Presentations and talks


Campbell, B., et al. (2013). Deletion of the GSTT1 genotype linked to tolerance of Brassicaceae in people with Crohn’s disease in a New Zealand cohort (poster) presented at the Otago University, Christchurch 40th Anniversary celebrations 20-22 February 2013, New Zealand.
Ulcerative colitis is a disease that causes inflammation in the intestine, particularly in the colon. Food components may prevent the occurrence and the extent of this inflammatory response in the intestine. The aim of our study is to test the anti-inflammatory response of some food flavonoids that have been reported to reduce intestinal inflammation. Multiple drug resistance mdr1a-/- knockout mice, that spontaneously develop ulcerative colitis because of a functional defect in an ATP dependent transporter, are used as an in vivo model of inflammatory bowel disease. Forty-eight 6.5 weeks old mdr1a-/- and forty-eight age-matched FVB control mice were obtained from Taconic (USA). All mice were housed individually under conventional housing conditions. Twelve mdr1a-/- and twelve FVB mice were either fed an AIN-76 control diet or the AIN-76A diet supplemented with either 0.2% curcumin, 0.1% rutin or 0.6% green tea polyphenol extract for 12 weeks. Fresh diets were fed ad libitum and food consumption was measured. All mice were weighed three times a week and weight loss, stool consistency, rectal bleeding and mobility was monitored and scored using a disease activity index. At 18.5 weeks of age, intestinal samples were collected for histology (inflammatory cell infiltrate, tissue destruction, tissue repair), microarray analysis of gene expression changes, proteomics and enzyme activity of myeloperoxidase, a marker of inflammation. Plasma samples were collected for cytokine analysis. Curcumin, rutin and green tea polyphenol and metabolite levels will be measured in urine, faeces and plasma. Urine samples were collected for metabolomics studies. Thymus, liver, spleen, kidneys and skeletal muscle were collected and stored for subsequent analysis. Overall, using nutritional genomics methods, our study will generate insight into the potential of flavonoids to beneficially affect gut health.


Keynote speaker


Ferguson, L. R. (2006). Nutrigenomics approach to establishing selenium requirements. 3rd Australian Health and Medical Research Congress. Melbourne, Australia.


Topical review


Invited talk


Ferguson, L. R. (2009). Could studies on gene-nutrient interaction maintain the promise of good health and/or prevention of chronic disease. First International Conference on Food-Omics. Cesena, Italy. 10.


Ferguson, L. R. (2010). Diet, mutation and prostate cancer. 20th International conference on antimitagenesis and anticarcinogenesis. Sao Paulo, Brazil.

  
  Keynote address


  
  Keynote address


Ferguson, L. R. (2014). Does what we eat affect how our bodies deal with disease? Invited talk for New Zealand Institute of Food Science & Technology, Tuesday 27 May.


Crohn’s disease, a chronic inflammatory disease of the gastrointestinal tract, is the initial target of the Nutrigenomics New Zealand research programme, since the disease may result from the interplay between diet and genotype. Important components of innate immune responses are the Toll-like receptors (TLR) and mutations in the genes for TLR4, TLR9 and NOD2 (linked with TLR2) are associated with Crohn’s disease. We have used specific TLR ligands to target an anti-inflammatory assay to these Crohn’s associated TLR pathways. Common foods were subjected to organic solvent or water extraction and assayed for anti-inflammatory activity by their ability to suppress production of TNFα from a macrophage cell line. Foods showing high activity (e.g. apple, kiwifruit and avocado) were selected for assay using specific TL4 (purified lipopolysaccharide), TLR 9 (bacterial CpG oligonucleotide), TLR 2 (purified gram positive peptidoglycan) and NOD2 (muramyl dipeptide) specific ligands. These extracts were then fractioned further to help to identify the pathway specific anti-inflammatory components of these foods. This preliminary screen allowed for the selection of foods ingredients that may be beneficial for people with Crohn’s disease and other inflammatory gut conditions. Funded by the Foundation for Research, Science and Technology, New Zealand. C02X0403 FRST contract number.


Crohn’s disease (CD) is associated with an abnormal increase in intestinal epithelial permeability and a defect in the intestinal tight junction (TJ) barrier has been proposed. Levels of the inflammatory mediator tumour necrosis factor-α (TNF-α) are markedly increased in CD patients, and as this mediator can increase intestinal TJ permeability, it may be a contributing factor in the intestinal permeability defects of CD. The objective of this study was to devise a food-based therapeutic approach to retighten the leaky TJ barrier. An in vitro model, consisting of filter-grown human intestinal epithelial Caco-2 monolayer was used to investigate the potential of polyphenols and other common foods on transepithelial electrical resistance (TEER), as a measure of TJ integrity. The effect on the functional localization of the TJ protein zona occludens-1 (ZO-1) by the immunofluorescent antibody method was also determined. TNF-α (10-100 ng/ml) was shown to produce a concentration- and time-dependent (up to 72 h) increase in TJ permeability in this model. Two NF-κB inhibitors, curcumin and triptolide, prevented the effect of TNF-α in a concentration- and time-dependent manner. Kiwifruit extracts prepared using solvent or water extraction methods were tested and some extracts were shown to inhibit the TNF-α induced TJ permeability. Progressive disturbances in the ZO-1 protein at cellular borders with a gap-like appearance were also noticed. These results demonstrate that some food-derived polyphenols have the ability to prevent TNF-α-induced intestinal epithelial tight junction permeability and foods or food components with this property may be useful for formulating personalized nutrition for CD and other intestinal disorders associated with an increase in intestinal epithelial permeability.


contributing compounds which are the most significant candidates for biomarkers so far identified through this research.


The simplest way to understand the complex mechanisms of a disease such as Inflammatory Bowel Disease


Dietary n-3 polyunsaturated fatty acids can ameliorate inflammation via a range of mechanisms like binding and activating peroxisome proliferator-activated receptor ? (PPAR?). This study tested how dietary eicosapentaenoic acid (EPA) reduced intestinal inflammation using interleukin 10 gene-deficient (IL10-/-) mice. Crohn’s Disease-like colitis was induced by inoculation of 12 IL10-/- mice with Enterococcus faecalis/faecium plus complex intestinal flora at five weeks of age (12 wild-type mice were also inoculated). These mice were randomly assigned to an AIN-76A diet (fat-free) containing 1% corn oil (plus 0.3% linoleic and 2-linolenic acid) supplemented with 3.7% purified ethyl esters of oleic acid (OA, control) or EPA. To identify colonic genes relevant to initiation and progression of inflammation, transcription profiling (micro-arrays), and bioinformatic analyses (Bioconductor, Ingenuity Pathway analysis) were used. Dietary EPA increased the expression
of genes associated with fatty acid and tryptophan metabolism (e.g. aldehyde dehydrogenases, cytochromes P450s) and fatty acid ß-oxidation in the colon of IL10-/- mice, likely through PPARγ enhancing energy utilization. The expression of genes related to oxidative stress was elevated in EPA-fed IL10-/- mice, showing induced xenobiotic-metabolizing enzymes. The expression of key inflammatory and immune response genes remained unchanged in EPA-fed compared to OA-fed IL10-/- mice suggesting that dietary EPA had anti-inflammatory properties.


L.R., F. (2011). Genes, diet and Inflammatory Bowel Diseases (keynote address). IPODD annual meeting.


Marlow, G., et al. (2013). Nutrigenomic technologies to study the effect of a Mediterranean-style diet on Inflammation (poster). NuGO.


Oxidative stress and deregulated immune response processes are involved in the development of inflammatory bowel diseases (IBD). Curcumin and rutin are polyphenolic flavonoid compounds known to have anti-oxidant and anti-inflammatory activities, but their mechanism(s) of action are yet to be fully elucidated. Mdr1a/- mice spontaneously develop intestinal inflammation predominantly in the colon and therefore this model is relevant to the study of IBD like Ulcerative Colitis and Crohn's Disease. This study tested the hypothesis that addition of curcumin and rutin to the food of mdr1a/- mice would alleviate colon inflammation. We also investigated the effect of dietary curcumin on gene expression in colon tissue. Mice were randomly assigned to one of three diets; control, control 0.1% rutin or control 0.2% curcumin (12 mdr1a/- mice per diet) and monitored from the age of 7 to 24 weeks. Curcumin, but not rutin, significantly reduced signs of colon inflammation in mdr1a/- mice. Micro-array and pathway analyses suggested that the effect of dietary curcumin on colon inflammation was mediated via: 1) up-regulation of xenobiotic metabolism mediated by the RXR receptor mechanism, which is activated by PXR and PPAR, 2) down-regulation of pro-inflammatory pathways. A series of pro-inflammatory cytokine and chemokine genes were down-regulated by dietary curcumin. Further research is warranted; but these results have clear implications in terms of potential dietary supplements for people with IBD. They also demonstrate the importance of nutrigenomic studies in understanding nutrient/gene interactions.


Inflammatory bowel disease (IBD) is thought result from the dysregulation of a combination of functional pathways; immunoregulation, maintenance of mucosal barrier integrity, microbial recognition and clearance, and/or homeostasis. Green tea extracts are non-nutritive polyphenolic-flavonoid compounds known to have anti-inflammatory activity, but the mechanism(s) of this are not fully understood. Mdr1a/- mice spontaneously develop intestinal inflammation predominantly in the colon and therefore are a relevant model for IBD. This study tested whether addition of green tea polyphenols to the food of mdr1a/- mice would alleviate colonic inflammation, allowing us to investigate the effect of dietary green tea polyphenols on relevant gene expression in colon tissue. This approach was designed to give insight into how this dietary compound might influence the metabolic pathways involved in the inflammatory response in mdr1a/- mice. Twelve mdr1a/- mice were randomly assigned to each of two experimental diets: control (AIN-76A), or control (AIN-76A) with 0.6% green tea extract (a polyphenol extract containing 35% epigallocatechin gallate). Mice were monitored from the age of 7 to 24 weeks, at which time colon tissues and blood were collected for histological and gene expression evaluation. Green tea extract significantly reduced the histological signs of colon inflammation and serum amyloid A concentration in the plasma of mdr1a/- mice (P<0.05). These results confirm the anti-
inflammatory effect of dietary green tea extract. Using the Ingenuity Pathways Analysis program, microarray data showed a total of 712 genes differentially expressed in the colon of mdr1a-/- mice as a result of dietary green tea extract that met the criteria for pathway analysis. Pathways involved in xenobiotic metabolism (five pathways) and immune and inflammatory response (eight pathways) were affected by green tea extract. Further research on the significance of these pathways is warranted; but these results have implications in terms of potential dietary supplements for people with IBD and demonstrate the importance and potential of nutrigenomic studies in understanding nutrient/gene interactions.

Nones, K., et al. (2008). What do gut microbes have to do with obesity? TNO Beneficial Microbes Conference. Amsterdam, the Netherlands: 72, Poster P22.

500 Million adult humans in the world are overweight and 250 million are obese which contributes to the fact that metabolic syndrome is one of the fastest growing global health problems. In a normal healthy adult human the number of microbial cells is approximately an order of magnitude higher than the number of cells making up the entire body, comprising 2-5% of their total body mass. Rather than being considered merely as colonising residents, scientists are discovering the contribution some of these microbes make to various metabolic process and the population of microbes are increasingly being referred to as the ‘microbial’. In fact there is evidence in the literature that obese and lean people have different bacterial populations. There is also speculation that gut microbes interact with fat metabolism via bile acids. The current study investigated the hypothesis that the health implications of diet induced obesity may be negated by including a fermentable vegetable fibre in the high fat diet. The theory behind the mechanism being that caecum microbes ferment the vegetable fibre which then affects a shift in microbial populations or microbial metabolism which has a knock on effect on host fat and energy metabolism via the bile acid pathway. Rats were randomised to receive either high-fat diet with cellulose (HF-C), high-fat diet with broccoli (HF-B), low-fat diet with cellulose (LF-C) or low-fat diet with broccoli (LF-B) with a sample size of n=16 per group. Two trials were run for different lengths of time (1 month and 4 months) to look at both acute and chronic effects. Early results concerning fat deposition, cholesterol and triglycerides will be presented as well as some histology and microbial analysis and their implications will be discussed.


Nutrigenomics studies the response of humans to food and food components, with the goal to develop f


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Innate immunity is the rapid and generalized inflammatory response that is the first organised reaction to infection. It involves the recognition of a limited number of pathogen associated molecules by Toll-like receptors (TLR) leading to the production of a complex variety of soluble mediators, such as interleukin -1(IL-1) and tumour necrosis factor á (TNF-á). Adaptive immunity is highly specific for a particular pathogen and like the innate response is directed by cytokines. Dysregulated inflammation leads to classic inflammatory diseases such as the inflammatory bowel diseases and other chronic conditions including cardiovascular disease. Nutrients, for example, fish oil and phytochemicals present in fruit, tea and spices, can modulate genes involved in regulating immune responses. Nutrient effects on inflammatory mediators have been shown to exhibit inter-individual variation based on specific single nucleotide polymorphisms (SNPs). Thus immune response genes are good targets for modulation by nutritional compounds. An objective of the Nutrigenomics NZ programme is to discover activities in foods that might rectify dysregulated inflammatory immune responses in patients with Crohn's disease. To screen for activity inflammatory pathways involving TLR4, TLR9 and NOD2 have been targeted, as some Crohn’s disease patients have SNPs in these receptors and a gene–nutrient sensor assay for NOD2 has been developed. Results from different types of common food extracts will be presented and those that that might modify gut mucosal immune responses discussed.
Defensins are an ubiquitous class of antimicrobial peptides found across the plant and animal kingdoms. In humans, two main sub-families exist; alpha and beta defensin which are expressed in multiple tissues but predominantly at epithelial surfaces. Both single nucleotide polymorphisms (for alpha defensins) and copy number variants (for beta defensins) exist in people with inflammatory bowel disease (Crohn’s disease and ulcerative colitis). As a result they have lower defensin expression and protein levels in their intestinal mucosa and less anti-microbial activity. The aetiology of Crohn’s disease is poorly understood but the involvement of microbial/host gut epithelial interactions is increasingly being accepted as central to pathology development. Whilst bacteria are known to stimulate defensins production, very few other stimulants of defensins expression are known. The aim of this work was to develop an assay to test food components and their effects on defensin production. A Crohn’s genotype colon cancer cell line HCT8 was incubated with various food extracts alone and with pathogenic bacteria (Escherichia coli LF82). Slot blots were performed to semi-quantitatively determine changes in the production of beta-defensin protein. Slot blots clearly show differences in the amount of protein produced by the cells in response to incubations with food and pathogenic bacteria. In conclusion, the assay has been optimised to detect changes in protein expression. Screening of food extracts, and ultimately their fractions, will follow to identify those that increase defensin production and potentially have a beneficial effect on the symptoms of Crohn’s disease.


Functional foods have been identified as a key trend in the food industry for some time. Demographic and social trends, along with an increasing body of scientific knowledge concerning food components and their physiological effects, have moved foods from a position of supplying simply basic nutrition to one where specialised foods are seen (by consumers and marketers) to protect against and (perhaps) prevent disease. The initial focus of the Nutrigenomics New Zealand research programme is the inflammatory bowel condition Crohn’s disease, a condition that may have both genetic and environmental contributions. From a food science perspective, two primary food outcomes are likely from the research programme: 1) public good information regarding good and bad foods for people with specific genetic profiles will likely become available and 2) intellectual property in the form of designed nutrigenomic foods are likely to emerge. Our studies into foods influencing Crohn’s disease have indicated that there may be certain foods or food fractions that could be active in reducing inflammation in this debilitating condition. How these materials might be integrated into hypothetical, personalised “Crohn’s positive” foods will be discussed, keeping in mind the difficulty of formulating specific types of food products with desired ratios of carbohydrate, protein and lipids, while maintaining textural properties or the need to mask adverse sensory properties from a desirable but unpalatable food fraction. An example from another health end-point oriented research project will be used
to demonstrate how some ideas, both preconceived and from the results of research, can not be adopted due to these practical limitations.


