however, the effects were subtle. In particular, expression levels across gene sets related to adaptive immune pathways were significantly reduced using three of the four KFE in C57BL/6J mice. The present study highlights the importance of investigating food components identified by cell-based assays with appropriate in vivo models before making dietary recommendations, as a food that looks promising in vitro may not be effective in vivo.


Inflammatory bowel disease (IBD) is a chronic, inflammatory disorder of the gastrointestinal tract involving an inappropriate immune response to commensal microorganisms in a genetically susceptible host. This study examined the effects of aqueous and ethyl acetate extracts of gold kiwifruit (Actinidia chinensis) or green kiwifruit (Actinidia deliciosa) using in vitro models of IBD. These models comprised primary macrophages and intestinal epithelial
cells isolated from C57BL/5J and interleukin-10 gene deficient (Il10−/−) mice and RAW 264.7, a murine macrophage-like cell line. All four kiwifruit extracts reduced the activation of these models after lipopolysaccharide stimulation, decreasing nitric oxide and cytokine secretion by both Il10−/− and wild-type cells. The ethyl acetate extracts exhibited the highest anti-inflammatory activity, with almost complete suppression of lipopolysaccharide-stimulated macrophage activation. These results suggest that kiwifruit extracts have significant anti-inflammatory activity relevant to IBD. We suggest that the Il10−/− mouse is a suitable model for further study of these compounds.


Variations in both the genome and epigenome can affect individual nutrient requirements. In order to optimise nutrient intake for good health, it becomes important to understand the way in which nutrients affect the expression of key genes. Epigenetic events imply a change of gene expression without a heritable change in DNA base pairs. These events may result from the action of transcription factors, the methylation of certain DNA bases, changes in chromatin structure through various histone modifications, or the action of non-coding RNAs. Each these classes of events is susceptible to both dietary and environmental influences. Transcription factors trigger gene expression in response to external signals, including certain dietary lipids. Changes in DNA methylation can occur directly, through an imbalance in the methyl donor pool. The key nutrient implicated here is folate, but vitamins B6 or B12, betaine, choline and selenium all play established roles. Dietary effects on DNA methylation may also occur indirectly, through inhibition of DNA methyltransferase enzymes. Inhibitors of such enzymes include various phytochemicals, including a range of polyphenols, such as epigallocatechin gallate, from green tea, or isothiocyanates, which are common in Brassicaceous vegetables. Post-translational modifications of histones play a key role, not only in regulating chromatin structure and gene expression, but also in genomic stability. A range of dietary compounds have been implicated as histone deacetylase inhibitors, including butyrate (produced through the digestion and fermentation of dietary fibres) and isothiocyanates. Single nucleotide polymorphisms in genes affecting methyl donor pools may impact individual susceptibility to epigenetic events, and these will be profoundly influenced by diet, not only pre-conception, but throughout the lifecycle. This paper addresses a hitherto neglected dimension in human nutrigenomics science literature - epigenetics and the importance of dietary effects on the epigenome - in the overarching context of tailoring diets to match people's genetic make-up. © 2009 Bentham Science Publishers Ltd.
Inflammation is a necessary part of the immune response. However, when inflammation persists, the resultant state of chronic inflammation may have a number of secondary consequences associated with increased risk of chronic disease. Among these is an increased rate of mutation. There is evidence to suggest that the accumulation of reactive oxygen and nitrogen species may be a causal factor in chronic inflammation. These reactive species are also produced through the oxidative burst associated with the inflammatory process, and may interact with various cellular components including proteins, lipids and, most important for mutagenesis, nucleic acids. DNA strand breaks are commonly produced, leading to chromosomal mutation. Oxidized bases, abasic sites, DNA-DNA intrastrand adducts, and DNA-protein cross-links also occur. Not only do the nucleic acid products act directly as pro-mutagenic lesions, lipid peroxidation products may also lead to secondary DNA damage, including pro-mutagenic exocyclic DNA adducts. While frameshift and chromosomal mutations have been associated with chronic inflammation, much of the evidence reveals base pair substitution mutations associated with polymerase stalling near the lesions, and base pair mis-incorporation. There are also indirect effects of ROS/RNS through inhibition of DNA repair enzymes and/or effects on metabolic activation of known carcinogens. Certain disease states, including the inflammatory bowel diseases, Crohn's disease and ulcerative colitis are associated with enhanced levels of chronic inflammation, and show evidence of enhanced levels of genetic damage in the colonic mucosa. Mutations may provide at least part of the cause of enhanced susceptibility to chronic diseases associated with chronic inflammation. (C) 2010 Elsevier B.V. All rights reserved.
identified. The probability with which these lead to mutations, and thereby cause cancer, is strongly impacted by variants in genes coding for xenobiotic metabolizing or DNA repair enzymes. Nutrient deficiencies also play a role, which will be exacerbated by variants in metabolic genes. However, many of the causal genes in sporadic CRC have hitherto proved elusive. The power of large international collaborations, coupled with genome-wide association studies, has implicated a major functional role of the tumour growth factor-β pathway in CRC susceptibility. Nutrient regulation of gene expression may be especially important here. Future large collaborative studies must consider gene-gene and gene-diet interactions, coupled with high throughput genomic technologies, in order to uncover the relative roles of genetic variants, mutagenic xenobiotics, nutrient imbalance and gene expression in the etiology of CRC.


Much early work on environmental stress, including ionizing radiation and environmental toxins, emphasised their action on DNA and subsequent mutagenesis in long term effects including germ cell mutagenesis, carcinogenesis and trans-generational effect. However, recent studies are increasingly pointing a complementary role of epigenetic effects in these processes. While a substantial part of the literature focuses on DNA methylation, there is increasing recognition of the role of non-coding RNAs, including small-, micro-, and pi-RNAs, as well as transposable elements. These play key roles in carcinogenesis, and in germ cell changes including trans-generational effects. © 2011.


Watching to see whether their pet has another explosive episode of bloody diarrhea, and the detailed characteristics of those episodes, must be every pet-owner's nightmare. Until now, the standard method of differentiating the two most common forms of chronic enteropathy in dogs, inflammatory bowel disease (IBD) and food-responsive diarrhea, has been to watch their response to various treatments, including an elimination diet. The manuscript by Ontsouka et al. in this issue of the European Journal of Lipid Science and Technology [p. 412-422], is of particular interest for several reasons. Firstly, it relates changes in duodenal gene expression profiles to a longer term reduction in diarrhea. This is important not only in providing a mechanism for this effect, but also implying a potential biomarker that might predict a reduction in the symptoms of chronic enteropathies, without having to wait for the disease process to occur. This thereby adds to a growing literature base endorsing genomic technologies in supporting health claims for pet foods. In addition, the study gives credibility to a fish-meal- and potato protein-based diet, enriched in omega-3 PUFA, in reducing the symptoms of spontaneous diarrhea lasting at least 6 wk. Consequent opportunities and challenges, for pets, other animals and humans, are discussed in the present commentary. See accompanying article http://dx.doi.org/10.1002/ejl.201100343. © 2012 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim.

Crohn's disease is a chronic relapsing condition that has no certain cure. Both genetic susceptibility and nutrition have key roles, but their level of involvement varies between patients. Interacting gene pathways influence the probability of disease development, but these are affected by stress and various environmental factors, including diet. In addition, the role of the gut microbiome must not be underestimated, as it is substantially altered in patients with Crohn's disease. Although an elemental diet might lead to disease remission, reintroducing real foods and sustainable diets in patients with Crohn's disease is currently difficult, and would benefit from the sensitivity and rapid feedback provided by the field of nutrigenomics. Nutrigenomics utilizes high-throughput genomics technologies to reveal changes in gene and protein expression that are modulated by the patient's nutrition. The most widely used technique thus far is transcriptomics, which permits measurement of changes in the expression of thousands of genes simultaneously in one sample. Given the volume of numbers generated in such studies, data-basing and bioinformatics are essential to ensure the correct application of nutrigenomics at the population level. These methods have been successfully applied to animal models of Crohn's disease, and the time is right to move them to human studies. © 2012 Macmillan Publishers Limited. All rights reserved.


Crohn's disease (CD), a form of inflammatory bowel disease (IBD), provides a complex model of host-microbe interactions underpinning disease pathogenesis. Although there is not widespread agreement on the etiology of CD, there is evidence that microorganisms lead to the often severe inflammatory response characteristic of the disease. Despite several microbial candidates, no specific microbe has been considered pathogenic. Instead, the concept of the 'pathogenic community' has emerged from the evidence, whereby the stability of the microbial ecosystem of the healthy human gut is disrupted in response to host genetics and destabilized immunity, perhaps through changing public health practices leading to altered microbial exposures over time. We discuss the complex microbial ecosystem of the mammalian gut, the underlying genetic factors that predispose to CD, and how these gene variants may alter host-microbe interactions and propagate inflammation. Over the next 5 years, the increased understanding of genes involved in CD and the way in which individuals with variants of these genes respond differently to nutrients and drugs will enable the rational development of personalized therapies, using pharmacogenomic and nutrigenomic approaches. © 2009 Expert Reviews Ltd.


Aim: Nutrigenomics reflects gene-diet interactions. In recent years, the science of nutrigenomics has become more sophisticated. We seek to answer the question as to what this might mean for the dietetics profession. Methods: We have critically reviewed recent developments in the area, and considered the importance of new business opportunities being opened up, which exploit the full potential of nutrigenomics for dietitians. Results: Whereas early business models sold genetic test results through direct-to-consumer testing, new business initiatives move dietitians to a central role. This now provides a robust framework that can inform dietitians in their practice. Conclusion: This field represents an


The role of minor variations in genotype and epigenetics in susceptibility to nutrition related diseases is reviewed, including folate requirements, the optimal omega-3 to omega-6 fatty acid ratio required and prenatal and postnatal dietary deficiencies.


Background Human Paneth cell defensins, especially DEFA5, are involved in maintaining homeostasis of the human microbial microflora. Since breakdown of normal mucosal antibacterial defence occurs in inflammatory bowel disease (IBD), variants in the DEFA5 gene could be associated with IBD risk. Subjects A cohort of 25 patients with indeterminate colitis (IC), 405 with ulcerative colitis (UC), and 385 with Crohn's disease (CD), were compared with 201 control individuals from the Canterbury region in New Zealand. Methods A 15 kb haplotype block surrounding DEFA5 contained 35 HapMap markers which were polymorphic in Caucasians. Four markers (A-D) were selected to tag 27 of the 35 markers at $r^2 > 0.68$, and were genotyped in DNA samples. Results Minor allele frequencies for all single nucleotide polymorphisms (SNPs) were somewhat elevated in patients. Subgroup analysis showed SNP A had odds ratio 1.44 in UC patients with panceolitis (95% C.I. 1.07-1.94), SNP B odds ratio 2.37 in CD patients with onset prior to 17 years age (95% C.I. 1.12-5.03), SNP C odds ratio 1.68 in UC patients with left colonic localisation (95% C.I. 1.12-2.52), and SNP D had odds ratio 1.56 in CD patients with one or more relatives with IBD (95% C.I. 1.03-2.35). Two two-marker haplotypes and one three-marker haplotype were associated with UC (p-values 0.025-0.05).


Ferguson, L. R., et al. (2009). "Tumor necrosis factor receptor superfamily, member 1B haplotypes increase or decrease the risk of inflammatory bowel diseases in a New Zealand caucasian population." Gastroenterology research and practice 2009: Article ID 591704.

Inflammatory bowel diseases (IBDs) comprising Crohn disease (CD) and ulcerative colitis (UC) are chronic inflammatory conditions with polygenic susceptibility. Interactions between TNF-alpha and TNF-alpha receptor play a fundamental role in inflammatory response. This study investigates the role that selected single nucleotide polymorphisms (SNPs) and haplotypes in the TNF-alpha receptor (TNSFRSF1B) gene play in the risk of IBD in a New Zealand Caucasian population. DNA samples from 388 CD, 405 UC, 27 indeterminate colitis patients, and 293 randomly selected controls, from Canterbury, New Zealand were screened for 3 common SNPs in TNSFRSF1B: rs1061622 (c.676T>C), rs1061624 (c.+1663A>G), and rs3397
(c.*1690T>C), using TaqMan technologies. Carrying the rs1061624 variant decreased the risk of UC in the left colon (OR 0.73, 95% CI=0.54–1.00) and of being a smoker at diagnosis (OR 0.62; 95% CI=0.40–0.96). Carrying the rs3397 variant decreased the risk of penetrating CD (OR 0.62, 95% CI=0.40–0.95). Three marker haplotype analyses revealed highly significant differences between CD patients and control subjects ($\chi^2=29.9$, df=7, $P<.0001$) and UC cases and controls ($\chi^2=46.3$, df=7, $P<.0001$). We conclude that carrying a 3-marker haplotype in the TNSFRSF18 gene may increase (e.g., haplotype of GGC was 2.9-fold more in the CD or UC patients) or decrease (e.g., TGT was 0.47-fold less in UC patients) the risk of IBD in a New Zealand Caucasian population.


DNA samples from 339 Crohn's disease (CD) and 407 randomly selected controls from the Auckland (New Zealand) IBD project, were genotyped for five common single nucleotide polymorphisms in IL-23R (rs11805303, rs7517847, rs1343151, rs11209026, and rs10889677) and two in IL-12B (rs1363670 and rs6887695). While the IL-12B variants did not show an overall association and other IL23R variants led to minor changes in the risk of CD, rs1343151 and/or rs7517847 variants in the IL-23R gene strongly reduced the risk of developing CD at both allelic and genotype levels. A significantly decreased risk of first diagnosis of childhood CD was observed in individuals carrying the A allele of rs1343151, or between 17-40 y in individuals carrying the G allele in rs7517847 of IL-23R. A significantly decreased risk of ileocolonic or structuring disease was observed in individuals carrying the A allele in either rs11209026 or rs1343151, or the G allele in rs7517847 of IL-23R, and when such individuals did develop the disease, they were unlikely to require a bowel resection. Certain haplotypes very strongly modified risk. There was evidence for interactions of IL-23R variants with the NOD2 wild-type (d/d) genotype. Down-regulating the function of the IL-23R gene may decrease CD risk in the normal population.


The Signal Transducers and Activators of Transcription (STAT)-Janus kinase OAK pathway controls signal transduction between cell surface receptors and the nucleus. Two members of that pathway, STAT3 and JAK2, enhanced the risk of Crohn's disease (CD) in recent genome-wide association studies. We replicated these findings in a New Zealand Caucasian case-control cohort, by genotyping two single nucleotide polymorphisms (SNPs) in STAT3 (rs744166(G >A) and rs3816769(C >T) and rs10758669(A> C) in JAK2, in 302 CD patients and 382 controls. For STAT3, there was a significant decrease in the frequency of the G allele of rs744166 and the C allele of rs3816769 in CD patients as compared with controls (OR = 0.76,95% CI = 0.61-0.95, p = 0.013; OR = 0.71, 95% CI = 0.56-0.89, p = 0.003). For the JAK2 rs10758669 polymorphism, the homozygous C/C or heterozygous A/C genotypes increased the risk of having CD as compared with the homozygous A/A (OR = 1.76,95% CI = 1.26-2.45 and OR = 2.36,95% CI = 1.44-3.86, respectively, p = 0.0003). Variant alleles in either gene significantly modified the likelihood of inflammatory disease in a colonic location, and of developing extra-intestinal manifestations. The JAK2 variant also strongly enhanced the risk of ileocolonic disease, with stricturing or ileal stricturing behaviour, requiring a bowel resection. We further studied a subset of our control population, stratified for JAK2 rs10758669 and/or STAT3 rs3816769 genotype. Carrying either the JAK2 or STAT3 IBD risk
allele was associated with significantly enhanced susceptibility to DNA damage, as estimated by comet assays in peripheral blood leukocytes, with or without a subsequent oxidative challenge. That is, both risk alleles enhance genomic instability. The JAK2 SNP is part of a haplotype previously associated with enhanced susceptibility to myeloproliferative neoplasms, but functional consequences of the STAT3 variant had not been previously demonstrated. It will be of interest to follow up CD patients carrying either JAK2 or STAT3 risk alleles for development of further secondary effects, including cancer. (C) 2010 Elsevier BM. All rights reserved.


Wheat bran protects against mutations and cancer, but contains different plant cell types that are likely to have different protective effects. We previously described the production and chemical characterisation of an aleurone-rich fraction (ARF) and a pericarp-rich fraction (PRF) from wheat grain. We compared these with whole bran (WB), fed to rats as 10% of a high fat AIN-76 diet. All bran-supplemented diets increased faecal bulk, in the order PRF>WB>ARF. PRF increased the activity of NAD(P)H:quinone acceptor oxidoreductase only in the forestomach, whereas ARF and WB enhanced levels of glutathione S-transferase in the duodenum. ARF but not PRF was digested and fermented, and also encouraged bacterial growth. Rats were gavaged with the radioactive mutagen (14)C-labelled IQ (2-amino-3-methylimidazo[4,5-f]quinoline), and effects of the brans on plasma radioactivity measured. Compared with the control diet, all bran-supplemented diets reduced the concentration of radioactivity in plasma, in the order ARF>PRF>WB. All brans increased faecal elimination of radioactivity, but only ARF and PRF enhanced urinary radioactivity. These data suggest that wheat bran may reduce mutation and cancers through direct adsorption and enhanced elimination of a dietary mutagen and/or its metabolites, and that wheat bran enriched in pericarp or aleurone cell walls may exert protective effects through different mechanisms.


AIM: To investigate the role that single nucleotide polymorphisms (SNPs) in the promoter of the tumour necrosis factor-alpha (TNF-alpha) gene play in the risk of inflammatory bowel diseases (IBDs) in a New Zealand population, in the context of international studies.

METHODS: DNA samples from 388 patients with Crohn's disease (CD), 405 ulcerative colitis
(UC), 27 indeterminate colitis (IC) and 201 randomly selected controls, from Canterbury, New Zealand were screened for 3 common polymorphisms in the TNF-alpha receptor: -238 G>A, -308 G>A and -857C>T, using a Taqman R assay. A meta-analysis was performed on the data obtained on these polymorphisms combined with that from other published studies. RESULTS: Individuals carrying the -308 G/A allele had a significantly (OR=1.91, chi 2=17.36, P<0.0001) increased risk of pancolitis, and a 1.57-fold increased risk (OR=1.57, chi 2=4.34, P=0.037) of requiring a bowel resection in UC. Carrying the -857 C/T variant decreased the risk of ileocolonic CD (OR=0.56, chi 2=4.32, P=0.037), and the need for a bowel resection (OR=0.59, chi 2=4.85, P=0.028). The risk of UC was reduced in individuals who were smokers at diagnosis, (OR=0.48, chi 2=4.86, P=0.028). CONCLUSION: TNF-alpha is a key cytokine known to play a role in inflammatory response, and the locus for the gene is found in the IBD3 region on chromosome 6p21, known to be associated with an increased risk for IBD. The -308 G/A SNP in the TNF-alpha promoter is functional, and may account in part for the increased UC risk associated with the IBD3 genomic region. The -857 C/T SNP may decrease IBD risk in certain groups. Pharmaco- or nutrigenomic approaches may be desirable for individuals with such affected genotypes.


Selenium (Se) is an essential micronutrient for humans, acting as a component of the unusual amino acids, selenocysteine (Se-Cys) and selenomethionine (Se-Met). Where Se levels are low, the cell cannot synthesise selenoproteins, although some selenoproteins and some tissues are prioritised over others. Characterised functions of known selenoproteins, include selenium transport (selenoprotein P), antioxidant/redox properties (glutathione peroxidases (GPxs), thioredoxin reductases and selenoprotein P) and anti-inflammatory properties (selenoprotein S and GPx4). Various forms of Se are consumed as part of a normal diet, or as a dietary supplement. Supplementation of tissue culture media, animal or human diets with moderate levels of certain Se compounds may protect against the formation of DNA adducts, DNA or chromosome breakage, and chromosome gain or loss. Protective effects have also been shown on mitochondrial DNA, and on telomere length and function. Some of the effects of Se compounds on gene expression may relate to modulation of DNA methylation or inhibition of histone deacetylation. Despite a large number of positive effects of selenium and selenoproteins in various model systems, there have now been some human clinical trials that have shown adverse effects of Se supplementation, according to various endpoints. Too much Se is as harmful as too little, with animal models
showing a "U"-shaped efficacy curve. Current recommended daily allowances differ among countries, but are generally based on the amount of Se necessary to saturate GPx enzymes. However, increasing evidence suggests that other enzymes may be more important than GPx for Se action, that optimal levels may depend upon the form of Se being ingested, and vary according to genotype. New paradigms, possibly involving nutrigenomic tools, will be necessary to optimise the forms and levels of Se desirable for maximum protection of genomic stability in all humans. © 2012 Elsevier B.V.


There is marked controversy on the beneficial levels of selenium (Se) to be used as a dietary supplement. The form of supplemented Se and the baseline plasma or serum Se status among supplemented populations are generally considered as crucial factors in this controversy. However, responses to supplemented Se can further vary with other factors, including health status, lifestyle, demographics and genetics. In the present study, the putative supplementation benefits of Se as 200 μg/day selenised yeast for six months were evaluated among a stratified male population from Auckland, New Zealand. Our study considered changes in surrogate biomarkers for cancer including antioxidant selenoenzymes glutathione peroxidase (GPx) and thioredoxin reductase activity (TR) levels, basal and peroxide-induced DNA damage levels. A total of 569 subjects self-reporting a European ancestry signed in for the study and provided answers to a basic demographic, health and lifestyle questionnaire. The effects of Se supplementation on biomarkers showed significant variability based on age, BMI, health status and seleno-genotypes of SELS rs4965373, GPx1 rs1050450, and SEPP1 rs3877899. The data indicate that the benefits of supplementary Se vary significantly across a population, based on demographics, lifestyle conditions and seleno-genotypes. As a contrast to "one-size-fits-all" nutritional interventions, these observations collectively inform rational targeting and personalisation of future Se-based dietary supplementation in regards to cancer chemoprevention strategies. This work also represents a way forward in critically understanding Se requirements in populations.


Nutrition-related disorders including cardiovascular disease, diabetes and various cancers rank highly among the causes of death and disability in New Zealand, with significant differences between racial groups in disease susceptibility. While the bulk of the population are Caucasians, a significant proportion are of Polynesian origins, including both Maori and Pacific Island groups, with an increasing Asian immigrant population. Maori have significantly lower colon cancer and significantly higher stomach, breast, lung and pancreatic cancers in comparison with the rest of the population. Both diabetes and cardiovascular disease develop at an earlier age in both Polynesian and Asian groups as compared with those of Caucasian origin. Thus, dietary manipulation has the potential to significantly affect health and disease-related outcomes in the different racial groups of New Zealand.

However, major dietary changes within the population are difficult to implement. Functional foods offer the solution of modifying the nutritive properties of foods that people already consume. New Zealand's high incidence of diet-related diseases makes it an ideal testing ground for new developments in functional foods. The key to these developments is nutrigenomics, which offers approaches powerful enough to explore the complex interactions between nutrients and biological systems, allowing the rational design of functional foods. Copyright © 2005 by New Century Health Publishers, LLC.
on signal transduction, epigenetic effects and modulation of the colonic microflora. Human intervention studies with broccoli and related foods, using standard biomarker methodologies, reveal part of a complex picture. Nutrigenomic approaches, especially transcriptomics, enable simultaneous study of various signalling pathways and networks. Phenotypic, genetic and/or metabolic stratification may identify individuals most likely to respond positively to foods or diets. Jointly, these technologies can provide proof of human efficacy, and may be essential to ensure effective market transfer and uptake of broccoli and related foods.


Inflammatory bowel diseases (IBDs), Crohn's disease (CD), and ulcerative colitis (UC) are chronic inflammatory conditions, which are increasing in incidence, prevalence, and severity, in many countries. While there is genetic susceptibility to IBD, the probability of disease development is modified by diet, lifestyle, and endogenous factors, including the gut microbiota. For example, high intakes of mono- and disaccharides, and total fats consistently increases the risk developing both forms of IBD. High vegetable intake reduces the risk of UC, whereas increased fruit and/or dietary fiber intake appears protective against CD. Low levels of certain micronutrients, especially vitamin D, may increase the risk of both diseases. Dietary patterns may be even more important to disease susceptibility than the levels of individual foods or nutrients. Various dietary regimes may modify disease symptoms, in part through their actions on the host microbiota. Both probiotics and prebiotics may modulate the microflora, and reduce the likelihood of IBD regression. However, other dietary factors
affect the microbiota in different ways. Distinguishing cause from effect, and characterizing the relative roles of human and microbial genes, diet, age of onset, gender, lifestyle, smoking history, ethnic background, environmental exposures, and medications, will require innovative and internationally integrated approaches.


New Zealand has one of the highest incidence rates of Crohn's Disease (CD), whilst the serum selenium status of New Zealanders is amongst the lowest in the world. A prospective case-control study in Auckland, New Zealand considered serum selenium as a potential CD risk factor. Serum selenium levels were significantly lower in CD patients compared to controls (101.8 ± 1.02 vs. 111.1 ± 1.01 ng/mL) (p = 5.91 × 10). Recent detailed studies in the United Kingdom have suggested an optimal serum level around 122 ng/mL, making the average CD patient in New Zealand selenium deficient. Of the 29 single nucleotide polymorphisms (SNPs) tested, 13 were found to significantly interact with serum selenium on CD. After adjustment for multiple testing, a significant interaction with serum selenium on CD was found for three SNPs, namely rs17529609 and rs7901303 in the gene SEPHS1, and rs1553153 in the gene SEPSECS. These three SNPs have not been reported elsewhere as being significantly associated with selenium or CD. It is unclear as to whether lower selenium levels are a cause or an effect of the disease. © 2012 by the authors; licensee MDPI, Basel, Switzerland.


Currently, the regulation of complementary and alternative medicines and related health claims in Australia and New Zealand is managed in a number of ways. Complementary medicines, including herbal, minerals, nutritional/dietary supplements, aromatherapy oils and homeopathic medicines are regulated under therapeutic goods/products legislation. The Therapeutic Goods Administration (TGA), a division of the Commonwealth Department of Health and Ageing is responsible for administering the provisions of the legislation in Australia. The New Zealand Medicines and Medical Devices Safety Authority (Medsafe) administers the provision of legislation in New Zealand. In December 2003 the Australian and New Zealand governments signed a Treaty to establish a single, bi-national agency to regulate therapeutic products, including medical devices prescription, over-the-counter and complementary medicines. A single agency will replace the Australian TGA and the New Zealand Medsafe. The role of the new agency will be to safeguard public health through regulation of the quality, safety and efficacy or performance of therapeutic products in both Australia and New Zealand. The major activities of the new joint Australia New Zealand therapeutic products agency are in product licensing, specifying labelling standards and setting the advertising scheme, together with determining the risk classes of medicines and creating an expanded list of ingredients permitted in Class I medicines. A new, expanded definition of complementary medicines is proposed and this definition is currently under consultation. Related Australian and New Zealand legislation is being developed to implement the joint scheme. Once this legislation is passed, the Treaty will come into force and the new joint regulatory scheme will begin. The agency is expected to commence operation no later than 1 July 2006 and will result in a single agency to regulate complementary and alternative medicines.
The success of the Human Genome Project and the spectacular development of broad genomics tools have catalyzed a new era in both medicine and nutrition. The terms pharmacogenomics and nutrigenomics are relatively new. Both have grown out of their genetic forbears as large-scale genomics technologies have been developed in the last decade. The aim of both disciplines is to individualize or personalize medicine and food and nutrition, and ultimately health, by tailoring the drug or the food to the individual genotype. This review article provides an overview of synergies and differences between these two potentially powerful science areas. Individual genetic variation is the common factor on which both pharmacogenomics and nutrigenomics are based. Each human is genetically (including epigenetics) unique and phenotypically distinct. One of the expectations of both technologies is that a wide range of gene variants and related single-nucleotide polymorphism will be identified as to their importance in health status, validated and incorporated into genotype based strategies for the optimization of health and the prevention of disease. Pharmacogenomics requires rigorous genomic testing that will be regulated and analyzed by professionals and acted on by medical practitioners. As further information is obtained on the importance of the interaction of food and the human genotype in disease prevention and health, pharmacogenomics can provide an opportunity driver for nutrigenomics. As we move from disease treatment to disease prevention, the two disciplines will become more closely aligned.

The traditional Mediterranean diet is thought to represent a healthy lifestyle; especially given the incidence of several cancers including colorectal cancer is lower in Mediterranean countries compared to Northern Europe. Olive oil, a central component of the Mediterranean diet, is believed to beneficially affect numerous biological processes. We used phenols extracted from virgin olive oil on a series of in vitro systems that model important stages of colon carcinogenesis. The effect the extract on DNA damage induced by hydrogen peroxide was measured in HT29 cells using single cell microgel-electrophoresis. A significant anti-genotoxic linear trend (\( p=0.011 \)) was observed when HT29 cells were pre-incubated with olive oil phenols (0, 5, 10, 25, 50, 75, 100 g/ml) for 24 hr, then challenged with hydrogen peroxide. The olive oil phenols (50, 100 g/ml) significantly (\( p=0.004, p=0.002 \)) improved barrier function of CACO2 cells after 48 hr as measured by trans-epithelial resistance. Significant inhibition of HT115 invasion (\( p<0.01 \)) was observed at olive oil phenols concentrations of 25, 50, 75, 100 g/ml using the matrigel invasion assay. No effect was observed on HT115 viability over the concentration range 0, 25, 50 75, 100 g/ml after 24 hr, although 75 and 100 g/ml olive oil phenols significantly inhibited HT115 cell attachment (\( p=0.011, p=0.006 \)). Olive oil phenols had no significant effect on metastasis-related gene expression in HT115 cells. We have demonstrated that phenols extracted from virgin olive oil are capable of inhibiting several stages in colon carcinogenesis in vitro.

Olive oil phenols had no significant effect on metastasis-related gene expression in HT115 cells. We have demonstrated that phenols extracted from virgin olive oil are capable of inhibiting several stages in colon carcinogenesis in vitro.

Long-chain (LC) n-3 PUFA have a broad range of biological properties that can be achieved at the gene expression level. This has been well described in liver, where LC n-3 PUFA modulate the expression of genes related to lipid metabolism. However, the complexity of biological pathway modulations and the nature of bioactive molecules are still under investigation. The present study aimed to investigate the dose-response effects of LC n-3 PUFA on the production of peroxidised metabolites, as potential bioactive molecules, and on global gene expression in liver. Hypercholesterolaemic rabbits received by daily oral administration (7 weeks) either oleic acid-rich oil or a mixture of oils providing 0.1, 0.5 or 1% (groups 1, 2 and 3 respectively) of energy as DHA. Levels of specific peroxidised metabolites, namely 4-hydroxyhexenal (4-HHE)-protein adducts, issued from LC n-3 PUFA were measured by GC/MS/MS in liver in parallel to transcription profiling. The intake of LC n-3 PUFA increased, in a dose-dependent manner, the hepatic production of 4-HHE. At the highest dose, LC n-3 PUFA provoked an accumulation of TAG in liver, which can be directly linked to increased mRNA levels of lipoprotein hepatic receptors (LDL-receptor and VLDL-receptor). In groups 1 and 2, the mRNA levels of microsomal TAG transfer protein decreased, suggesting a possible new mechanism to reduce VLDL secretion. These modulations of genes related to lipoprotein metabolism were independent of PPAR alpha signalling but were probably linked to the activation of the farnesol X receptor pathway by LC n-3 PUFA and/or their metabolites such as HHE.


Children born small-for-gestational-age (SGA) are at increased risk of developing obesity and metabolic diseases later in life, a risk which is magnified if followed by accelerated postnatal growth. We investigated whether common gene variants associated with adult obesity were associated with increased postnatal growth, as measured by BMI z-score, in children born SGA and appropriate for gestational age (AGA) in the Auckland Birthweight Collaborative.


Proanthocyanidins (PAs) are products of the flavonoid pathway, which also leads to the production of anthocyanins and flavonols. Many flavonoids have antioxidant properties and may have beneficial effects for human health. PAs are found in the seeds and fruits of many plants. In apple fruit (Malus x domestica Borkh.), the flavonoid biosynthetic pathway is most active in the skin, with the flavan-3-ols, catechin, and epicatechin acting as the initiating units for the synthesis of PA polymers. This study examined the genes involved in the production of PAs in three apple cultivars: two heritage apple cultivars, Hetlina and Devonshire Quarrenden, and a commercial cultivar, Royal Gala. HPLC analysis shows that tree-ripe fruit from Hetlina and Devonshire Quarrenden had a higher phenolic content than Royal Gala. Epicatechin and catechin biosynthesis is under the control of the biosynthetic enzymes anthocyanidin reductase (ANR) and leucoanthocyanidin reductase (LAR1), respectively. Counter-intuitively, real-time quantitative PCR analysis showed that the expression levels of Royal Gala LAR1 and ANR were significantly higher than those of both Devonshire Quarrenden and Hetlina. This suggests that a compensatory feedback mechanism may be active, whereby low concentrations of PAs may induce higher expression of gene transcripts. Further investigation is required into the regulation of these key enzymes in apple.


BACKGROUND: Single nucleotide polymorphisms (SNPs) in the multidrug transporter MDR1 have been associated with inflammatory bowel disease (IBD) in different studies. However, the data are highly controversial. Recently, 6 haplotype tagging SNPs (tSNPs), representing the haplotype variations of the MDR1 gene, were identified. The aims of this study were to genotype these variants and correlate them to disease phenotype in New Zealand IBD patients.

MATERIALS AND METHODS: A total of 784 IBD patients and 200 healthy subjects were genotyped for 5 tSNPs and the triallelic MDR1 variant G2677T/A using the Sequenom MassArray platform. Furthermore, the effects of these variants were examined in correlation with phenotypic clinical features.

RESULTS: Heterozygous carriers for the variants C1236T, rs2235046 (an SNP in intron 16), and G2677T/A showed a lower risk of developing ulcerative colitis (C1236T: odds ratio [OR] = 0.63, 95% confidence interval [CI] = 0.42-0.93, P = 0.03; G2677T/A: OR = 0.59, CI = 0.39-0.89, P = 0.02; and rs2235046: OR = 0.59, 95% CI = 0.38-0.91, P = 0.009) as compared with homozygotes. None of the analyzed markers were associated with Crohn's disease on a genotypic level. Subgroup analysis revealed an association for 2 variants with IBD when stratified for age of onset (C1236T SNP and rs3789243). The MDR1 variant C3435T was associated with disease behavior in CD (OR = 1.45, 95% CI = 1.01-2.08, P = 0.04), whereas the SNP rs3789243 was found to be associated with pancolitis in UC patients (OR = 1.35, CI = 1.00-1.82, P = 0.05).

CONCLUSIONS: The results of our study support the role of MDR1 as a candidate gene for ulcerative colitis. Furthermore, our results suggest the possibility of a heterozygous advantage for certain MDR1 variants for this disease. Copyright 2009 Crohn's & Colitis Foundation of America, Inc.


Increased numbers of adherent invasive Escherichia coli (AIEC) have been found in Crohn's disease (CD) patients. In this report, we investigate the potential of the probiotic Escherichia coli Nissle 1917 (EcN) to reduce features associated with AIEC pathogenicity in an already established infection with AIEC reference strain LF82.


Background. The nucleotide-binding oligomerization domain containing 1 (NOD1) gene encodes a pattern recognition receptor that senses pathogens, leading to downstream responses characteristic of innate immunity. We investigated the role of NOD1 single nucleotide polymorphisms (SNPs) on IBD risk in a New Zealand Caucasian population, and studied Nod1 expression in response to bacterial invasion in the Caco2 cell line. Findings. DNA samples from 388 Crohn's disease (CD), 405 ulcerative colitis (UC), 27 indeterminate colitis patients and 201 randomly selected controls, from Canterbury, New Zealand were screened for 3 common SNPs in NOD1, using the MassARRAY iPLEX Gold assay. Transcriptional activation of the protein produced by NOD1 (Nod1) was studied after infection of Caco2 cells with Escherichia coli LF82. Carrying the rs2075818 G allele decreased the risk of CD (OR = 0.66, 95% CI = 0.50-0.88, p < 0.002) but not UC. There was an increased frequency of the three SNP (rs2075818, rs2075822, rs2907748) haplotype, CTG (p = 0.004) and a decreased frequency of the GTG haplotype (p = 0.02).in CD. The rs2075822 CT or TT genotypes were at an increased frequency (genotype p value = 0.02), while the rs2907748 AA or AG genotypes showed decreased frequencies in UC (p = 0.04), but not in CD.
Functional assays showed that Nod1 is produced 6 hours after bacterial invasion of the Caco2 cell line. Conclusion. The NOD1 gene is important in signalling invasion of colonic cells by pathogenic bacteria, indicative of its key role in innate immunity. Carrying specific SNPs in this gene significantly modifies the risk of CD and/or UC in a New Zealand Caucasian population. © 2009 Ferguson et al.


Kiwifruit are nutrient-dense fruit with a reputation for promoting good health. Although this could be attributed to the high vitamin C content of kiwifruit, other phytochemicals could also provide health benefits. Kiwifruit are commonly reported to be a good source of vitamin E and in addition contain phenolics and carotenoids. The antioxidant properties of kiwifruit have received attention as possible mechanisms for their health-promoting effects. In this review, the antioxidant capacity of kiwifruit is discussed in the context of biologically relevant in vitro assays for predicting antioxidant activity in a biological setting compared with chemical antioxidant assays, and the ability of kiwifruit to protect cells from dying after exposure to an oxidative insult by hydrogen peroxide (cytoprotection). Some recent data are included, where extracts from twenty kiwifruit genotypes, derived from germplasm held at The New Zealand Institute for Plant & Food Research Ltd, were compared for their cellular antioxidant activity and cytoprotection, using human gut derived epithelial cell lines. Our knowledge of how this type of result is currently reflected in vivo is summarised, together with the ‘naturally protective’ properties of kiwifruit that involve modulating immune responses in a positive way. Finally, the ways in which these antioxidant and natural protective properties of kiwifruit may influence human health and wellness are discussed.


Crohn's disease and ulcerative colitis, the two common forms of inflammatory bowel disease (IBD), affect over 2.5 million people of European ancestry, with rising prevalence in other populations. Genome-wide association studies and subsequent meta-analyses of these two diseases as separate phenotypes have implicated previously unsuspected mechanisms, such as autophagy, in their pathogenesis and showed that some IBD loci are shared with other
inflammatory diseases. Here we expand on the knowledge of relevant pathways by undertaking a meta-analysis of Crohn's disease and ulcerative colitis genome-wide association scans, followed by extensive validation of significant findings, with a combined total of more than 75,000 cases and controls. We identify 71 new associations, for a total of 163 IBD loci, that meet genome-wide significance thresholds. Most loci contribute to both phenotypes, and both directional (consistently favouring one allele over the course of human history) and balancing (favouring the retention of both alleles within populations) selection effects are evident. Many IBD loci are also implicated in other immune-mediated disorders, most notably with ankylosing spondylitis and psoriasis. We also observe considerable overlap between susceptibility loci for IBD and mycobacterial infection. Gene co-expression network analysis emphasizes this relationship, with pathways shared between host responses to mycobacteria and those predisposing to IBD. © 2012 Macmillan Publishers Limited. All rights reserved.


Nutrigenomics is the study of how constituents of the diet interact with genes, and their products, to alter phenotype and, conversely, how genes and their products metabolise these constituents into nutrients, antinutrients, and bioactive compounds. Results from molecular and genetic epidemiological studies indicate that dietary unbalance can alter gene–nutrient interactions in ways that increase the risk of developing chronic disease. The interplay of human genetic variation and environmental factors will make identifying causative genes and nutrients a formidable, but not intractable, challenge. We provide specific recommendations for how to best meet this challenge and discuss the need for new methodologies and the use of comprehensive analyses of nutrient–genotype interactions involving large and diverse populations. The objective of the present paper is to stimulate discourse and collaboration among nutrigenomic researchers and stakeholders, a process that will lead to an increase in global health and wellness by reducing health disparities in developed and developing countries.


Prostate cancer is a leading public health burden worldwide, and in New Zealand it is the most commonly registered cancer and the third leading cause of cancer deaths among males. Genetic variability and its associations with diet, demographic and lifestyle factors could influence the risk of this disease.

Selenium (Se) supplementation was tested in a group of healthy men from Auckland, New Zealand with selenized yeast (Selplex, 200 μg/day) as the supplementation mode. A set of biomarkers, including DNA damage levels and seleno-antioxidant enzyme levels, were evaluated at pre- and postsupplementation time points. Supplementation produced significant increases in serum Se levels, red blood cell (RBC) thioredoxin reductase (TR) activity and peroxide-induced DNA damage, when the mean baseline serum Se level was 110 ng/ml. Those with higher baseline serum Se levels gained less serum Se and showed a significant reduction of RBC glutathione peroxidase (GPx) activity by supplementation. The optimum benefits of supplementation on DNA stability are observed when the serum Se level reaches between >120 and <160 ng/ml. However, the most significant observation was that those with highest baseline DNA damage benefit the most from Se supplementation, whereas those having lower baseline DNA damage are disadvantaged. A dose of 200 μg/day selenized yeast was also shown to be a safer supplementation option compared to a similar dose of selenomethionine (SeMet). This study highlights the requirement for prestratification of a population by standing serum Se level and baseline DNA damage level, before any Se supplementation is carried out.
reaction cell-mass spectrometry, while selenoprotein SNPs were estimated using TaqMan(*) SNP genotyping assays. While antioxidant enzyme activities and DNA damage recorded after a peroxide challenge increased with increasing serum selenium, the inherent DNA damage levels in leukocytes showed no statistically significant relationship with serum selenium. However, these relationships and dietary Se requirements at the individual level were modified by several different SNPs in genes for selenoproteins. The GPx1 rs1050450 C allele was significantly associated with GPx activity. Significant correlations between serum Se level and GPX activity were seen with all genotypes except for homozygous minor allele carriers, while the GPx1 rs1050450 CT genotype showed the highest correlation. Several genotypes showed significant correlations between serum Se and TR activity with SEPP1 rs3877899 GG genotype showing the highest correlation. A significant decreasing trend in DNA damage with increasing serum Se was seen among GPx1 rs1050450 CC and GPx4 rs713041 TT genotype carriers up to a serum Se level of 116 and 149 ng/ml, respectively. In the absence of this genetic information, we would recommend a serum Se concentration in the region of 100-150 ng/ml as providing a useful compromise.


Multiple single nucleotide polymorphisms (SNPs) associated with prostate cancer (PC) have been reported in statistically robust studies in the past but these require an in-depth mechanistic understanding with respect to the biological pathways leading to disease. The current study was carried out to examine the PC and benign urology disease risk associations with lifestyle, demographic and genetic factors in a group of men between the ages 40-81 years from Auckland, New Zealand. The data presented herein support a significant positive association of PC risk with tobacco smoking, and a negative association with alcohol intake. The BMI was not associated with disease risk. The SRD5A2 rs632148 G allele was associated with PC compared to those with benign urology disease, after adjustments were made for the confounding variables. The Gleason score as well as disease aggressiveness of the PC group showed no association with lifestyle, demographic factors or the SNPs studied. The levels of prostate-specific antigen (PSA) significantly increased with age, smoking status and BMI, and decreased with alcohol consumption. The AKR1C3 rs12529 G allele was significantly associated with lower PSA levels in PC and benign urology disease groups compared to healthy controls. The G allele of the SRD5A2 rs632148 SNP has shown a significant interaction with PSA and a higher Gleason score outcome. Taken together, these findings show the utility of these gene variants and patient lifestyle history, together with the diagnostic serum PSA levels, to collectively enhance the understanding of the clinical-pathological variables of PC. Such information will support the selection of more personalised treatment options for this disease greatly impacting public health. © 2013 Bentham Science Publishers.


The kiwifruit is, by definition, a berry: it has a large number of seeds embedded in fleshy, edible tissue. The Latin name of kiwifruit is Actinidia and there are two main species of Actinidia that are commercially important: Actinidia chinensis and Actinidia deliciosa. Kiwifruit are not only enjoyable to eat. They are exceptionally good sources of vitamin C and
they are also excellent sources of potassium and folate and possibly of vitamin E and vitamin K. They contain a most effective laxative. There is very little, if any, loss of nutritional quality during storage. However, the risks from the allergic response to kiwifruit should not be underestimated. © Springer 2006.


Oleic acid (OA) has been used as a control fatty acid in dietary polyunsaturated fatty acid (PUFA) intervention studies due to its lack of effect on eicosanoid biosynthesis. Since the effect of OA as a control fatty acid has not yet been investigated for transcriptomics and proteomics studies, this study aimed to test whether colonic transcriptome and proteome profiles associated with colitis development in mice fed a linoleic acid-rich corn oil-AIN-76A diet (Il10−/− compared to C57 mice) where similar to those of OA-fed Il10−/− compared to C57 mice (genotype comparison). A close clustering of colonic gene and protein expression profiles between the mice fed the AIN-76A or OA diet was observed. Inflammation-induced regulatory processes associated with cellular and humoral immune responses, cellular stress response and metabolic processes related to energy utilization were identified in Il10−/− compared to C57 mice fed either diet. Thus OA was considered as a suitable control unsaturated fatty acid for use in multi-omics PUFA studies. The second aim of this study was to test the effect of an OA-enriched AIN-76A diet compared to a linoleic acid-rich corn oil-AIN-76A diet on colonic transcriptome and proteome changes within Il10−/− or C57 mice (diet comparison). Overall, there was a limited concordance observed between measureable transcriptomics and proteomics profiles for genotype and diet comparisons. This underlines the importance and validity of a systems biology approach to understand the effects of diet on gene expression as a function of the genotype.


The interleukin-10 gene-deficient (Il10−/−) mouse is a model of human inflammatory bowel disease and Ppara has been identified as one of the key genes involved in regulation of colitis in the bacterially inoculated Il10−/− model. The aims were to (1) characterize colitis onset and progression using a histopathological, transcriptomic, and proteomic approach and (2) investigate links between PPARα and IL10 using gene network analysis. Bacterial inoculation resulted in severe colitis in Il10−/- mice from 10 to 12 weeks of age. Innate and adaptive immune responses showed differences in gene expression relating to colitis severity. Actin cytoskeleton dynamics, innate immunity, and apoptosis-linked gene and protein expression data suggested a delayed remodeling process in 12-week-old Il10−/− mice. Gene expression changes in 12-week-old Il10−/− mice were related to PPARα signaling likely to control colitis, but how PPARα activation might regulate intestinal IL10 production remains to be determined.


Increased levels of n-6 arachidonic acid (AA), a precursor of pro-inflammatory eicosanoids, have been found in the colon mucosa of inflammatory bowel disease patients when
compared with healthy subjects. The hypothesis was that dietary AA would aggravate colon inflammation by changing expression of genes in inflammatory signaling pathways. AA-enriched diet was fed to IL10 gene-deficient (Il10-/-) mice, model of a inflammatory bowel disease, and compared with Il10-/ mice fed an oleic acid control diet. Effects of AA on gene expression profiles during colitis were examined using whole genome microarray analysis. Dietary AA decreased the expression levels of some colonic genes in ER stress, complement system, nuclear respiratory factor 2-mediated oxidative stress and positive acute phase response pathways compared with Il10-/ mice fed an oleic acid diet. AA increased the expression levels of fatty acid catabolism genes, but decreased that of lipid synthesis genes during colitis, likely by sterol regulatory element binding transcription factor 1 and target gene regulation. A link has been suggested between AA and reduction of intestinal fibrosis by down-regulating the expression levels of pro-inflammatory and fibrotic marker genes. Contrary to the hypothesis, these findings suggest that dietary AA, in the present experimental conditions, is not pro-inflammatory, reduces ER stress and protects colonocytes from oxidative stress in Il10-/ mice.


The use of "omics" techniques in combination with model systems and molecular tools allows to understand how foods and food components act on metabolic pathways to regulate transcriptional processes. Polyunsaturated fatty acids have distinctive nutritional and metabolic effects because they give rise to lipid mediated products and affect the expression of various genes involved in intestinal inflammation. The present review focuses on the molecular effects of dietary polyunsaturated fatty acids on intestinal inflammation.


**Background/Aims:** Dietary n-3 polyunsaturated fatty acids can reduce inflammation via a range of mechanisms. This study tested the effect of dietary eicosapentaenoic acid (EPA) on intestinal inflammation using interleukin-10 gene-deficient (Il10-) mice. **Methods:** At 35 days of age, 12 weaned Il10-/ and 12 C57 mice were randomly assigned to one of two modified AIN-76A diets, supplemented with 3.7% purified ethyl esters of either EPA (n-3) or oleic acid (OA, control). To identify genes relevant to colon inflammation, transcription profiling (microarrays and qRT-PCR) and bioinformatic analyses were used. **Results:** In this study, dietary EPA reversed the decrease in colon fatty acid -oxidation gene expression observed in OA-fed Il10-/ compared to C57 mice. Il10-/ mice fed the OA diet showed decreased expression of antioxidant enzyme genes, as well as those involved in detoxification of xenobiotics, compared to C57 mice on the same diet. In contrast, dietary EPA increased the expression of these genes in Il10-/ mice. **Conclusions:** These data indicate that dietary EPA-induced endogenous lipid oxidation which might have a potential anti-inflammatory effect on colon tissue. This is supported by the activation of the Ppara gene that regulates the expression of pro-inflammatory and immunomodulatory genes and proteins.


Interleukin-10 gene-deficient (//10(-/-)) mice show a hyper-reaction to normal intestinal bacteria and develop spontaneous colitis similar to that of human Crohn's disease when raised under conventional (but not germ-free) conditions. The lack of ID0 protein in these mice leads to changes in intestinal metabolic and signalling processes. The first aim of this study was to identify changes in the bacterial community of the caeca at 7 weeks of age (preclinical colitis) and at 12 weeks of age (when clinical signs of colitis are present), and establish if there were any changes that could be associated with the mouse genotype. We have previously shown that dietary n-3 and n-6 polyunsaturated fatty acids (PUFA) have anti-inflammatory effects and affect colonic gene expression profiles in //10/-/- mice; therefore, we also aimed to test the effect of the n-3 PUFA eicosapentaenoic acid (EPA) and the n-6 PUFA arachidonic acid (AA) on the bacterial community of caeca in both //10(-/-) and C57 mice fed these diets. The lower number of caecal bacteria observed before colitis (7 weeks of age) in //10(-/-) compared to C57 mice suggests differences in the intestinal bacteria that might be associated with the genotype, and this could contribute to the development of colitis in this mouse model. The number and diversity of caecal bacteria increased after the onset of colitis (12 weeks of age). The increase in caecal Escherichia coli numbers in both inflamed //10/-/- and healthy C57 mice might be attributed to the dietary PUFA (especially dietary AA), and thus not be a cause of colitis development. A possible protective effect of E. coli mediated by PUFA supplementation and associated changes in the bacterial environment could be a subject for further investigation to define the mode of action of PUFA in colitis.


Four ellagitannins from boysenberry, a cross between Rubus loganbaccus and Rubus baileyanus Britt., were isolated by preparative HPLC and the exact structures determined by a combination of LC–ESI-MS/MS, MALDI-TOF-MS and NMR spectroscopy. The two most abundant ellagitannins were identified as sanguin H-6, which is known to be abundant in Rubus species, and the other was identified as an isomer of sanguin H-10, which has not previously been reported in Rubus. The two less abundant ellagitannins were identified as sanguin H-2 and [galloyl–bis-HHDP–glucose]_2-gallate. Sanguin H-2 has been previously reported in Rubus, whereas both sanguin H-2 and [galloyl–bis-HHDP–glucose]_2-gallate have been previously reported as hot-water degradation products of lambertianin C. Even though lambertianin C is reported to be a major ellagitannin in other Rubus species, it was not found in any of the fractions, suggesting that both sanguin H-2 and [galloyl–bis-HHDP–glucose]_2-gallate are present naturally in boysenberry.


Increasing demand for eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) containing fish oils is putting pressure on fish species and numbers. Fisheries provide fish for human consumption, supplement production and fish feeds and are currently supplying fish at a maximum historical rate, suggesting mass-scale fishing is no longer sustainable. However, the health properties of EPA and DHA long-chain (LC) omega-3 polyunsaturated fatty acids (PUFA) demonstrate the necessity for these oils in our diets. EPA and DHA from fish oils show favourable effects in inflammatory bowel disease, some cancers and cardiovascular complications. The high prevalence of these diseases worldwide indicates the requirement for alternative sources of LC-PUFA. Strategies have included plant-based fish diets, although this may compromise the health benefits associated with fish oils. Alternatively, stearidonic acid, the product of α-linolenic acid desaturation, may act as an EPA-enhancing fatty acid. Additionally, algae oils may be a promising omega-3 PUFA source for the future. Algae are beneficial for multiple industries, offering a source of biodiesel and livestock feeds. However, further research is required to develop efficient and sustainable LC-PUFA production from algae. This paper summarises the recent research for developing prospective substitutes for omega-3 PUFA and the current limitations that are faced.


Interleukin-10 is an immunosuppressive cytokine involved in the regulation of gastrointestinal mucosal immunity toward intestinal microbiota. Interleukin-10-deficient (IL10−/−) mice develop Crohn’s disease-like colitis unless raised in germ-free conditions. Previous gas chromatography–mass spectrometry (GC–MS) metabolomic analysis revealed urinary metabolite differences between IL10−/− and wildtype C57BL/6 mice. To determine which of these differences were specifically associated with intestinal inflammation arising from IL10-deficiency, urine samples from IL10−/− and wildtype mice, housed in either conventional or specific pathogen-free conditions, were subjected to GC–MS metabolomic analysis. Fifteen metabolite differences, including fucose, xanthurenic acid, and 5-aminovaleric acid, were associated with intestinal inflammation. Elevated urinary levels of xanthurenic acid in IL10−/− mice were attributed to increased production of kynurenine metabolites that may induce T-cell tolerance toward intestinal microbiota. Liquid chromatography–mass spectrometry analysis confirmed that plasma levels of kynurenine and 3-hydroxykynurenine were elevated in IL10−/− mice. Eleven metabolite differences, including glutaric acid, 2-hydroxyglutaric acid, and 2-hydroxyxidipic acid, were unaffected by the severity of inflammation. These metabolite differences may be associated with residual genes from the embryonic stem cells of the 129P2 mouse strain that were used to create the IL10−/− mouse, or may indicate novel functions of IL10 unrelated to inflammation.

Crohn’s disease is an inflammatory disorder of the bowel, believed to arise from the dysregulation of intestinal mucosal immunity. The interleukin-10-deficient (IL10−/−) mouse, which develops intestinal inflammation in the presence of gut microflora, serves as a mouse model of Crohn’s disease. Nontargeted urinary metabolite profiling was carried out to identify systemic metabolic changes associated with the development of intestinal inflammation caused by IL10-deficiency. Spot urine samples, collected from IL10−/− and wildtype mice at ages 5.5, 7, 8.5, and 10.5 weeks old were analyzed by gas chromatography–mass spectrometry (GCMS). The data were analyzed using XCMS software, multiple t tests, and ANOVA. Among the key metabolic differences detected were elevated urinary levels of xanthurenic acid and fucose in IL10−/− mice relative to wildtype, indicating upregulation of tryptophan catabolism and perturbed fucosylation in IL10−/− mice. Three short-chain dicarboxylic acid metabolites were decreased in urine of IL10−/− mice relative to wildtype, suggesting the downregulation of fatty acid oxidation in IL10−/− mice. These metabolic differences were reproducible in an independent set of mice. This study demonstrates that nontargeted GCMS metabolite profiling of IL10−/− mice can provide insights into the metabolic effects of IL10-deficiency and identify potential markers of intestinal inflammation.


The interleukin-10-deficient (IL-10−/−) mouse, a model of inflammatory bowel disease (IBD), develops intestinal inflammation unless raised in germ-free conditions. The metabolic effects of consuming extracts from the fruits of yellow (*Actinidia chinensis*) or green-fleshed (*A. deliciosa*) kiwifruit that displayed in vitro anti-inflammatory activity were investigated in IL-10−/− mice by metabolomic analysis of urine samples. Kiwifruit-derived metabolites were detected at significantly higher levels in urine of IL-10−/− mice relative to those of wild-type mice, indicating that the metabolism of these metabolites was affected by IL-10−/−-wild-type genotypic differences. Urinary metabolites previously associated with inflammation were not altered by the kiwifruit extracts. This study demonstrates the use of metabolomic analysis to study dietary effects and the influence of genotype on food metabolism, which may have implications on the development of functional foods for the treatment of IBD.


Crohn’s disease (CD) and ulcerative colitis (UC) are inflammatory bowel diseases (IBD) attributed to a dysregulated immune response towards intestinal microbiota. Although various susceptibility genes have been identified for CD and UC, the exact disease etiology is unclear and complicated by the influence of environmental factors. Metabolomic analysis enables high sample throughput measurements of multiple metabolites in biological samples. The use of metabolomic analysis in medical sciences has revealed metabolite perturbations associated with diseases. This article provides a summary of the current understanding of IBD, and describes potential applications and previous metabolomic analysis in IBD research to understand IBD pathogenesis and improve IBD therapy.


Peroxisome proliferator activated receptor gamma (PPARγ) is a ligand-dependent transcription factor and a member of the nuclear receptor superfamily. Acting as sensors of hormones, vitamins, endogenous metabolites and xenobiotic compounds, the nuclear receptors control the expression of a very large number of genes. PPARγ has been known for some time to regulate adipocyte differentiation, fatty acid storage and glucose metabolism, and is a target of anti-diabetic drugs. More recently, PPARγ has been recognized as playing a fundamentally important role in the immune response through its ability to inhibit the expression of inflammatory cytokines and to direct the differentiation of immune cells towards anti-inflammatory phenotypes. A feature of PPARγ is the structural diversity of its ligands, which encompass endogenous metabolites, dietary compounds and synthetic drugs. The high and increasing incidence of inflammatory and allergic disease, coupled with encouraging results from recent clinical trials, suggest that natural PPARγ agonists found in foods may be beneficial to human health by acting as anti-inflammatory molecules. PPARγ is therefore not only a target of the pharmaceutical industry, but also of great potential interest to the food industry, since it is activated by several natural dietary constituents. The prospects for dietary intervention in inflammatory disease have improved somewhat over the last few years, and are reviewed here.

Martin, H., et al. (2014 (in press)). "JAK2 and AMP-kinase inhibition in vitro by food extracts, fractions and purified phytochemicals."
A high-throughput, homogeneous, fluorescence polarization, and fluorescence intensity assay has been developed for the measurement of folate in fruits and vegetables. This assay is based on the competitive displacement of the fluorescent folate ligands Alexa Fluor (Alexa) 594-folate and Alexa 660-folate from bovine milk folate-binding protein by folates in fruit and vegetable extracts. These fluorescent ligands are employed because their excitation and emission maxima are in regions of the spectrum with minimal autofluorescence in many extracts. Folate-binding protein and Alexa-folate were typically used at concentrations of 0.5 microg/ml and 5nM, respectively, in 20-microl volumes in 384-well microplates. The assay is complete within 100 min. The folate estimate is unaffected by the heterogeneity of polyglutamyl residues that complicates the liquid chromatography-mass spectrometry (LC-MS)-based methods of quantification. In this assay, folic acid had an apparent affinity 2.5-fold greater than 5-methyltetrahydrofolate (5MTHF); therefore, it cannot be used to quantify folate when both natural and synthetic folate are present. 5MTHF-equivalent values were measured in broccoli (240 microg/100g), strawberry (113 microg/100g), white grape (32 microg/100g), orange (44 microg/100g), tomato (12 microg/100g), raspberry (31 microg/100g), banana (29 microg/g), and kiwifruit (36 microg/100g). These data are similar to published values. However, the assay will not detect 5-formyltetrahydrofolate which is a significant constituent of the total folate in lettuce, spinach, carrot, and peppers.


Scope There is evidence that a mammalian lignan, enterolactone (ENL), decreases the proliferation rate of prostate cancer cells, although previous studies have used concentrations difficult to achieve through dietary modification. We have therefore investigated the anti-proliferative effects of ENL in an in vitro model of prostate tumourigenesis at concentrations reported to occur in a range of male populations. Methods and results The effects of 0.1 and 1 muM ENL on three markers of viability and proliferation (metabolic activity, growth kinetics, and cell cycle progression) were assessed in the RWPE-1, WPE1-NA22, WPE1-NB14, WPE1-NB11, WPE1-NB26, LNCaP, and PC-3 cell lines over 72 h. Based on these data, we quantified the expression levels of 12 genes involved in the control of DNA replication initiation using TaqMan real-time PCR in the WPE1-NA22, WPE1-NB14,
WPE1-NB11, and WPE1-NB26 cell lines. ENL significantly inhibited the abnormal proliferation of the WPE1-NB14 and WPE1-NB11 cell lines and appears to be a consequence of decreased expression of abnormal chromatin licensing and DNA replication factor 1. Conclusion In contrast to previous studies, concentrations of ENL that are reported after dietary intervention restrict the proliferation of early-stage tumorigenic prostate cell lines by inhibiting the abnormal formation of complexes that initiate DNA replication.


Metabolomics, comprehensive metabolite analysis, is finding increasing application as a tool to measure and enable the manipulation of the phytochemical content of foods, to identify the measures of dietary intake, and to understand human and animal responses to phytochemicals in the diet. Recent applications of metabolomics directed toward understanding the role of phytochemicals in food and nutrition are reviewed.


The major anthocyanins of boysenberry fruit, a cross between Rubus loganbaccus and Rubus baileyanus Britt., were isolated by preparative high-performance liquid chromatography (HPLC). The structures of cyanidin-3-[2-(glucosyl)glucoside] (1) and cyanidin-3-[2-(glucosyl)-6-(rhamnosyl)glucoside] (2) were determined by NMR in 1% DCOOD/D2O. An unusually high chemical shift (2.5) is reported for H-5'" of cyanidin-3-[2-(glucosyl)glucoside].


Metallothioneins (MTs) are excellent candidate genes for Inflammatory Bowel Disease (IBD) and have previously been shown to have altered expression in both animal and human studies of IBD. This is the first study to examine genetic variants within the MT genes and aims to determine whether such genetic variants have an important role in this disease. 28 tag SNPs in genes MT1 (subtypes A, B, E, F, G, H, M, X), MT2, MT3 and MT4 were selected for genotyping in a well-characterized New Zealand dataset consisting of 406 patients with Crohn's Disease and 638 controls. We did not find any evidence of association for MT genetic variation with CD. The lack of association indicates that genetic variants in the MT genes do not play a significant role in predisposing to CD in the New Zealand population.


Increased production of matrix metalloproteinases (MMPs) plays an important role in tissue damage in inflammatory bowel disease (IBD). Genetically encoded variation between individuals in MMP production may therefore contribute to disease onset, type, or severity. We undertook an extensive candidate gene single nucleotide polymorphism (SNP) study of MMP-1, -2, -3, -7, -8, -9, -10, -12, -13, and -14 and tissue inhibitor of metalloproteinases (TIMPs)-1, -3, and -4 in ulcerative colitis (UC). We identified tagging SNPs across these genes, and genotyped these SNPs in a Caucasian New Zealand dataset consisting of 419 UC patients and 907 controls. SNPs in a number of MMP genes were associated with UC. After correcting for multiple testing SNPs in MMP-3, MMP-8, MMP-10, and MMP-14 remained significant in their associations with UC. In a second study, using samples from a Dutch cohort, most of the significant findings in the New Zealand cohort were not replicated. However, data from an international meta-analysis provide some support for the initial findings. In conclusion, this study provides preliminary evidence to suggest that genetic variation in the MMPs may play a role in interindividual differences in UC susceptibility and clinical outcome. Further studies are needed in other cohorts to determine the robustness of these observations in different populations. © 2011 American Society for Histocompatibility and Immunogenetics.


Recent genome-wide association studies have provided evidence for the involvement of 3p21 in the pathogenesis of Crohn's disease (CD). Here we attempted to validate the 3p21 region in a well characterized CD case-control New Zealand dataset of 329 CD patients and 521 controls by genotyping tagging single nucleotide polymorphisms (SNPs) across this region. Analysis revealed significant differences between patients and controls for six of 14 SNPs: rs9874472, rs1800668, rs11716445, rs4283605, rs2131109, and rs6446298. Five of these demonstrated strong interaction with CARD15 and phenotypic analysis demonstrated association of these SNPs with age at first diagnosis, CD location, CD behavior and requirement of bowel resection. The results from this study support the accumulating evidence that suggests the 3p21 region is a CD-associated locus, although it remains unclear which is the causative SNP and/or gene.


Several lines of evidence suggest a possible functional role of Matrix metalloproteinase -2 (MMP-2) in obesity. The aim of this study was to evaluate the role of MMP-2 promoter polymorphisms in percentage body fat (PBF) as a measure of childhood obesity in a New Zealand population.


Background

In a double-blind, randomized, placebo-controlled birth cohort, we have recently shown a beneficial effect of Lactobacillus rhamnosus HN001 (HN001) for the prevention of eczema in children through to 6 years of age but no effect of Bifidobacterium animalis subsp lactis HN019 (HN019).
Objective
Among this cohort of children, we aim to investigate whether these probiotics could modify the expression of genetic predisposition to eczema conferred by genetic variation in susceptibility genes.

Methods
Thirty-three eczema susceptibility SNPs (in eleven genes) were genotyped in 331 children of European ancestry.

Results
Children who carried a genetic variant that put them at a high risk of developing eczema were less likely to develop eczema if they had been randomized to the HN001 intervention group compared to those in the placebo group. HN019 was also able to protect against the effects of some SNPs. As well as modifying genetic susceptibility to childhood eczema, HN001 was also found to modify genetic susceptibility to eczema severity and atopy risk.

Conclusion and Clinical Relevance
This is the first study to show an effect of a probiotic on reducing eczema risk amongst those with particular eczema-associated genotypes. Our findings suggest that Lactobacillus rhamnosus HN001 may be particularly effective in preventing eczema in children with specific high-risk genotypes.


The gene ULK1 is an excellent candidate for Crohn's disease (CD) due to its role in autophagy. A recent study provided evidence for the involvement of ULK1 in the pathogenesis of CD (Henckaerts et al., 2011). We attempted to validate this association, using a candidate gene SNP study of ULK1 in CD. We identified tagging SNPs and genotyped these SNPs using the Sequenom platform in a Caucasian New Zealand dataset consisting of 406 CD patients and 638 controls. In this sample, we were able to demonstrate an association between CD and several different ULK1 SNPs and haplotypes. Phenotypic analysis showed an association with age of diagnosis 17-40 years and inflammatory behaviour. The findings of this study provide evidence to suggest that genetic variation in ULK1 may play a role in interindividual differences in CD susceptibility and clinical outcome.


Toll-like receptors (TLRs) play an important role in the induction and regulation of the innate immune system and have been implicated in both infectious and inflammatory diseases. Recently the first association of TLR10 with Crohn's disease (CD) was reported. Here, we attempted to validate this association, using a candidate gene single nucleotide polymorphism (SNP) study of TLR10 in CD. We identified tagging SNPs, and genotyped these SNPs in a Caucasian New Zealand dataset consisting of 406 CD patients and 638 controls. In
this sample, we were able to demonstrate an association between CD and several different TLR10 SNPs and haplotypes. Phenotypic analysis showed an association with early age at first diagnosis, inflammatory and ileocolonic CD behavior, requirement of bowel resection, and extra intestinal manifestations. This study provides evidence to suggest that genetic variation in TLR10 plays a role in interindividual differences in CD susceptibility and clinical outcome.


Background: Accurate estimates of endogenous ileal total nitrogen and amino acid flows are necessary to ascertain true dietary amino acid digestibility coefficients and for the factorial estimation of dietary amino acid requirements. Objective: The objective was to ascertain endogenous amino acid losses from the small bowel in human subjects consuming a protein-free diet or a diet with enzyme-hydrolyzed casein (EHC; MW <5000) as the sole source of nitrogen. Design: The subjects were 8 men and women with terminal ileum ileostomies after ulcerative colitis who consumed the protein-free and EHC-based diets in a crossover design. Each subject received each test diet in single meals followed by 2 consecutive 9-h total collections of digesta. Digesta samples for the EHC treatment were centrifuged and ultrafiltered (10 000 MW cutoff), with the precipitate-plus-retentate fraction (>10 000 MW) providing a measurement of endogenous ileal amino acids. Results: The mean endogenous flows for most of the amino acids and nitrogen were significantly (P < 0.05) higher when determined with the EHC-based diet than with the protein-free diet. Mean (n = 8) endogenous ileal nitrogen flows were 2061 and 4233 µg/g dry matter intake for the protein-free and EHC-based diets, respectively. Conclusion: The traditional protein-free method underestimates endogenous ileal amino acid loss in adults.


There are millions of microbes that live in the human gut. These are important in digestion as well as defense. The host immune system needs to be able to distinguish between the harmless bacteria and pathogens. The initial interaction between bacteria and the host happen through the pattern recognition receptors (PRRs). As these receptors are in direct
contact with the external environment, this makes them important candidates for regulation by dietary components and therefore potential targets for therapy. In this review, we introduce some of the main PRRs including a cellular process known as autophagy, and how they function. Additionally we review dietary phytochemicals from plants which are believed to be beneficial for humans. The purpose of this review was to give a better understanding of how these components work in order to create better awareness on how they could be explored in the future.


Ng L, K. N., Benjamin CS, Ferguson LR (2012). "Beyond PSA: are new prostate cancer biomarkers of potential value to New Zealand doctors?." New Zealand Medical Journal 125(1353): 59-86.


Background: Dairy products have been perceived as having the potential to cause adverse effects in individuals with Crohn's disease (CD) and are often avoided, potentially increasing the risk of osteoporosis and related morbidity associated with inadequate dietary calcium intake. Objective: To evaluate the self-reported effects of dairy products on CD symptoms and to determine whether these effects differed between types of dairy products consumed and disease state or location. Design: Secondary analysis of dietary survey and clinical data from participants in the Genes and Diet in Inflammatory Bowel Disease study based in Auckland, New Zealand. Subjects/setting: One hundred and sixty-five men and women diagnosed with CD for which both dietary survey data and clinical information were available. Statistical analyses performed: X analysis was conducted to assess whether significant differences in the proportions of responses relating to a worsening of CD symptoms from individual dairy products were evident between individuals with active or quiescent CD, or ileal or colonic disease locations. Odds ratios with confidence interval were calculated to determine whether CD location was associated with risk of any type of adverse reaction to milk products. Logit scales were utilized to depict self-reported CD symptoms associated with individual dairy product consumption for ileal and colonic CD patients. Results: Dairy products had no effect on self-reported CD symptoms for most people. Dairy products with a high fat content were most frequently reported to worsen perceived CD symptoms. Clinically, self-reported CD activity status did not influence responses to dairy products; however, colonic inflammation was more frequently associated with adverse CD effects in comparison to ileal CD involvement. Conclusions: Research outcomes question the necessity of dairy product avoidance in CD patients and illustrate the highly individual nature of dairy product tolerance in this clinical population. © 2011 American Dietetic Association.

Background. Mycobacterium avium subspecies paratuberculosis (MAP) is an infective agent found in ruminants and milk products, which has been suggested to increase the risk of gastrointestinal inflammation in genetically susceptible hosts. It is hypothesized that lactase persistence facilitates exposure to such milk products increasing the likelihood of adverse outcomes. Individuals either homozygous or heterozygous for the T allele of DNA variant, rs4988235, located 14kb upstream from the LCT locus, are associated with having lactase persistence. The aim of this study was to determine whether lactase persistence as evident by the T allele of rs4988235 is associated with Crohn's Disease (CD) in a New Zealand population. Findings. Individuals homozygous for the T allele (T/T genotype) showed a significantly increased risk of having CD as compared with those homozygous for the C allele (OR = 1.61, 95% CI = 1.03-2.51). Additionally, a significant increase in the frequency of the T allele was observed in CD patients (OR = 1.30, 95% CI = 1.05-1.61, p = 0.013), indicating that the T allele encoding lactase persistence was associated with an increased risk of CD. Conclusions. Our findings indicate that lactase persistence as evident by the presence of the T allele of rs4988235 is associated with risk of CD in this New Zealand Caucasian population.


Damage of the intestinal epithelial barrier by xenobiotics or reactive oxygen species and a dysregulated immune response are both factors involved in the pathogenesis of inflammatory bowel diseases (IBD). Curcumin and rutin are polyphenolic compounds known to have antioxidant and anti-inflammatory activities, but their mechanism(s) of action are yet to be fully elucidated. Multidrug resistance gene-deficient (mdr1a--/) mice spontaneously develop intestinal inflammation, predominantly in the colon, with pathology similar to IBD, so this mouse model is relevant for studying diet–gene interactions and potential effects of foods on remission or development of IBD. The present study tested whether the addition of curcumin or rutin to the diet would alleviate colonic inflammation in mdr1a--/ mice. Using whole-genome microarrays, the effect of dietary curcumin on gene expression in colon tissue was also investigated. Twelve mice were randomly assigned to each of three diets (control (AIN-76A), control 0.2 % curcumin or control 0.1 % rutin) and monitored from the age of 7 to 24 weeks. Curcumin, but not rutin, significantly reduced histological signs of colonic inflammation in mdr1a--/ mice. Microarray and pathway analyses suggested that the effect of dietary curcumin on colon inflammation could be via an up-regulation of xenobiotic metabolism and a down-regulation of pro-inflammatory pathways, probably mediated by pregnane X receptor (Pxr) and peroxisome proliferator-activated receptor ? (Ppara) activation of retinoid X receptor (Rxr). These results indicate the potential of global gene expression and pathway analyses to study and better understand the effect of foods in modulating colonic inflammation.


Abstract

Aim: To compare caecal microbiota from mdr1a-/- and wild type (FVB) mice to identify differences in the bacterial community that could influence the intestinal inflammation.

Methods and Results: Caecal microbiota of mdr1a-/- and FVB mice were evaluated at 12 and 25 weeks of age using denaturing gradient gel electrophoresis (DGGE) and quantitative real-time PCR. DGGE fingerprints of FVB and mdr1a-/- mice (with no intestinal inflammation) at 12 weeks revealed differences in the presence of DNA fragments identified as Bacteroides fragilis, B. thetaiotaomicron, B. vulgatus and an uncultured alphaproteobacterium. Escherichia coli and Acinetobacter sp. were only identified in DGGE profiles of mdr1a-/- mice at 25 weeks (with severe intestinal inflammation), which also had a lower number of total bacteria in the caecum compared with FVB mice at same age.

Conclusions: Differences found in the caecal microbiota of FVB and mdr1a-/- mice (12 weeks) suggest that the lack of Abcb1 transporters in intestinal cells due to the disruption of the mdr1a gene might lead to changes in the caecal microbiota. The altered microbiota along with the genetic defect could contribute to the development of intestinal inflammation in mdr1a-/- mice.

Significance and Impact of the Study: Differences in caecal microbiota of mdr1a-/- and FVB mice (12 weeks) suggest genotype specific colonization. The results provide evidence that Abcb1 transporters may regulate host interactions with commensal bacteria. Future work is needed to identify the mechanisms involved in this possible cross-talk between the host intestinal cells and microbiota.


The interleukin-10-deficient (IL10-/-) mouse develops colon inflammation in response to normal intestinal microflora and has been used as a model of Crohn’s disease. Short-Column LCMS metabolite profiling of urine from IL10-/- and wild-type (WT) mice was used, in two independent experiments, to identify mass spectral ions differing in intensity between these two genotypes. Three differential metabolites were identified as xanthurenic acid and as the glucuronides of xanthurenic acid and of α-CEHC (2,5,7,8-tetramethyl-2-(2′-carboxyethyl)-6-hydroxycroman). The significance of several differential metabolites as potential biomarkers of colon inflammation was evaluated in an experiment which compared metabolite concentrations in IL10-/- and WT mice housed, either under conventional conditions and dosed with intestinal microflora, or maintained under specific pathogen-free (SPF) conditions. Concentrations of xanthurenic acid, α-CEHC glucuronide, and an unidentified metabolite m/z 495/-497+ were associated with the degree of inflammation in IL10-/- mice and may prove useful as biomarkers of colon inflammation.


The effect of common dietary polyphenols on growth of human gut bacteria and their adhesion to enterocytes was investigated. The influence on the growth of a probiotic (Lactobacillus rhamnosus), a commensal (Escherichia coli) and two pathogenic bacteria (Staphylococcus aureus, Salmonella typhimurium) was determined, together with effects on adhesion of pathogenic and probiotic bacteria to cultured Caco-2 cells. All polyphenols, except rutin, were found to affect the viability of representative gut flora in vitro, at doses likely to be present in the gastrointestinal tract, but to differing degrees. Naringenin and quercetin were the most active with the lowest minimum inhibitory concentrations for all the four bacteria tested. The remaining polyphenols had the most marked effect on the Gram positive enteropathogen S. aureus. Naringenin and phloridzin were the most effective inhibitors of S. typhimurium adherence to Caco-2 enterocytes while phloridzin and rutin enhanced the adherence of the probiotic L. rhamnosus. Polyphenols appear to have
potential to alter gut microecology and, by affecting the total number of beneficial microflora in the gut, may confer positive gut health benefits.


The rate and extent of in situ digesta transit after ingestion of diets containing dietary fibres differing in their susceptibility to large intestine fermentation were investigated. One hundred and twenty rats were fed diets containing 7.5% cellulose, inulin, potato fibre or maize starch for 3 days, then the same diets with titanium dioxide (TiO$_2$) for 3 days, followed by diets without TiO$_2$ for 2 days. In all diets, TiO$_2$ ratios rapidly increased within 24 h and reached a maximum level in duodenum, caecum and colon within 2–3 days. Inulin, potato fibre and maize starch-fed rats showed higher levels of caecal short-chain fatty acids, lower faecal polysaccharide concentrations, and reduced faecal output than the rats fed cellulose. Inulin was highly susceptible to caecal microbial fermentation compared to the other dietary fibres. Transit of these dietary fibres through the GI tract was rapid, and the rate of digesta transit was not affected by dietary fibre fermentability in the large intestine.


Enteric microbiota has been shown to be associated with various pathological conditions such as inflammatory bowel disease (IBD). This study aimed to determine the anti-inflammatory colonic effects of blueberries and broccoli in mdr1a⁻/⁻ mice (IBD mouse model) through modification of microbiota composition in the gastrointestinal tract. The mdr1a⁻/⁻ mice were fed either a control diet or the control diet supplemented with either 10% blueberry or broccoli for 21 wk. We investigated the influence of these diets on cecal microbiota and organic acids, colon morphology, and bacterial translocation to mesenteric lymph nodes. In comparison to mice fed the control diet, blueberry and broccoli supplementation altered cecum microbiota similarly with the exception of Faecalibacterium prausnitzii, which was found to be significantly lower in broccoli-fed mice. High concentrations of butyric acid and low concentrations of succinic acid were observed in the cecum of broccoli-fed mice. Blueberry- and broccoli-supplemented diets increased colon crypt size and the number of goblet cells per crypt. Only the broccoli-supplemented diet significantly lowered colonic inflammation compared to mice fed the control diet. Translocation of total microbes to mesenteric lymph nodes was lower in broccoli-fed mice compared to blueberry and control diet groups. Dietary blueberries and/or broccoli altered the composition and metabolism of the cecal microbiota and colon morphology. Overall, these results warrant further investigation through clinical studies to establish whether the consumption of blueberries and/or broccoli is able to alter the composition and metabolism of large intestine microbiota and promote colon health in humans.

Carrying a functional single nucleotide polymorphism (L503F, c. 1672 C>T) in the gene for the Na-dependent organic cation transporter (OCTN1), increases the risk of Crohn's disease (CD) in some, but not all, populations. Case–control data on New Zealand Caucasians show no differences for CD risk between individuals carrying the L503F OCTN1 C-allele when compared with those carrying the variant T-allele. However, more of the New Zealand CD cases report intolerance to maize and mushrooms than those who report beneficial effects or no differences. The OCTN1 gene encodes a transporter for ergothionine, a fungal metabolite at high levels in mushrooms but not widely common in other dietary items. An inability to tolerate mushrooms showed statistically significant associations with the variant OCTN1 genotype. That is, among those individuals reporting adverse effects from mushrooms, there was a higher frequency of the variant T-allele when compared with the general population, or with CD patients overall. We believe that this is a novel gene–diet association, suggesting that individuals carrying the OCTN1 variant single nucleotide polymorphism may have an enhanced risk of adverse symptoms associated with consuming mushrooms. Nutrigenomic approaches to dietary recommendations may be appropriate in this group.


Inflammatory bowel diseases (IBDs) such as Crohn's disease are highly debilitating. There are inconsistencies in response to and side effects in the current conventional medications, failures in adequate drug delivery, and the lack of therapeutics to offer complete remission in the presently available treatments of IBD. This suggests the need to explore beyond the horizons of conventional approaches in IBD therapeutics. This review examines the arena of the evolving IBD nanomedicine, studied so far in animal and in vitro models, before comprehensive clinical testing in humans. The investigations carried out so far in IBD models have provided substantial evidence of the nanotherapeutic approach as having the potential
to overcome some of the current drawbacks to conventional IBD therapy. We analyze the pros and cons of nanotechnology in IBD therapies studied in different models, aimed at different targets and mechanisms of IBD pathogenesis, in an attempt to predict its possible impact in humans.


This review focuses on tools for studying a cell's transcriptome, the collection of all RNA transcripts produced at a specific time, and the tools available for determining how these changes in gene expression relate to the functional changes in an organism. While the microarray-based (analog) gene-expression profiling technology has dominated the 'omics' era, Next-Generation Sequencing based gene-expression profiling (RNA-Seq) is likely to replace this analog technology in the future. RNA-Seq shows much promise for transcriptomic studies as the genes of interest do not have to be known a priori, new classes of RNA, SNPs and alternative splice variants can be detected, and it is also theoretically possible to detect transcripts from all biologically relevant abundance classes. However, the technology also brings with it new issues to resolve: the specific technical properties of RNA-Seq data differ to those of analog data, leading to novel systematic biases which must be accounted for when analysing this type of data. Additionally, multireads and splice junctions can cause problems when mapping the sequences back to a genome, and concepts such as cloud computing may be required because of the massive amounts of data generated.

In vivo models of Inflammatory Bowel Diseases (IBD) elucidate important mechanisms of chronic inflammation. Complex intestinal responses to food components create a unique "fingerprint" discriminating health from disease. Five-week-old IL10-/- and C57BL/6J (C57; control) mice were inoculated orally with complex intestinal microflora (CIF) and/or pure cultures of Enterococcus faecalis and E. faecalis (EF) aiming for more consistent inflammation of the intestinal mucosa. Inoculation treatments were compared to non-inoculated IL10-/- and C57 mice, either kept in specific pathogen free (SPF) or conventional conditions (2 × 5 factorial design). At 12 weeks of age, mice were sacrificed for intestinal histological (HIS) and transcriptomic analysis using limma and Ingenuity Pathway Analysis Software. Colonic HIS was significantly affected (P < 0.05) in inoculated IL10-/- mice and accounted for approximately 60% of total intestinal HIS. Inoculation showed a strong effect on colonic gene expression, with more than 2000 genes differentially expressed in EF-CIF-inoculated IL10-/- mice. Immune response gene expression was altered (P < 0.05) in these mice. The second study investigated the effect of arachidonic (AA) and eicosapentaenoic acid (EPA) on colonic HIS and gene expression to test whether EPA, contrary to AA, diminished intestinal inflammation in EF-CIF IL10-/- mice. Immune response gene expression was altered (P < 0.05) in these mice. The second study investigated the effect of arachidonic (AA) and eicosapentaenoic acid (EPA) on colonic HIS and gene expression to test whether EPA, contrary to AA, diminished intestinal inflammation in EF-CIF IL10-/- mice (2 × 4 factorial design). AIN-76A (5% corn oil) and AIN-76A (fat-free) 1% corn oil supplemented with either 3.7% oleic acid (OA), AA or EPA were used. IL10-/- mice fed EPA- and AA-enriched diets had at least 40% lower colonic HIS (P < 0.05) than those fed control diets (AIN-76A and OA diets). The expression of immune response and ‘inflammatory disease’ genes (down-regulated: TNFa, IL6, S100A8, FGF7, PTGS2; up-regulated: PPARa, MGLL, MYLK, PPSS23, ABCB4 with EPA and/or AA) was affected in IL10-/- mice fed EPA- and AA-enriched diets, compared to those fed AIN-76A diet.


We examined the effect of a 9-week diet and physical activity intervention provided in the workplace by a group education session where personal dietary and physical activity goals were proposed. Measurements of anthropometry, fasting blood lipids, glucose and insulin, assays for antioxidant activity (AOA) and questionnaires were completed at 0, 3, 6, 9, and 12 weeks in 50 healthy workers (50 male, mean age 46y). Followup measurements in 39 (56 male) were possible at 52 weeks. At week 3 a group dietary and physical activity motivational seminar was held. At week 6, half the group were supplied daily kiwifruit for 3 weeks with cross over at week 9 until week 12. Compared to baseline, lipid, glucose, insulin and AOA measurements were improved at 12 and 52 weeks. Body measurements did not change. Group diet and physical activity advice reinforced over 9 weeks is associated with a sustained improvement in cardiovascular risk factors at 52 weeks. Copyright © 2009 Elaine C. Rush et al.


Many milk-derived components have immunomodulatory and anti-inflammatory properties, and some of these reduce intestinal inflammation when orally administered to animal models of colitis. However, the potential for ruminant milk or milk components to benefit people with intestinal inflammatory disorders (such as Inflammatory Bowel Disease) has not been well-researched. This review describes published research into mechanisms by which ruminant milk and its components may have beneficial effects when consumed by people who have intestinal inflammation.


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Lactobacillus species can exert health promoting effects in the gastrointestinal tract (GIT) through many mechanisms, which include pathogen inhibition, maintenance of microbial balance, immunomodulation, and enhancement of the epithelial barrier function. Different species of the genus Lactobacillus can evoke different responses in the host, and not all strains of the same species can be considered beneficial. Strain variations may be related to diversity of the cell surface architecture of lactobacilli and the bacteria's ability to express certain surface components or secrete specific compounds in response to the host environment. Lactobacilli are known to modify their surface structures in response to stress factors such as bile and low pH, and these adaptations may help their survival in the face of harsh environmental conditions encountered in the GIT. In recent years, multiple cell surface-associated molecules have been implicated in the adherence of lactobacilli to the GIT lining, immunomodulation, and protective effects on intestinal epithelial barrier function. Identification of the relevant bacterial ligands and their host receptors is imperative for a better understanding of the mechanisms through which lactobacilli exert their beneficial effects on human health.


Early-life methyl-donor deficiency is implicated in growth restriction and later-life development of type 2 diabetes mellitus. We ascertained whether dietary methyl-donor deficiency in the mother during pregnancy or during postweaning growth in the rat would impair glucose homeostasis, insulin secretion and pancreatic endocrine development in young adults.


Recent research indicates that antioxidants do not work in quite the way we thought, but may still have beneficial health effects through helping the body respond to and manage oxidative stress (covered in Part 1). This has prompted a rethink of antioxidants in the diet and how we can use them beneficially in the foods we eat. We discuss some examples of new science-based approaches to improving human health and the development and proof of efficacy of future functional foods targeted at assisting the benefits of physical exercise and slowing of the human ageing process.


Polyphenolic phytochemicals are ubiquitous in plants, in which they function in various protective roles. A ‘recommended’ human diet contains significant quantities of polyphenolics, as they have long been assumed to be ‘antioxidants’ that scavenge excessive, damaging, free radicals arising from normal metabolic processes. There is recent evidence that polyphenolics also have ‘indirect’ antioxidant effects through induction of endogenous protective enzymes. There is also increasing evidence for many potential benefits through polyphenolic-mediated regulation of cellular processes such as inflammation. Inductive or signalling effects may occur at concentrations much lower than required for effective radical scavenging. Over the last 2 – 3 years, there have been many exciting new developments in the elucidation of the in vivo mechanisms of the health benefits of polyphenolics. We summarise the current knowledge of the intake, bio-availability and metabolism of polyphenolics, their antioxidant effects, regulatory effects on signalling pathways, neuroprotective effects and regulatory effects on energy metabolism and gut health.


A panel of 148 extracts from 37 food products was prepared using organic and aqueous solvents and both neutral and acidic conditions. The panel of food products tested included fruits, vegetables, grains, herbs and spices, most of which are common in a normal European-style diet. The impact of these extracts on the growth of selected probiotic bacteria (Lactobacillus reuteri, Lactobacillus rhamnosus, Bifidobacteria lactis) and pathogenic bacteria (Escherichia coli O157:H7 and Escherichia coli LF82) was assessed using a standard minimum inhibitory concentration method. The results showed that aqueous extractions of garlic and black peppercorns significantly enhanced the growth of one strain of probiotic bacteria (L. reuteri) whilst inhibiting both pathogenic strains of E. coli at a 1:50 dilution. Aqueous extracts of banana, apple and orange all enhanced the growth of the three probiotic strains significantly, and inhibited the pathogens to approximately 80% of the controls (not significant). Both aqueous and organic extractions of ginger significantly inhibited the growth of one or both E. coli strains, respectively (also at the 1:50 dilution).


The idea that diet and health are related is not new but the concept of direct nutrient–gene interactions is a new one for the food industry and the public to deal with. The ultimate goal of nutrigenomics is the development of foods that can be matched to individual human genotypes in order to benefit the health of those individuals. This paper discusses how personalised, nutrigenomic foods might be developed. Early results from research into food fractions that have the potential to ameliorate Crohn's disease are presented along with illustrations of candidate foods. Issues covering food customisation, consumer response and the ethics of genetic testing for food selection are also discussed briefly.


The functional polymorphism Val158Met in the catechol-O-methyltransferase (COMT) gene was analysed to determine its association with maternal stress and childhood total difficulties.


Micronutrients influence multiple metabolic pathways including oxidative and inflammatory processes. Optimum micronutrient supply is important for the maintenance of homeostasis in metabolism and, ultimately, for maintaining good health. With advances in systems biology and genomics technologies, it is becoming feasible to assess the activity of single and multiple micronutrients in their complete biological context. Existing research collects fragments of information, which are not stored systematically and are thus not optimally disseminated. The Micronutrient Genomics Project (MGP) was established as a community-driven project to facilitate the development of systematic capture, storage, management, analyses, and dissemination of data and knowledge generated by biological studies focused on micronutrient-genome interactions. Specifically, the MGP creates a public portal and open-source bioinformatics toolbox for all "omics" information and evaluation of micronutrient and health studies. The core of the project focuses on access to, and visualization of, genetic/genomic, transcriptomic, proteomic and metabolomic information related to micronutrients. For each micronutrient, an expert group is or will be established combining the various relevant areas (including genetics, nutrition, biochemistry, and epidemiology). Each expert group will (1) collect all available knowledge, (2) collaborate with bioinformatics teams towards constructing the pathways and biological networks, and (3) publish their findings on a regular basis. The project is coordinated in a transparent manner, regular meetings are organized and dissemination is arranged through tools, a toolbox web portal, a communications website and dedicated publications. © 2010 The Author(s).


Interleukin (IL)-10 has important effects in immunoregulation and inflammation, and previous studies have provided evidence for the involvement of IL-10 in the pathogenesis of Crohn's disease (CD). In this study, we investigated whether genetic variants of the IL-10 gene were associated with CD in a New Zealand population. Three single nucleotide polymorphisms (SNPs) in the promoter region of IL-10 (rs1800871, rs1800872, and rs1800896) and a flanking SNP, rs3024505, were genotyped in a well-characterized New Zealand dataset consisting of 342 CD cases and 610 controls. Furthermore, we measured serum IL-10 levels in a number of the CD patients and controls and examined whether a relationship existed between these polymorphisms and serum IL-10 levels. We demonstrated an association with CD for SNPs rs3024505 and rs1800896, and phenotypic analysis indicated an association of rs3024505 with an early age at first diagnosis, strictureing CD behavior, and requirement for bowel resection. We also observed that IL-10 concentration was significantly higher in CD patients than in the controls and that the T allele of rs1800896, the A allele of rs1800871, and the T allele of rs1800872 were associated with increased serum IL-10 levels.


Prostate cancer runs in families and shows a clear dietary involvement. Until recently, the key risk gene(s) have proved elusive. We summarise current understandings of nutrient-gene interactions in prostate cancer risk and progression.


OBJECTIVES: Serologic testing is increasingly being utilized to evaluate children with suspected inflammatory bowel disease (IBD). The aim of this paper was to evaluate the sensitivity and specificity of a currently available panel involving four antibodies: deoxyribonuclease (DNase)-sensitive perinuclear antineutrophil cytoplasmic antibody (DNase-sensitive pANCA), IgA and IgG antibodies to Saccharomyces cerevisiae (IgA and IgG ASCA), and antibody to Escherichia coli outer membrane porin (anti-OmpC). We also wished to determine whether antibody levels correlated with disease activity, and whether a
specific antibody pattern correlated with location and outcome of disease in children. METHODS: We studied sera from 81 children with Crohn's disease (CD), 54 with ulcerative colitis (UC), and 63 controls. Clinical data, disease activity, and disease diagnosis were gathered at the time of serum sampling, and charts were re-reviewed at time of the study to determine long-term outcome. Enzyme-linked immunosorbent assay was utilized to determine titers of antibodies to ASCA, DNase-sensitive pANCA, and anti-OmpC; the presence of perinuclear staining for ANCA was confirmed by immunofluorescence. RESULTS: We identified ASCA antibodies in 44% of CD patients, 0% of UC patients, and 1 control patient. DNase-sensitive pANCA antibodies were found in 70% of patients with UC, 18% of CD patients (predominantly Crohn's colitis), and 3% of controls. Anti-OmpC as an isolated assay had low sensitivity for both CD (24%) and UC (11%), and displayed a 5% false-positive rate. However, anti-OmpC did identify a small number of IBD patients not detected by the other assays. If any one or more of the four antibodies was positive, the overall sensitivity of the four antibody panel was 65% for CD and 76% for UC, with a specificity of 94%. Patients who were ASCA-positive were more likely to have disease of the ileum or ileum and right colon than patients who were ASCA-negative (58% vs 18%, p<0.001). Patients with ASCA-positive were also more likely to require ileocecal resection (36% vs 13%, p<0.05). CONCLUSIONS: A currently available commercial antibody panel has good sensitivity and excellent specificity for CD and UC. The ASCA antibodies, while highly specific for CD, identify predominantly the subset of children with disease of the ileum and ascending colon who may be at increased risk of surgery.