J Proteome Res. 2010 Aug 19. [Epub ahead of print]

Proteomics in Nutrition: Status Quo and Outlook for Biomarkers and Bioactives.

Kussmann M, Panchaud A, Affolter M.

Abstract

Food and beverages are the only physical matter we take into our body, if we disregard the air we inhale and the drugs we may have to apply. While traditional nutrition research has aimed at providing nutrients to nourish populations and preventing specific nutrient deficiencies, it more recently explores health-related aspects of individual bioactive components as well as entire diets and this at group rather than population level. The new era of nutrition research translates empirical knowledge to evidence-based molecular science. Modern nutrition research focuses on promoting health, preventing or delaying the onset of disease, optimizing performance and assessing risk. Personalized nutrition is a conceptual analogue to personalized medicine and means adapting food to individual needs. Nutrigenomics and nutrigenetics build the science foundation for understanding human variability in preferences, requirements, and responses to diet and may become the future tools for consumer assessment motivated by personalized nutritional counseling for health maintenance and disease prevention. The scope of this paper is to review the current and future aspects of nutritional proteomics, focusing on the two main outputs: identification of health biomarkers and analysis of food bioactives.

PMID: 20718507


Molecular Mechanisms of Pediatric Nutrition.

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Abstract

Over the last years, major scientific advances allowed to decrypt the human genome with over 22,000 protein-coding genes. We do know some of these genes, but yet only few of their functions and even less of their control and regulation as well as the complex interplay between different genes and their products. Genotyping allows to analyze particular genes, but it cannot predict phenotypes. What can we expect from the recent scientific advances with regard to the needs of the developing child or adult and the intention to prevent disease and/or to improve life quality? We address two particular points in this review: the (direct/indirect) interaction of nutrition with genes of the host and the impact of genetic variations (polymorphisms) on requirements, tolerance or metabolism of nutrition. Over the last 5 years, major research efforts were made to address the potential interaction of nutrition and genes, now named nutrigenomics (interaction of nutrition and genes) and nutrigenetics (impact of gene variants on nutrition and/or their metabolism). We give in this review examples of molecular approaches in the understanding of this bidirectional interaction between nutrition and genes, focusing also on epigenetic imprinting.

PMID: 20664216


Review: Nutriceuticals as antithrombotic agents.

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Abstract

Thrombus formation in a disrupted endothelium is influenced not only by the platelet redox state and reactive oxygen and nitrogen species but also by the presence of endogenous or exogenous antioxidants. Thrombus formation in the stenotic arteries is triggered predominantly by attenuated shear stress. Superoxide and nitric oxide production, as well as their metabolism, potentially influence platelet activation and thrombosis. Antioxidant supplementation has not been generally associated with better cardiovascular
outcome and is often compounded by bleeding and hemorrhagic stroke. Because of recent developments like the human genome project and personalized medicine, an emerging new area of nutrigenomics and nutraceuticals offers a scientific approach of diet-based therapeutics applicable to a plethora of human diseases, including cardiovascular inflammation and thrombosis. Therefore, further mechanistic research using nutrigenomics and nutraceuticals in the prevention and management of thrombosis offers great potential and may be effective in limiting the problems associated with antioxidant-based therapeutics. In the present review, we have summarized the effect of dietary antioxidants in the modulation of platelet-mediated thrombosis. In addition, therapeutic opportunities in the area of nutrigenomics and nutraceuticals in vascular and nonvascular diseases are also discussed.

PMID: 20553290


Future nutrigenetics: in search of the missing genetic variation.

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Abstract

Despite considerable effort, genetic analysis of complex disorders and traits, including those related to nutrition, has revealed only a very small part of the expected genetic variation. Missing variation may occur as conditional variation depending on the presence of defined lifestyle factors, as epigenetic variation or as low-moderate effect size variation not detected by mutation screening and genome-wide association studies. Experience with genetic analysis of patients with neural tube defects provides evidence of the existence of the latter type of variation and demonstrates that candidate gene analysis is an efficient approach to discover part of this missing variation. By reviewing the genes with rare and common variation associated with obesity or related parameters, guidelines are proposed for the proper selection of candidate genes. This selection fits into an analytic strategy to deal with the complex and massive data sets expected to arise from the application of routine whole genome sequencing.

PMID: 20453519
Biomarkers of meat intake and the application of nutrigenomics.

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Abstract

Objective dietary intake markers for meat would be useful to assess meat intake in observational studies and as compliance markers in dietary intervention studies. A number of compounds are specific to meat compared with most other dietary items but there is some overlap between protein rich foods. A number of single compounds have been analysed in urine, plasma, serum or hair samples in studies of their relationship to meat or total protein intake. Among potential markers of dietary meat intake are urea, creatine, creatinine, carnitine, camosine, anserine, ophidine, 1- and 3-methylhistidine, and sulphate or sulphite. Anserine and 1-methylhistidine come close to being meat-specific markers but true quantitative biomarker may not exist. Modern profiling techniques are increasingly used to look for useful biomarkers or for constructing them from latent information in complex profiles. Metabolomics by NMR spectroscopy of urine has also been applied to search for meat intake markers. Studies on single compounds or metabolomics markers are shortly reviewed here.

PMID: 20374789

Omega-3 fatty acids, inflammation and angiogenesis: basic mechanisms behind the cardioprotective effects of fish and fish oils.

Massaro M, Scoditti E, Carluccio MA, Campana MC, De Caterina R.

C.N.R. Institute of Clinical Physiology, Pisa, and Lecce, Italy.

Abstract

Atherosclerosis is now widely accepted to be an inflammatory disease, characterized by degenerative as well as proliferative changes and extracellular accumulation of lipid and cholesterol, in which an ongoing
inflammatory reaction plays an important role both in initiation and progression/destabilization, converting a chronic process into an acute disorder. Neovascularization has also been recognized as an important process for the progression/destabilization of atherosclerotic plaques. In fact, vulnerable atherosclerotic plaques prone to rupture are characterized by an enlarged necrotic core, containing an increased number of vasa vasorum, apoptotic macrophages, and more frequent intraplaque haemorrhage. Various functional roles have been assigned to intimal microvessels, however the relationship between the process of angiogenesis and its causal association with the progression and complications of atherosclerosis are still challenging and controversial. In the past 30 years, the dietary intake of omega-3 (n-3) polyunsaturated fatty acids--mainly derived from fish--has emerged as an important way to modify cardiovascular risk through beneficial effects on all stages of atherosclerosis, including plaque angiogenesis. This review specifically focuses on the modulating effects of n-3 fatty acids on molecular events involved in early and late atherogenesis, including effects on endothelial expression of adhesion molecules, as well as pro-inflammatory and pro-angiogenic enzymes. By accumulating in endothelial membrane phospholipids, omega-3 fatty acids have been shown to decrease the transcriptional activation of several genes through an attenuation of activation of the nuclear factor-kappaB system of transcription factors. This occurs secondary to decreased generation of intracellular reactive oxygen species. This series of investigations configures a clear example of nutrigenomics--i.e., how nutrients may affect gene expression, ultimately affecting a wide spectrum of human diseases.

PMID: 20196971


Omega-3 fatty acids, inflammation and angiogenesis: nutrigenomic effects as an explanation for anti-atherogenic and anti-inflammatory effects of fish and fish oils.

Massaro M, Scoditti E, Carluccio MA, Montinari MR, De Caterina R.

CNR Institutes of Clinical Physiology, Pisa and Lecce, Italy.

Abstract

Atherosclerosis is a dynamic process with inflammatory aspects playing a considerable pathogenetic role. In this process, the vascular endothelium is the key regulator of vascular function, promoting the maintenance of vascular homeostasis or the progression towards vascular disease. In the past 30 years,
the dietary intake of omega-3 (n-3) polyunsaturated fatty acids - mainly derived from fish - has emerged as an important way to modify cardiovascular risk through beneficial effects on all stages of atherosclerosis. This review specifically focuses on the modulating effects of n-3 fatty acids on molecular events involved in early and late atherogenesis, including effects on endothelial expression of adhesion molecules, as well as pro-inflammatory and pro-angiogenic enzymes. By accumulating in endothelial membrane phospholipids, omega-3 fatty acids have been shown to decrease the transcriptional activation of several genes through a decreased activation of the nuclear factor-kappaB system of transcription factors. This occurs secondary to decreased generation of intracellular reactive oxygen species. This series of investigations configures a clear example of nutrigenomics, i.e. how nutrients may affect gene expression, ultimately affecting a wide spectrum of human diseases.

PMID: 19918111


Nutrigenetics/Nutrigenomics.

Simopoulos AP.

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Comment in:


Abstract

All diseases have a genetic predisposition. Genome-wide association studies (GWASs) by large international consortia are discovering genetic variants that contribute to complex diseases. However, nutrient information is missing, which is essential for the development of dietary advice for prevention and management of disease. Nutrigenetics/nutrigenomics studies provide data on mechanisms of nutrient and gene interactions in health and disease needed for personalized nutrition. A process will be needed to define when gene-nutrient-disease associations are ready to be evaluated as potential tools to improve public health.

PMID: 20070200
Overview of the symposium on public health significance of genomics and eco-genetics.

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Comment on:

Abstract
Genomic and genetic information is rapidly becoming a major element in public health research and emerging public health practice. This symposium reviews the methods, findings, and significance of genome-wide association studies from epidemiological and statistical points of view. We examine infectious and inflammatory components of gene-environment interaction in the respiratory system. We note the need for nutrient and dietary data and many other kinds of environmental exposure data in population-based genomic studies. Then we explore the sufficiency of a well-informed family history for public health and family counseling purposes. Finally, in an era of direct-to-consumer genomic test promotion, we review the evidence on the critical question, will genetic risk profiles motivate individuals and families to choose more healthful behaviors? This symposium builds on the foundation of the symposium on Public Health Genetics in Volume 21 (2000) of the Annual Review of Public Health.

PMID: 20001819

Nutrition, immunology, and genetics: future perspectives.

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Abstract
This review surveys some of the areas in which nutrients have been shown to have an impact on specific immune functions, the use of molecular and genetic tools to study molecular responses to dietary factors, and the metabolic consequences of food. It also explores the relationships between nutrient molecules, genetic polymorphisms, and the biological system as a whole, while providing a short introduction to nutrition immunology, nutrient-gene interactions and the novel technologies employed in nutrigenomics and nutrigenetics research.

PMID: 19906227


Advances in Nutrigenomics research: novel and future analytical approaches to investigate the biological activity of natural compounds and food functions.

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Abstract
In recent years, nutrition research has moved from classical epidemiology and physiology to molecular biology and genetics. Following this trend, Nutrigenomics has emerged as a novel and multidisciplinary research field in nutritional science that aims to elucidate how diet can influence human health. It is already well known that bioactive food compounds can interact with genes affecting transcription factors, protein expression and metabolite production. The study of these complex interactions requires the development of advanced analytical approaches combined with bioinformatics. Thus, to carry out these studies Transcriptomics, Proteomics and Metabolomics approaches are employed together with an
adequate integration of the information that they provide. In this article, an overview of the current methodologies and a thorough revision of the advances in analytical technologies and their possibilities for future developments and applications in the field of Nutrigenomics is provided.

PMID: 19467817


[Application of nutrigenomics in clinical nutrition]

[Article in Chinese]

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Abstract

In the past decade, the focus of nutritional study shifted from epidemiology and physiology to molecular biology. Advanced research strategies and technologies including genomics, transcriptomics, proteomics, metabolomics, and system biology have been gradually applied in clinical nutrition. This article reviews the effects of nutrients on gene expressions, application of modern molecular biology in clinical nutrition, as well as the advances and challenges in recent years.

PMID: 17260482


Use of metagenomics to understand the genetic basis of malnutrition.

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Abstract
Childhood malnutrition is not just due to lack of nutrients, it can also be caused by enteric infections leading to intestinal inflammation and malabsorption of nutrients. Human genetic polymorphisms can alter host genes that affect nutrient absorption and metabolism. Changes in intestinal microbial ecology and the microbiome (the collective genome of the intestinal microbiota) can also affect the harvest of nutrients from the diet. A substantial proportion of malnourished children fail to recover due to inappropriate treatment. However, there may be other causes for treatment failure, including changes in the microbiome and infection with an enteropathogen, and a genetic predisposition to malnutrition may exist. It is, therefore, logical to undertake the following: 1) investigate genetic predisposition to malnutrition, 2) determine the genetic markers and biomarkers that can help identify children at risk of malnutrition, and 3) look for new treatment modalities that can improve the clinical management of children with malnutrition.

PMID: 19906224


**Nutrigenetics in the light of human evolution.**

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**Abstract**

Bio-cultural adaptations to new foods played a key role in human evolution. The fossil record and sequence differences between human and chimpanzee genes point to a major dietary shift at the stem of human evolution. The earliest representatives of the human lineage diverged from the ancestors of chimpanzees because of their better adaptation to hard and abrasive foods. Bipedalism and modifications of the hand, which allowed tool manufacture and use, impacted on dietary flexibility, facilitating access to foods of animal origin. This promoted major anatomic, physiologic and metabolic adaptations. Encephalization, which requires high-quality diet, characterizes the evolutionary sequence that, through the Homo ergaster/erectus stages, led to our species, Homo sapiens, which originated in Africa about 200,000 years ago. At the end of the Ice Age, climatic changes and human impact determined a major food crisis, which triggered the agricultural revolution. This affected nutrition and health, with rapid evolutionary adaptations through the selection of genetic variants that allowed better utilization of new
foods, different in relation to geography and culture. Today population growth, globalization and economic pressure powerfully affect diets worldwide. We must take into account our evolutionary past to meet the present nutritional challenges.

PMID: 19690436


**Investigating micronutrients and epigenetic mechanisms in relation to inflammatory bowel disease.**

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**Abstract**

Epigenomic regulation, via DNA methylation, histone modification and non-coding RNA, is increasingly recognised as having a key role in normal development and function of an organism, acting to control cellular and tissue growth and differentiation. It is also thought to be involved in many complex diseases now common in the Western world, including cardiovascular disease, type 2 diabetes, obesity and inflammatory bowel disease (IBD). There is a range of evidence to suggest that nutrition plays a vital role in the protection from such diseases. However, there is little information about the role of nutrition on the epigenetic regulation of IBD. This review aims to elucidate the interactions of nutrients and the epigenome in IBD. More specifically, the plasticity of epigenetic modifications that occur due to low selenium and folate levels in the diet during gestation and lactation will be discussed. A better understanding of this plasticity, and of nutrient-epigenome interactions, will have important implications for enhancing human health through foods.

PMID: 20188748


**Contribution of genomics to the understanding of physiological functions.**
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Abstract
Genomics has brought with it a true biological revolution and can be applied to all areas of life sciences. The advent of genomics is thus linked to the development of high-throughput techniques which allows the genome of organisms as a whole to be studied. The first high-throughput techniques to be developed were sequencing methods. These advances will allow new approaches to a variety of problems in biology. For instance, the emerging fields of genomic medicine in humans and genomic selection in livestock are promising. After the sequencing of genomes, genomics has shifted to the study of gene expression and function. This is called the "post-genomic area" by some authors or "functional genomics" by others. The most recent "omics" to be developed are associated with the study of the metabolism (e.g. metabolomics).
Integrative "omics" approaches (e.g. nutrigenomics) are based on the association of the omics tools at different levels (DNA, RNA, proteins, metabolites) for a specific objective (here nutrition). In terms of perspectives, it is likely that methods for collecting data will outstrip our capacity to adequately analyse these data. So scientists must develop bioinformatic tools and methods to overcome this difficulty. In addition, high-throughput techniques need to be developed in physiology in order to match the increasing amount of genomic information with true biological data. Finally, there is no doubt that all these new approaches will allow important new genes and novel biological mechanisms to be discovered.
Physiological models with invalidated or over-expressed genes will be precious tools to check these new biological discoveries.

PMID: 19996478


Negotiating the boundary between medicine and consumer culture: online marketing of nutrigenetic tests.

Saukko PM, Reed M, Britten N, Hogarth S.
Abstract

Genomics researchers and policy makers have accused nutrigenetic testing companies—which provide DNA-based nutritional advice online—of misleading the public. The UK and USA regulation of the tests has hinged on whether they are classed as "medical" devices, and alternative regulatory categories for "lifestyle" and less-serious genetic tests have been proposed. This article presents the findings of a qualitative thematic analysis of the webpages of nine nutrigenetic testing companies. We argue that the companies, mirroring and negotiating the regulatory debates, were creating a new social space for products between medicine and consumer culture. This space was articulated through three themes: (i) how "genes" and tests were framed, (ii) how the individual was imagined vis a vis health information, and (iii) the advice and treatments offered. The themes mapped onto four frames or models for genetic testing: (i) clinical genetics, (ii) medicine, (iii) intermediate, and (iv) lifestyle. We suggest that the genomics researchers and policy makers appeared to perform what Gieryn (Gieryn, T.F. (1983). Boundary-work and the demarcation of science from non-science: strains and interests in professional ideologies of scientists. American Sociological Review, 48, 781-795.) has termed "boundary work", i.e., to delegitimize the tests as outside proper medicine and science. Yet, they legitimated them, though in a different way, by defining them as lifestyle, and we contend that the transformation of the boundaries of science into a creation of such hybrid or compromise categories is symptomatic of current historical times. Social scientists studying medicine have referred to the emergence of "lifestyle" products. This article contributes to this literature by examining the historical, regulatory and marketing processes through which certain goods and services become defined this way.

PMID: 20022680


[Anti-oxidants, controversies and perspectives: how can the failure of clinical studies using anti-oxidants be explained?]

[Article in French]
Abstract
Since several decades anti-oxidants have been much studied, and scientists have tried to prove the preventive and curative effects in many chronic diseases. However, it is not uncommon to find highly contradictory clinical results, which may explain that consumers are less enthusiastic for anti-oxidants food supplements. First of all, definitions should be reviewed, such as that of free radicals (FR); all of them are not toxic. Some of them, such as nitric oxide, are necessary for the proper physiological functioning of the body, and eliminating them would be a mistake! However, other reactive oxygen species (ROS), which are not FR, are toxic, such as hydrogen peroxide. We have also redefined the oxidative stress, which it is not only the result of an imbalance between oxidants and anti-oxidants, but also the consequence of imbalance in the cellular redox status. The mechanisms of action, bioavailability, synergy and methods to determine the level of anti-oxidants are very sensitive topics, and it is crucial to study them if we want to obtain reliable clinical studies. Given the failure of clinical studies about anti-oxidant, we try to explain strategies which should be followed. First of all, the nature of the anti-oxidant is important; and an anti-oxidant from a natural origin must be preferred. Then, we proposed that the dose-effect was certainly responsible for the failure of tests. Indeed, doses administered in the studies was either too weak to obtain significant results, or too high, becoming pro-oxidative and eliminating the basal concentration of ROS (physiological role). Involvement of mitochondria and glycation are particularly discussed. Nutrigenomics and nutrigenetics are also discussed, which study the interactions between genetics and nutrition. Genetic polymorphism can explain the variable absorption of micronutrients. This concept leads to a truth believed by all scientists, namely the need to provide the right anti-oxidant, in adequate quantity, at the right place, at the right time and for a particular individual. To increase the anti-oxidant capacity of the body, the exogenous intake of anti-oxidants must be increased or the endogenous synthesis of anti-oxidants (SOD, GPX, GSH) must be stimulated. Targeting mitochondria and increasing their overall anti-oxidant defence system will be a challenge. Increasing the bioavailability of anti-oxidants and studying their passage through the blood-brain barrier must be also taken in consideration.

PMID: 19833072


Role of proteomics in nutrigenomics and nutrigenetics.
Vitamin-regulated cytokines and growth factors in the CNS and elsewhere.

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Abstract

There is a growing awareness that natural vitamins (with the only exception of pantothenic acid) positively or negatively modulate the synthesis of some cytokines and growth factors in the CNS, and various mammalian cells and organs. As natural vitamins are micronutrients in the human diet, studying their effects can be considered a part of nutritional genomics or nutrigenomics. A given vitamin selectively modifies the synthesis of only a few cytokines and/or growth factors, although the same cytokine and/or growth factor may be regulated by more than one vitamin. These effects seem to be independent of the effects of vitamins as coenzymes and/or reducing agents, and seem to occur mainly at genomic and/or epigenetic level, and/or by modulating NF-kappaB activity. Although most of the studies reviewed here have been based on cultured cell lines, but their findings have been confirmed by some key in vivo studies. The CNS seems to be particularly involved and is severely affected by most avitaminoses, especially in the case of vitamin B(12). However, the vitamin-induced changes in cytokine and growth factor synthesis may initiate a cascade of events that can affect the function, differentiation, and morphology of the cells and/or structures not only in the CNS, but also elsewhere because most natural vitamins, cytokines, and growth factors cross the blood-brain barrier. As cytokines are essential to CNS-immune and CNS-hormone system communications, natural vitamins also interact with these circuits. Further studies of such vitamin-mediated effects could lead to vitamins being used for the treatment of diseases which, although not true avitaminoses, involve an imbalance in cytokine and/or growth factor synthesis.
Learning from the past and looking to the future.

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Abstract

BACKGROUND/AIMS: Leaders in the fields of nutrigenomics/genetics can benefit from studying the ethical and social issues raised by comparable biomedical developments in the recent past and their consequences for science and society.

METHODS: Experience with recombinant DNA research, beginning in the early 1970s, and its commercial application, and with pharmacogenetics/genomics, beginning two decades later, is analyzed.

RESULTS: Particular lessons are drawn from both experiences. As to the first, the conclusions are to encourage open discussion among scientists of the possible negative or risky consequences of their research; not to conduct such discussions behind closed doors, so as to involve rather than to surprise the public; and to keep in mind the international characteristics of science but the domestic nature of the manner in which it is regulated. As to the second, the lessons are to beware of hype, avoid genetic determinism, take account of the problems raised by similarities to traditional genetic screening/testing, overcome the medical system’s lack of preparation to use the new information, and recognize that differences in access may exacerbate inequities in health and health care.

CONCLUSION: Awareness of these problems, which are likely to recur, can at least prepare those working in the field.

PMID: 19690435

Proteomics at the center of nutrigenomics: comprehensive molecular understanding of dietary health effects.

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**Abstract**

Apart from the air we breathe, food is the only physical matter we take into our body during our life. Nutrition exhibits therefore the most important life-long environmental impact on human health. Food components interact with our body at system, organ, cellular, and molecular levels. These dietary components come in complex mixtures, in which not only the presence and concentrations of a single compound but also interactions of multiple compounds determine ingredient bioavailability and bioefficacy.

Modern nutritional and health research focuses on promoting health, preventing or delaying the onset of disease, and optimizing performance. Deciphering the molecular interplay between food and health requires therefore holistic approaches because nutritional improvement of certain health aspects must not be compromised by deterioration of others. In other words, in nutrition, we have to get everything right.

Proteomics is a central platform in nutrigenomics that describes how our genome expresses itself as a response to diet. Nutrigenetics deals with our genetic predisposition and susceptibility toward diet and helps stratify subject cohorts and discern responders from non-responders. Epigenetics represent DNA sequence-unrelated biochemical modifications of DNA itself and DNA-binding proteins and appears to provide a format for life-long or even transgeneration imprinting of metabolism. Proteomics in nutrition can identify and quantify bioactive proteins and peptides and addresses questions of nutritional bioefficacy. In this review, we focus on these latter aspects, update the reader on technologic developments, and review major applications.

PMID: 19665868m


**N-3 fatty acids in glucose metabolism and insulin sensitivity.**

**Abstract**
Polyunsaturated fatty acids (PUFA) of the n-3 series are essential for normal growth and development. The health effects of these fatty acids include reduction of cardiovascular risk due to antiarrhythmic, antiinflammatory, anti-thrombotic and lipid lowering actions. An increase in unsaturation of the muscle membrane fatty acids is associated with improved insulin sensitivity. Higher proportion of n-3 fatty acids may have beneficial roles, such as antiobesity effects and protection against the metabolic syndrome and type 2 diabetes mellitus through a number of metabolic effects. However, controversy exists on the different effects of n-6 and n-3 polyunsaturated fatty acids as well as on the interacting effect of dietary saturated and monounsaturated fat. In addition, some adverse effects have been described concerning the use of fish oil supplements containing high doses of n-3 fatty acids. Several studies show Eskimos diabetes risk, while results of nutritional interventions on the influence of consuming diets rich in oily fish or other food rich in n-3 fatty acids is very limited. This article reviews the possible mechanisms through which n-3 PUFA are involved in glucose level control and insulin sensitivity. Intervention and epidemiological studies together with recent findings on the nutrigenomic field related with this subject are also briefly reviewed.

PMID: 19593479


Nutrigenomic targeting of carbohydrate craving behavior: can we manage obesity and aberrant craving behaviors with neurochemical pathway manipulation by Immunological Compatible Substances (nutrients) using a Genetic Positioning System (GPS) Map?

Downs BW, Chen AL, Chen TJ, Waite RL, Braverman ER, Kerner M, Braverman D, Rhoades P, Prihoda TJ, Palomo T, Oscar-Berman M, Reinking J, Blum SH, DiNubile NA, Liu HH, Blum K.

Department of Nutrigenomics and Personalized Medicine, LifeGen, Inc., La Jolla, CA, USA.

Abstract

Genetic mediated physiological processes that rely on both pharmacological and nutritional principles hold great promise for the successful therapeutic targeting of reduced carbohydrate craving, body-friendly fat loss, healthy body recomposition, and overall wellness. By integrating an assembly of scientific knowledge on inheritable characteristics and environmental mediators of gene expression, we review the relationship of genes, hormones, neurotransmitters, and nutrients as they correct unwanted weight gain coupled with
unhappiness. In contrast to a simple one-locus, one-mechanism focus on pharmaceuticals alone, we hypothesize that the use of nutrigenomic treatment targeting multi-physiological neurological, immunological, and metabolic pathways will enable clinicians to intercede in the process of lipogenesis by promoting lipolysis while attenuating aberrant glucose cravings. In turn, this approach will enhance wellness in a safe and predictable manner through the use of a Genetic Positioning System (GPS) Map. The GPS Map, while presently incomplete, ultimately will serve not only as a blueprint for personalized medicine in the treatment of obesity, but also for the development of strategies for reducing many harmful addictive behaviors and promoting optimal health by using substances compatible with the body's immune system.

PMID: 19450935


[Human nutrition in the context of evolutionary medicine]

[Article in German]

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Abstract

Evolutionary medicine has gained increasing attention in recent years by implying that a food selection similar to that of the Paleolithic may prevent diseases. This article is an attempt to characterize the food selection during hominid evolution based on current paleontologic research. Hominid evolution can be divided into multiple phases; and the nutrition ecology of the plio-pleistocene hominids can be tentatively characterized. According to new results of isotope analysis, the Australopithecines did ingest small amounts of animal food already 4.5-2.5 million years ago, while consuming a mainly plant based abrasive diet, which was similar to that of recent chimpanzees. Compared to the Australopithecines, the first representatives of Homo such as H. erectus and H. habilis (2.5-1.5 million years before today) were likely to consume a diet providing more energy and nutrients, which might also have been related to the more gracile dentition. Like H. sapiens the members of this species also consumed an omnivore diet. Assumptions about the nutrition ecology of the archaic and the modern H. sapiens are often concluded by
analogies based on the living of historic and recent foragers (hunter-gatherers). As the few detailed ethnographic data show, the diet composition of the individual hunter-gatherer groups varied considerably and ranged from a nearly pure animal-based diet to a diet dominated by plants. All in all the eating behaviour of prehistoric humans was, like that of their pleistocene ancestors, very flexible. Except for focussing on an energy and nutrient-rich diet there was neither specialization in certain foods, nor a typical plant-animal ratio nor a defined macronutrient distribution. Correspondingly, it is impossible to justify details given by representatives of evolutionary medicine on "the Paleolithic diet" empirically.

PMID: 19412746


Future perspectives of nutrigenomics foods: benefits vs. risks.

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Abstract

Nutrigenomics, defined as the application of high-throughput genomics tools in nutrition research is now past its incubation phase. The poorly understood associations of diet and disease prevention in particular will likely be the single most important catalyst to its accelerated and continued growth. Whether the goal of matching foods to individual genotypes to improve the health of those individuals can be attained, and personalised nutrigenomic foods enter the world's food markets, depends on numerous hurdles being overcome: some scientific in nature, some technical and others related to consumer, market or ethical issues. Public adoption of new technologies is an important determinant for their success. Many of the drivers behind the trend in personalisation of food are now known, particularly ethical, legal, and social issues (ELSI) are the major drivers. Future development in the field of nutrigenomics undoubtedly will place its seemingly huge potential in better perspective. From the scientific responsibility point of view, one hopes that the new perspectives to be gained and progress to be made in this field will be so managed as to take the public at large on board, if we are to avoid another nutrition education disaster of the genetically modified organism type and dimension.

PMID: 19374251

Nutrigenomics patents and commercialization: old wine in a new bottle?

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Abstract

This paper looks at the ethical, legal, and social issues (ELSI) associated with commercialization and patenting through the lens of nutrigenomics. These are two areas have generated a great deal of ELSI literature, although very little specific to nutrigenomic research. Nutrigenomic researchers seem likely to face the same patent concerns as those associated with gene patents more generally--specifically, that patents will hurt research and the distribution and uptake of useful technologies. Likewise, there is concern that commercialization pressure will lead to the inappropriate and premature implementation of nutrigenomic services. This paper concludes that while the patenting issues do not seem unique or particularly worrisome in the context of nutrigenomics, the early commercialization of testing is cause for concern and worthy of careful policy consideration.

PMID: 19290812


Nutrigenomics approaches to functional foods.

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Abstract

By definition, functional foods benefit human health beyond the effect of nutrients alone. However, few are accompanied by convincing health claims, partly because human responses are variable. Nutritional biochemistry explains why polymorphisms in genes for the absorption, circulation, or metabolism of
essential nutrients, such as n-3 polyunsaturated fatty acids, would affect the efficacy of that nutrient. However, functional foods often incorporate bioactive compounds, such as epigallocatechin-3-gallate, without considering the interaction with genetic polymorphisms. For either example there will be individuals whose genotype precludes their deriving significant benefit from an increased intake of such foods, and a small segment of the population that may be disadvantaged. Large-scale, whole-genome association studies are providing unprecedented understanding of the genetic basis of health and chronic disease. This rapidly evolving genomic science often fails to consider the interaction with environmental exposure like diet. It is important that the dietetics profession ensures rigorous nutrition science alongside genetic evaluation as part of future study design to derive informed information on gene-diet interactions that may enable clients to rationally select foods leading to optimal health or reduced risk of chronic disease.

PMID: 19248861


Biomarkers for diet and cancer prevention research: potentials and challenges.

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Abstract

As cancer incidence is projected to increase for decades there is a need for effective preventive strategies. Fortunately, evidence continues to mount that altering dietary habits is an effective and cost-efficient approach for reducing cancer risk and for modifying the biological behavior of tumors. Predictive, validated and sensitive biomarkers, including those that reliably evaluate "intake" or exposure to a specific food or bioactive component, that assess one or more specific biological "effects" that are linked to cancer, and that effectively predict individual "susceptibility" as a function of nutrient-nutrient interactions and genetics, are fundamental to evaluating who will benefit most from dietary interventions. These biomarkers must be readily accessible, easily and reliably assayed, and predictive of a key process(es) involved in cancer. The response to a food is determined not only by the effective concentration of the bioactive food component(s) reaching the target tissue, but also by the amount of the target requiring modification. Thus, this threshold response to foods and their components will vary from individual to individual. The key to
understanding a personalized response is a greater knowledge of nutrigenomics, proteomics and metabolomics.

PMID: 17723162


Using nutrigenomics to evaluate apoptosis as a preemptive target in cancer prevention.

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**Abstract**

Apoptosis, a form of programmed cell death, is a pivotal defense against cancer and is essential in maintaining tissue homeostasis. Many diseases including cancer have been associated with aberrantly regulated apoptotic cell death, thus elucidation of events associated with both apoptosis and carcinogenesis provides the opportunity for dietary intervention with the plethora of bioactive components in the diet. Apoptosis occurs primarily through two well-recognized pathways in cells including the intrinsic, mitochondrial-mediated pathway and the extrinsic, death receptor-mediated pathway. Dietary components can modulate apoptosis through effects on protein expression and function, mRNA expression, and on the human genome, either directly or indirectly, to modulate gene expression. Thus, apoptosis is an emerging target of dietary bioactive agents. However, apoptosis is a complex process, with numerous specific targets within each pathway that may or may not overlap. Furthermore, biological systems are also extremely complex and exhibit properties that extend far beyond observations associated with each independent cellular process. This is further complicated by the temporal nature of many of these effects. As a result, it is critical to evaluate the entire biological system from the nutrigenomics perspective to include critical evaluation of DNA polymorphisms or SNPs of a gene, expression of that specific gene, expression of specific processed mRNA (alternative splicing), protein production from that mRNA, post-translational modification of the resultant protein, and formation of respective metabolites. Evolution of the fields of nutrigenetics, epigenomics, transcriptomics, proteomics, and metabolomics has begun to permit this approach so that a comprehensive picture emerges from not only a single cell but tissues and whole organisms. Studies such as these can ultimately be used to study tumors to understand the molecular
events that accompany carcinogenesis and perturbations that occur during cell death processes and how an individual's response to diet can impact these processes.

PMID: 17691903


[Nutrigenomics. Scientific basis, status and perspectives of application]

[Article in German]

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Abstract

Nutrigenomics investigates the interaction between nutrition and the genome, thereby combining nutritional research with functional genomics. Its aims are (1) to correlate heterogeneous effects of nutrients with sequence variations in the genome and (2) to investigate the effects of nutrients and other food components on gene expression at a genome-wide scale (mRNA profiling), and on patterns of metabolite alterations in serum (metabolite profiling). The field will provide important information as to the biological effects of food components, and to the functional consequences of genetic variance. This information will improve the prevention of nutrition-related diseases, e. g. by establishing personalised nutritional recommendations.

PMID: 17013774


Dietary small molecules and large-scale gene expression studies: an experimental approach for understanding their beneficial effects on the development of malignant and non-malignant proliferative diseases.

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Abstract

Epidemiological studies have repeatedly demonstrated a correlation between nutrition, development and the severity of malignant and non-malignant proliferative diseases such as cancer and atherosclerosis. Therefore, the prevention of chronic proliferative diseases through dietary intervention is currently receiving considerable attention. Until now, much of the research is being focused on the cellular and molecular action mechanisms of dietary small molecules explaining their beneficial effects. Dietary chemicals may affect gene expression in several human diseases. However, significant progress has been made and several molecular action mechanisms have been proposed. Alteration of genetical pathways by nutrition, also called "Nutrigenomics", may offer a new approach for understanding the beneficial effects of dietary compounds on the development of severe polygenic diseases, such as cardiovascular disease, diabetes and hypertension. This review focuses on the nutritional genomics of dietary chemicals with a special emphasis on catechins. Catechins belong to the flavonoid family, which are polyphenolic compounds available in foods of plant origin. Several epidemiological studies have reported that consumption of flavonoids, and especially catechins might function as chemopreventive agents against cancer and cardiovascular diseases.

PMID: 16787199

Bioactive substances of plant origin in food--impact on genomics.

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Department of Physiological Sciences, Faculty of Veterinary Medicine, Warsaw Agricultural University, Poland.

Erratum in:

Abstract

In the past decade, substantial progress has been made concerning our knowledge of bioactive components in plant foods and their links to health. Human diets of plant origin contain many hundreds of compounds which cannot be considered as nutrients, but appear to play a role in the maintenance of health. These substances are called nutraceuticals. In some cases where the disease process is at least partially understood, elements of protection can be related to a single compound or structurally related group of compounds in the diet. Bioactive components of food which are of special interest include the following groups: polyphenols, phytoestrogens, phytosterols, phytates and polyunsaturated fatty acids. Most of them are featured by antioxidant properties. In the first part of this review, we indicate the main groups of bioactive compounds giving a description of their localisation, chemical properties and biological actions. Recently, it was shown, however, that the bioavailability of potential antioxidants from plant foods is generally too low to have any substantial direct effect on reactive oxygen species. As a result of that it is postulated that dietary compounds, even in very low concentrations, may have a far greater impact than previously appreciated on the regulation of gene expression. The second part of this paper concerns the action of the literally most important bioactive substances on the molecular mechanisms of the control of genes which in turn affect cellular metabolism. A few current studies on the action of selected nutraceuticals on the activity of transcription factors such as AP-1, NF-kappaB, SREBPs, PPARs as final targets in the signal transduction cascade and gene regulation are included. A detailed analysis of numerous factors of dietary origin with their targets is far beyond the scope of this paper. However, continuing research on the effects of nutraceuticals on gene expression should provide insight into the mechanisms of prevention of diseases such as obesity, diabetes, atherosclerosis, hypertension and cancer by dietary manipulations.

PMID: 12537256

Am J Med. 2002 Dec 30;113 Suppl 9B:71S-88S.

Bioactive compounds in foods: their role in the prevention of cardiovascular disease and cancer.

Kris-Etherton PM, Hecker KD, Bonanome A, Coval SM, Binkoski AE, Hilpert KF, Griel AE, Etherton TD.

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"Bioactive compounds" are extranutritional constituents that typically occur in small quantities in foods. They are being intensively studied to evaluate their effects on health. The impetus sparking this scientific inquiry was the result of many epidemiologic studies that have shown protective effects of plant-based diets on cardiovascular disease (CVD) and cancer. Many bioactive compounds have been discovered. These compounds vary widely in chemical structure and function and are grouped accordingly. Phenolic compounds, including their subcategory, flavonoids, are present in all plants and have been studied extensively in cereals, legumes, nuts, olive oil, vegetables, fruits, tea, and red wine. Many phenolic compounds have antioxidant properties, and some studies have demonstrated favorable effects on thrombosis and tumorogenesis and promotion. Although some epidemiologic studies have reported protective associations between flavonoids or other phenolics and CVD and cancer, other studies have not found these associations. Various phytoestrogens are present in soy, but also in flaxseed oil, whole grains, fruits, and vegetables. They have antioxidant properties, and some studies demonstrated favorable effects on other CVD risk factors, and in animal and cell culture models of cancer. However, because phytoestrogens act both as partial estrogen agonists and antagonists, their effects on cancer are likely complex. Hydroxytyrosol, one of many phenolics in olives and olive oil, is a potent antioxidant. Resveratrol, found in nuts and red wine, has antioxidant, antithrombotic, and anti-inflammatory properties, and inhibits carcinogenesis. Lycopene, a potent antioxidant carotenoid in tomatoes and other fruits, is thought to protect against prostate and other cancers, and inhibits tumor cell growth in animals. Organosulfur compounds in garlic and onions, isothiocyanates in cruciferous vegetables, and monoterpenes in citrus fruits, cherries, and herbs have anticarcinogenic actions in experimental models, as well as cardioprotective effects. In summary, numerous bioactive compounds appear to have beneficial health effects. Much scientific research needs to be conducted before we can begin to make science-based dietary recommendations. Despite this, there is sufficient evidence to recommend consuming food sources rich in bioactive compounds. From a practical perspective, this translates to recommending a diet rich in a variety of fruits, vegetables, whole grains, legumes, oils, and nuts.

PMID: 12566142


Non-nutrient bioactive substances of pulses.

Champ MM.
Abstract

Pulses supply many bioactive substances found in minor amounts in food, but which may have significant metabolic and/or physiological effects. These compounds have long been classified as antinutritional factors, but many studies have reconsidered their impact on health. Some could play a role in the prevention of the major diseases of affluent societies. As these compounds can be beneficial or adverse, depending on conditions, an assessment of their various physiological effects is necessary to determine whether they should be preserved or eliminated in each main nutritional situation.

PMID: 12498631


Nutrigenomics: integrating genomic approaches into nutrition research.

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Abstract

It has been suggested that the supermarket of today will be the pharmacy of tomorrow. Such statements have been derived from recognition of our increasing ability to optimize nutrition, and maintain a state of good health through longer periods of life. The new field of nutrigenomics, which focuses on the interaction between bioactive dietary components and the genome, recognizes that current nutritional guidelines may be ideal for only a relatively small proportion of the population. There is good evidence that nutrition has significant influences on the expression of genes, and, likewise, genetic variation can have a significant effect on food intake, metabolic response to food, individual nutrient requirements, food safety, and the efficacy of disease-protective dietary factors. For example, a significant number of human studies in various areas are increasing the evidence for interactions between single nucleotide polymorphisms (SNPs) in various genes and the metabolic response to diet, including the risk of obesity. Many of the
same genetic polymorphisms and dietary patterns that influence obesity or cardiovascular disease also affect cancer, since overweight individuals are at increased risk of cancer development. The control of food intake is profoundly affected by polymorphisms either in genes encoding taste receptors or in genes encoding a number of peripheral signaling peptides such as insulin, leptin, ghrelin, cholecystokinin, and corresponding receptors. Total dietary intake, and the satiety value of various foods, will profoundly influence the effects of these genes. Identifying key SNPs that are likely to influence the health of an individual provides an approach to understanding and, ultimately, to optimizing nutrition at the population or individual level. Traditional methods for identification of SNPs may involve consideration of individual variants, using methodologies such as restriction fragment length polymorphisms or quantitative real-time PCR assays. New developments allow identification of up to 500,000 SNPs in an individual, and with increasingly lowered pricings these developments may explode the population-level potential for dietary optimization based on nutrigenomic approaches.

PMID: 16669608


OMICS-driven biomarker discovery in nutrition and health.

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Abstract

While traditional nutrition research has dealt with providing nutrients to nourish populations, it nowadays focuses on improving health of individuals through diet. Modern nutritional research is aiming at health promotion and disease prevention and on performance improvement. As a consequence of these ambitious objectives, the disciplines "nutrigenetics" and "nutrigenomics" have evolved. Nutrigenetics asks the question how individual genetic disposition, manifesting as single nucleotide polymorphisms, copy-number polymorphisms and epigenetic phenomena, affects susceptibility to diet. Nutrigenomics addresses the inverse relationship, that is how diet influences gene transcription, protein expression and metabolism.

A major methodological challenge and first pre-requisite of nutrigenomics is integrating genomics (gene analysis), transcriptomics (gene expression analysis), proteomics (protein expression analysis) and
metabonomics (metabolite profiling) to define a “healthy” phenotype. The long-term deliverable of nutrigenomics is personalised nutrition for maintenance of individual health and prevention of disease. Transcriptomics serves to put proteomic and metabolomic markers into a larger biological perspective and is suitable for a first “round of discovery” in regulatory networks. Metabonomics is a diagnostic tool for metabolic classification of individuals. The great asset of this platform is the quantitative, non-invasive analysis of easily accessible human body fluids like urine, blood and saliva. This feature also holds true to some extent for proteomics, with the constraint that proteomics is more complex in terms of absolute number, chemical properties and dynamic range of compounds present. Apart from addressing the most complex “-ome”, proteomics represents the only platform that delivers not only markers for disposition and efficacy but also targets of intervention. The Omics disciplines applied in the context of nutrition and health have the potential to deliver biomarkers for health and comfort, reveal early indicators for disease disposition, assist in differentiating dietary responders from non-responders, and, last but not least, discover bioactive, beneficial food components. This paper reviews the state-of-the-art of the three Omics platforms, discusses their implication in nutrigenomics and elaborates on applications in nutrition and health such as digestive health, allergy, diabetes and obesity, nutritional intervention and nutrient bioavailability. Proteomic developments, applications and potential in the field of nutrition have been specifically addressed in another review issued by our group.

PMID: 16600411


Understanding the nutrigenomic definitions and concepts at the food-genome junction.

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Abstract

The marked differences in individual response to dietary factors have led to major controversies in nutrition and puzzled nutrition scientists over the last century. The emerging field of nutrigenomics helps us to understand the basis for some of these differences and also promises us the ability to tailor diet based on individual genetic makeup. Great advances in Human Genome Project, documentation of single nucleotide
polymorphisms (SNPs) in candidate genes and their association with metabolic imbalances have gradually added new tests to the nutrigenomic panel. Studies based on ethnopharmacology and phytotherapy concepts showed that nutrients and botanicals can interact with the genome causing marked changes in gene expression. This has led to the commercial development of nutraceuticals and functional foods that can modify negative health effects of individual genetic profile bringing the field to the "food/genome" junction. Despite the promise of nutrigenomics to personalize diet, there is skepticism whether it can truly bring about meaningful modification of the risk factors connected to chronic diseases, due to the lack of large scale nutrition intervention studies. Several intervention studies currently underway in the United States and abroad (Israel, Spain, and France) will further help validate nutrigenomic concepts. France has already introduced a National Nutrition and Health Program to assess nutritional status and risk of major metabolic diseases. As the field(s) related to nutritional genomics advance in their scope, it is essential that: (a) strict guidelines be followed in the nomenclature and definition of the subdisciplines; and (b) the state/federal regulatory guidelines be updated for diagnostic laboratories, especially for those offering tests directly to the public (without a physician's request) to help protect the consumer.

PMID: 18687041

Transl Res. 2007 Feb;149(2):55-61.

Nutrigenetics and nutraceuticals: the next wave riding on personalized medicine.

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Abstract

The Human Genome Project and subsequent identification of single nucleotide polymorphisms (SNPs) within populations has played a major role in predicting individual response to drugs (pharmacogenetics) leading to the concept of "personalized medicine." Nutritional genomics is a recent off-shoot of this genetic
revolution that includes (1) nutrigenomics: the study of interaction of dietary components with the genome and the resulting proteonomic and metabolomic changes; and (2) nutrigenetics: understanding the gene-based differences in response to dietary components and developing nutraceuticals that are most compatible with health based on individual genetic makeup. Despite the extensive data on genetic polymorphisms in humans, its translation into medical practice has been slow because of the time required to accumulate population data on SNP incidence, understand the significance of a given SNP in disease, and develop suitable diagnostic tests. Nutrigenomics revitalized the field by showing that nutrients and botanicals can interact with the genome and modify subsequent gene expression, which has provided a great impetus for nutrigenetic research and nutraceutical development based on nutrigenetics.

Polymorphisms in methylene tetrahydrofolate reductase (MTHFR) (involved in folate metabolism), apolipoprotein E (Apo E) and ApoA1 (in cardiovascular disease), and leptin/leptin receptor (obesity) genes are some good examples for understanding basic nutrigenetics. Developing nutraceuticals to prevent and manage thrombosis risk in women with thrombophilic gene mutations are discussed in the context of the opportunities that exist at the nutrigenetic/pharmacogenetic interphase leading to "personalized nutrition."

Further research on individual differences in genetic profiles and nutrient requirements will help establish nutrigenetics as an essential discipline for nutrition and dietetics practice.

PMID: 17240315


Nutritional genomics and dietetic professional practice.

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Comment in:


Abstract

Nutrigenomics is concerned with the role of nutrients in gene expression, and nutrigenetics is the study of how genetic variants or polymorphisms (mutations) can affect responses to nutrients; nutritional genomics is the umbrella term. Nutritional genomics can be expected to revolutionize the way dietitians and other
health professionals identify people with chronic diseases and treat those diseases. Understanding the science of nutritional genomics is important to dietitians and other health professionals because major scientific advancements such as this usually have a significant impact on ethics, policy, and practice. Blood lipid profiles are one area in which nutritional genomics has quickly advanced knowledge. New knowledge is available on blood lipid profiles and associated conditions, such as obesity and type 2 diabetes. New technology has also had an impact on policy and practice issues, and ethics is an important issue to consider.

PMID: 19063807


**Diet-related disease, nutritional genomics, and food and nutrition professionals.**

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PMID: 19248855


**Nutritional genomics in practice: where do we begin?**

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**Abstract**

Nutritional genomics, which studies the genome-wide influences of nutrition, has far-reaching potential in the prevention of diet-related disease. It is highly likely that during the next decade the nutritional supplement and functional food industries will continue robust growth in response to advances in nutritional genomics research and its applications. Parallel to this growth will be impressive progress in
understanding the specific influence of certain food components on metabolic pathways and on long-term risk for disease. As genetic information about individuals becomes available, such data are likely to redefine the current concept of preventive medicine. Dietetics professionals have the potential to harness this information and influence health promotion and disease prevention on a global scale. For these reasons, the dietetics profession has an exciting opportunity that, if seized and properly executed, could enhance the scientific foundation of clinical practice, improve therapeutic outcomes, and significantly expand career and economic opportunities for practitioners. The future of dietetics is unquestionably intertwined with nutritional genomics.

PMID: 15800562

J Nutr. 2005 Dec;135(12 Suppl):3027S-3032S.

Nutrient-gene interaction: tracer-based metabolomics.

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Abstract

Understanding nutrient-gene interaction requires tools for both the study of nutrigenomics and the characterization of phenotype. Metabolomics or metabolite profiling is a powerful tool for characterizing metabolic phenotype, and tracer-based metabolomics is a subset of metabolomics that focuses on metabolite distribution and flux determination using tracers. In this review, the characterizations of metabolic phenotype by metabolite profiling and by metabolic flux measurements are compared. The rationale and methodologies of tracer-based metabolomics are explained. Tracer-based metabolomics provides a relational database of metabolites linked by the relationship of shared metabolic pathways, common substrates, and cofactors. Such a collection of flux measurements provides precise and accurate information on the operation of the cellular metabolic network and its response to genetic and nutrient environment changes. Nutrient-gene interaction can be studied using the concept of constraint-based modeling, which states that the observed metabolic phenotype is a consequence of constraints from genetic factors and the nutrient environment. Thus, genetic inheritance (genomic constraints) confers a
wide range of possible phenotypes whereas selection by metabolic (structural and pathway relationship) and environmental (physical environment and nutrient availability) constraints determines the final observed phenotype. The study of the contribution from nutrient and genetic factors to the survival advantage of cancer cells using flux measurements is a critical first step in our understanding of the relationship between nutrient intake and cancer risk.

**PMID:** 16317166

é FRee mas não entrou


Nutritional "omics" technologies for elucidating the role(s) of bioactive food components in colon cancer prevention.

**Davis CD, Hord NG.**

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**Abstract**

Evidence continues to implicate dietary components and genetic susceptibilities as important determinants of cancer risk and tumor behavior. Variation in cancer incidence among and within populations with similar dietary patterns suggests that an individual's response may reflect interactions with genetic factors, which may modify gene, protein, and metabolite expression patterns. Nutrigenomics, defined as the interaction between nutrition and an individual's genome, will likely provide important clues about responders and nonresponders. In this symposium, the role of bioactive food components in colon cancer susceptibility was used to exemplify the application of "omic" technologies for cancer prevention. Topics that were addressed included dietary changes and gene polymorphisms (nutrigenetics), DNA methylation (nutritional epigenomics), gene expression (nutritional transcriptomics), altered formation or bioactivation of proteins (proteomics), and characterizing how the quantity and timing of exposure influence small molecular weight cellular constituents (metabolomics). The final presentation focused on exfoliated cells as a surrogate sample for the evaluation of bioactive food components in cancer prevention. The goal of the symposium was to provide an example of each of the "omic" technologies as they relate to nutrition, cancer risk, and
tumor behavior, and to help the participants understand that an integrated framework that simultaneously examines all of the "omic" technologies is needed.

PMID: 16251632

é FRee mas não entrou


[Advances in molecular nutrition: nutrigenomics and/or nutrigenetics]

[Article in Spanish]

**Marti A, Moreno-Aliaga MJ, Zulet A, Martínez JA.**

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**Abstract**

The application of molecular biology techniques and the success of the Human Genome Project have opened a new era for both Medicine and Nutrition. To date, at least 1,000 human genes causing disease have been identified and partially characterized, 97% of which we now know that are the cause of monogenic diseases. However, other diseases such as obesity, cardiovascular disease, diabetes, and cancer are due to complex interactions between several genes and environmental factors. In spite of the many association studies, over 600 published since 2002, the molecular base of chronic diseases is still uncertain. Information about nucleotide polymorphisms and haplotypes maps is an additional resource for identifying genes implicated in diseases. Genomic development gets close, however we frequently do not accurately know the dietary components and their mechanisms that importantly influence on genetic information expression and its pathologic impairments. The food industry has the opportunity for utilizing the bioactive components of foods to improve health and prevent diseases while considering the consumers’ genetic constitution. This new era of molecular nutrition--gene-nutrient interactions--may evolve in several ways, although two of them are essential. On the one hand, the study of the influence of nutrients on gene expression (nutrigenomics) and, on the other hand, to know the influence of genetic variations in the organism response to nutrients (nutrigenetics).

PMID: 15989061
Nutrigenomics: the Rubicon of molecular nutrition.

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Abstract

The success of the Human Genome Project and the powerful tools of molecular biology have ushered in a new era of medicine and nutrition. The pharmaceutical industry expects to leverage data from the Human Genome Project to develop new drugs based on the genetic constitution of the patient; likewise, the food industry has an opportunity to position food and nutritional bioactives to promote health and prevent disease based on the genetic constitution of the consumer. This new era of molecular nutrition—that is, nutrient-gene interaction—can unfold in dichotomous directions. One could focus on the effects of nutrients or food bioactives on the regulation of gene expression (ie, nutrigenomics) or on the impact of variations in gene structure on one's response to nutrients or food bioactives (ie, nutrigenetics). The challenge of the public health nutritionist will be to balance the needs of the community with those of the individual. In this regard, the excitement and promise of molecular nutrition should be tempered by the need to validate the scientific data emerging from the disciplines of nutrigenomics and nutrigenetics and the need to educate practitioners and communicate the value to consumers—and to do it all within a socially responsible bioethical framework.

PMID: 14666500


[Advances in molecular nutrition: nutrigenomics and/or nutrigenetics]

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Abstract

The application of molecular biology techniques and the success of the Human Genome Project have opened a new era for both Medicine and Nutrition. To date, at least 1,000 human genes causing disease have been identified and partially characterized, 97% of which we now know that are the cause of monogenic diseases. However, other diseases such as obesity, cardiovascular disease, diabetes, and cancer are due to complex interactions between several genes and environmental factors. In spite of the many association studies, over 600 published since 2002, the molecular base of chronic diseases is still uncertain. Information about nucleotide polymorphisms and haplotypes maps is an additional resource for identifying genes implicated in diseases. Genomic development gets close, however we frequently do not accurately know the dietary components and their mechanisms that importantly influence on genetic information expression and its pathologic impairments. The food industry has the opportunity for utilizing the bioactive components of foods to improve health and prevent diseases while considering the consumers’ genetic constitution. This new era of molecular nutrition--gene-nutrient interactions--may evolve in several ways, although two of them are essential. On the one hand, the study of the influence of nutrients on gene expression (nutrigenomics) and, on the other hand, to know the influence of genetic variations in the organism response to nutrients (nutrigenetics).

PMID: 15989061
Significant advances have been made in understanding the relation between dietary factors and disease prevention. However, the identification of those who will or will not benefit from dietary intervention strategies remains a major obstacle. The execution of the Human Genome Project has brought forth a wealth of information about the structure of the genome and the spectacular development of broad genomics technologies have catalyzed a new era in both medicine and nutrition. Each person is genetically unique and phenotypically distinct, and the genetic makeup that individuals inherit from their ancestors is responsible for variation in responses to food. Evidence continues to implicate dietary components and genetic susceptibilities as important determinants of chronic diseases, cancer risk and tumor behavior. Variation in incidence among and within populations with similar dietary patterns suggests that an individual's response may reflect interactions with genetic factors, which may modify gene, protein, and metabolite expression patterns. Nutrigenetics studies the genetic basis of the different individual responses to the same nutritional stimulus and Nutrigenomics is defined as the interaction between nutrition and an individual's genome. With the application of "omic" technologies, proteomic, metabolomic, transcriptomic, will increase our fundamental knowledge of the interaction between life processes and diet. The identification of diet-gene interactions will offers an opportunity to develop dietary interventions that will lead to evidence-based dietary strategies for restoring health and fitness, obviate the effects of genetic factors for preventing diet-related diseases and provide important clues about gene expression and gene modulation by environmental factors.

PMID: 18410060


Nutrigenomics and nutrigenetics: the 'omics' revolution in nutritional science.

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Abstract

The execution of the Human Genome Project has brought forth a wealth of information about the structure of the genome, which can now be used to study how the interplay between our genes and factors from the environment such as nutrition relate to a state of health or disease. To enable such studies, novel
technologies have been designed in particular to monitor the activity of multiple genes simultaneously at
the level of the RNA by transcriptomics, or the level of the proteins by proteomics. In addition, genome
information has boosted approaches to study the role of genetic variation to explain individual differences
in responses to nutrition, underlying in part the susceptibility for nutrition-related disorders. These new
areas of science referred to as 'nutrigenomics' and 'nutrigenetics' respectively, will increase our
fundamental knowledge of the interaction between life processes and our diet or specific components
thereof, which may in time lead to the development of novel functional foods to improve the health status
of the general population, and to the personalized diet to prevent the onset of nutrition-related disorders in
genetically predisposed individuals.

PMID: 16704375


[Nutritional genomics: toward a personalized diet]

[Article in Italian]

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Abstract

Nutrigenomics is the application of high-throughput genomics tools to the study of diet-gene interactions in
order to identify dietetic components having beneficial or detrimental health effects. Nutrition becomes
indeed one of the environmental factors influencing gene expression. We can consider nutrigenomics as a
multidisciplinary science that comes after the human genome characterization and that put the genomic
techniques besides the biochemical and epidemiological aspects, with the aim to understand the etiologic
aspects of chronic diseases such as cancer, type 2 diabetes mellitus (T2DM), obesity, cardiovascular
diseases (CVD), metabolic syndrome, etc. Nutrigenomics is linked to nutrigenetics, which studies the
genetic basis of the different individual response to the same nutritional stimulus. This phenomenon arises
from gene polymorphism. As a consequence genes are important in determining a function, but nutrition is
able to modify the degree of gene expression. These are however theories only at an early stage, but a
perspective in the change of dietetic intervention is emerging. A really personalized diet will be a diet
considering the nutritional status, the nutritional needs based on age, body composition, work and physical activities, but also considering the genotype. The integration of all these information and in particular the ones arising from genomic, proteomic and metabolomic analyses will be useful to define the "nutritional phenotype".

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[Advances in molecular nutrition: nutrigenomics and/or nutrigenetics]

[Article in Spanish]

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**Abstract**

The application of molecular biology techniques and the success of the Human Genome Project have opened a new era for both Medicine and Nutrition. To date, at least 1,000 human genes causing disease have been identified and partially characterized, 97% of which we now know that are the cause of monogenic diseases. However, other diseases such as obesity, cardiovascular disease, diabetes, and cancer are due to complex interactions between several genes and environmental factors. In spite of the many association studies, over 600 published since 2002, the molecular base of chronic diseases is still uncertain. Information about nucleotide polymorphisms and haplotypes maps is an additional resource for identifying genes implicated in diseases. Genomic development gets close, however we frequently do not accurately know the dietary components and their mechanisms that importantly influence on genetic information expression and its pathologic impairments. The food industry has the opportunity for utilizing the bioactive components of foods to improve health and prevent diseases while considering the consumers’ genetic constitution. This new era of molecular nutrition--gene-nutrient interactions--may evolve in several ways, although two of them are essential. On the one hand, the study of the influence of nutrients on gene expression (nutrigenomics) and, on the other hand, to know the influence of genetic variations in the organism response to nutrients (nutrigenetics).
The evidence of a direct link between increased genome/epigenome damage and elevated risk for adverse health outcomes during the various stages of life, such as infertility, foetal development and cancer is becoming increasingly stronger. The latter is briefly reviewed against a background of evidence indicating that genome and epigenome damage biomarkers, in the absence of overt exposure of genotoxins, are themselves sensitive indicators of deficiency in micronutrients required as cofactors or as components of DNA repair enzymes, for maintenance methylation of CpG sequences and prevention of DNA oxidation and/or uracil incorporation into DNA. The latter is illustrated with cross-sectional and dietary intervention data obtained using the micronucleus assay and other efficient biomarkers for diagnosing genome and/or epigenome instability. The concept of recommended dietary allowances for genome stability and how this could be achieved is discussed. The 'Genome Health Nutrigenomics' concept is also introduced to define and focus attention on the specialized research area of how diet impacts on genome stability and how genotype determines nutritional requirements for genome health maintenance. The review concludes with a vision for a paradigm shift in disease prevention strategy based on the diagnosis and nutritional treatment of genome/epigenome damage on an individual basis, i.e. The Genome Health Clinic.
Butyrate may enhance toxicological defence in primary, adenoma and tumor human colon cells by favourably modulating expression of glutathione S-transferases genes, an approach in nutrigenomics.


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Abstract

Butyrate, formed by bacterial fermentation of plant foods, has been suggested to reduce colon cancer risks by suppressing the proliferation of tumor cells. In addition, butyrate has been shown to induce glutathione S-transferases (GSTs) in tumor cell lines, which may contribute to the detoxification of dietary carcinogens. We hypothesize that butyrate also affects biotransformation in non-transformed colon cells. Thus, we have investigated the gene expression of drug metabolism genes in primary human colon tissue, premalignant LT97 adenoma and HT29 tumor cells cultured in an appropriate medium+/−butyrate. A total of 96 drug metabolism genes (including 12 GSTs) spotted on cDNA macroarrays (Superarray; n = 3) were hybridized with biotin-labeled cDNA probes. To validate the expression detected with Superarray, samples of LT97 cells were also analyzed with high density microarrays (Affymetrix U133A), which include biotransformation genes that overlap with the set of genes represented on the Superarray. Relative expression levels were compared across colon samples and for each colon sample+/−butyrate. Compared with fresh tissue, 13 genes were downregulated in primary cells cultured ex vivo, whereas 8 genes were upregulated. Several genes were less expressed in LT97 (40 genes) or in HT29 (41 and 17 genes, grown for 72 and 48 h, respectively) compared with primary colon tissue. Butyrate induced GSTP1, GSTM2, and GSTA4 in HT29 as previously confirmed by other methods (northern blot/qPCR). We detected an upregulation of GSTs (GSTA2, GSTT2) that are known to be involved in the defence against oxidative stress in primary cells upon incubation with butyrate. The changes in expression detected in LT97 by Superarray and Affymetrix were similar, confirming the validity of the results. We conclude that low GST expression levels were favourably altered by butyrate. An induction of the toxicological defence system possibly contributes to reported chemopreventive properties of butyrate, a product of dietary fibre fermentation in the gut.

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Towards a systems biology understanding of human health: interplay between genotype, environment and nutrition.

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Abstract

Sequencing of the human genome has opened the door to the most exciting new era for the holistic system description of human health. It is now possible to study the underlying mechanisms of human health in relation to diet and other environmental factors such as drugs and toxic pollutants. Technological advances make it feasible to envisage that in the future personalized drug treatment and dietary advice and possibly tailored food products can be used for promoting optimal health on an individual basis, in relation to genotype and lifestyle. Life-Science research has in the past very much focused on diseases and how to reestablish human health after illness. Today, the role of food and nutrition in human health and especially prevention of illness is gaining recognition. Diseases of modern civilization, such as diabetes, heart disease and cancer have been shown to be effected by dietary patterns. The risk of disease is often associated with genetic polymorphisms, but the effect is dependent on dietary intake and nutritional status. To understand the link between diet and health, nutritional-research must cover a broad range of areas, from the molecular level to whole body studies. Therefore it provides an excellent example of integrative biology requiring a systems biology approach. The current state and implications of systems biology in the understanding of human health are reviewed. It becomes clear that a complete mechanistic description of the human organism is not yet possible. However, recent advances in systems biology provide a trajectory for future research in order to improve health of individuals and populations. Disease prevention through personalized nutrition will become more important as the obvious avenue of research in life sciences and more focus will need to be put upon those natural ways of disease prevention. In particular, the new discipline of nutrigenomics, which investigates how nutrients interact with humans, taking predetermined genetic factors into account, will mediate new insights into human health that will finally have significant positive impact on our quality of life.

Cancer nutrigenomics.

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Nutrition and cancer: essential elements for a roadmap.

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Abstract

Personalizing nutrition for cancer prevention and therapy will require a comprehensive understanding of "genotypes/phenotypes" in order to identify, evaluate, and prioritize appropriate points for dietary intervention. This nutritional preemption roadmap must begin with accurately assessing intakes/exposures of which bioactive food component(s) is needed to bring about a desired response in critical cellular processes (carcinogen metabolism, DNA repair, cell proliferation, apoptosis, inflammation, immunity, differentiation, angiogenesis, hormonal regulation and cellular energetic) within an individual. Understanding this "individuality" through a better understanding of the "omics" is fundamental to arriving at the correct destination and thus interpreting biological variables which establish the magnitude or direction of a response to bioactive food components.

Nutritional genomic approaches to cancer prevention research.

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Abstract

A wealth of evidence points to the diet as one of the most important modifiable determinants of the risk of developing cancer, but a greater understanding of the interaction between diet and genes may help distinguish who will and will not respond to dietary interventions. The term nutrigenomics or nutritional genomics refers to the bidirectional interactions between genes and diet. Nutritional genomics encompasses an understanding about how the response to bioactive food components depends on an individual's genetic background (nutrigenetics), nutrient induced changes in DNA methylation, histone posttranslational modifications, and other chromatin alterations (nutritional epigenetics), and nutrient induced changes in gene expression (nutritional transcriptomics). These approaches to the study of nutrition will assist in understanding how genetic variation, epigenetic events, and regulation of gene expression alter requirements for, and responses to, nutrients. Recognition of the interplay between genes and diet could ultimately help identify modifiable molecular targets for preventing, delaying, or reducing the symptoms of cancer and other chronic diseases.

Mutat Res. 2004 Jul 13;551(1-2):51-64.

Frontiers in nutrigenomics, proteomics, metabolomics and cancer prevention.

Davis CD, Milner J.
Abstract

While dietary habits continue to surface as a significant factor that may influence cancer incidence and tumor behavior, there is considerable scientific uncertainty about who will benefit most. Adequate knowledge about how the responses depend on an individual's genetic background (nutrigenetic effects), the cumulative effects of food components on genetic expression profiles (nutritional transcriptomics and nutritional epigenomics effects), the occurrence and activity of proteins (proteomic effects) and/or the dose and temporal changes in cellular small molecular weight compounds (metabolomics effects) will assist in identifying responders and non-responders. Expanding the information about similarities and differences in the "omic" responses across tissues will not only provide clues about specificity in response to bioactive food components but assist in the identification of surrogate tissues and biomarkers that can be used for predicting a response. Deciphering the importance of each of these potential sites of regulation will be particularly challenging but does hold promise in explaining many of the inconsistencies in the literature.

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There is strong epidemiologic evidence to show that differences in diet explain a significant proportion of the variation in cancer incidence worldwide. However, because of the complex nature of eating behaviour and the chemical heterogeneity of foods, it remains very difficult to ascertain which aspects of diet, in what quantities and over what time-frames are responsible for modifying risk. In addition, there are few dietary intervention studies demonstrating reduction in cancer risk. Much faster progress has been made in understanding the biological basis of cancer. It is now clear that damage to the genome resulting in aberrant expression of genes (principally suppression of tumour suppressor genes (TSGs) and inappropriate expression of oncogenes) is fundamental to tumorigenesis. It is also becoming clear that much of the inter-individual variation in cancer experience is due to differences in the amount of damage experienced and/or the capacity to repair that damage. Both of these processes are influenced strongly by dietary factors and by genetic predisposition (polymorphisms in the requisite genes). It is possible that understanding diet:gene interactions in DNA damage and in repair will not only explain much of the inter-individual variation in risk but also offer opportunities to design better dietary intervention studies aimed at chemoprevention. The Human Genome maps and the SNPs databases, together with the rapid development of tools suitable for investigating genetic and epigenetic changes in small tissue biopsies provide the means to begin to test hypotheses about the mechanisms by which diet influences cancer risk directly in human subjects. This is likely to form a significant component of the emerging science of nutrigenomics.

PMID: 15225580


Activation of MAP kinases, apoptosis and nutrigenomics of gene expression elicited by dietary cancer-prevention compounds.

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