NUTRITIONAL GENOMIC APPROACHES TO CANCER PREVENTION RESEARCH

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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.

Key Words: nutrition, epigenetics, gene expression, nutrigenetics.

INTRODUCTION

The World Cancer Research Fund and the American Institute of Cancer Research (WCRF/AICR) have recently updated their 1997 summary [1] of the available epidemiological evidence on food, nutrition, and the prevention of cancer, which continues to support the suggestion that cancer incidence and death are potentially avoidable by modification of the diet as well as by physical activity [2]. In addition to such observational evidence, both in vitro and in vivo studies have suggested that several bioactive food components, including phytochemicals found in plants [3], zootechnicals found in animals such as conjugated linoleic acid [4] and omega-3 fatty acids [5] present in certain types of fish, fungochemicals found in mushrooms [6], and bacteriochemicals [7] formed from food fermentation (pre) and those resulting from intestinal flora (pro) are likely to alter susceptibility to cancer. In fact, both essential and non-essential nutrients, have been implicated in many of the pathways of cancer, including apoptosis, cell cycle control, differentiation, inflammation, angiogenesis, DNA repair, and carcinogen metabolism [8]. Examples of bioactive components from the plant kingdom that have been shown to influence cancer pathways in experimental models include folate from green leafy vegetables, selenium from grains and nuts, diallyl disulfide and other organosulphur compounds from garlic, lycopene from tomato products, genistein and other isoflavones from soy products, epigallocatechin-3-gallate and other polyphenols in tea, and isothiocyanates and indole-3-carbinol from cruciferous vegetables.

Interestingly, the Women’s Healthy Eating and Living (WHEL) study [9], which included survivors of early stage breast cancer, recently reported that adoption of a diet that was very high in vegetables, fruit, and fiber and low in fat did not reduce additional breast cancer events or mortality during a 7.3-year follow-up period. To the optimist, these null results suggest that it is not that diet does not matter, but that the diet-cancer connection may be more complicated than previously expected. The results lead us to consider the possibility that there may be responders and non-responders to different exposures (amounts and patterns) of fruits and vegetables. In fact, genetic variation in pathways affecting absorption, metabolism, and distribution of phytochemicals are likely to influence exposure at the tissue level, thus modifying disease risk in individuals [10]. Few experimental clinical studies have examined these gene-diet interactions in humans. Although study design (cancer site, model system or population, food and/or total diet, timing and exposure level) may also be an important determinant of the direction and magnitude of the response to diet, variation in genetic influences on the diet due to gene polymorphisms (nutrigenetics) and/or dietary influences on gene expression (nutrigenomics), on DNA methylation and other epigenetic events, and on post-translational modification of proteins may also account for inconsistencies or variations in response.

It has long been recognized that humans have displayed individual responsiveness to the foods they consume. Phenotypic variation to foods can be as subtle as sensitivity to bitterness, as reflected by the response to compounds like phenylthiocarbamide [11], or as gross as obesity as reflected by differences in energy utilization [12]. Collectively, the scientific study of the way foods or their components interact
with genes to influence phenotype is referred to as ‘nutrigenomics’ or ‘nutritional genomics’ [13, 14]. The
science of nutrigenomics is beginning to provide clarity to the genetic pathways and associated molecular
targets which account for the ability of food components
to result in a physiologically relevant response. Using
examples from the cancer prevention literature, the
focus of this summary is on nutrigenomics, including
(a) how the response to bioactive food components
depend on an individual’s genetic background or nutrigenetics, (b) nutrient induced changes in DNA
methylation, histone postranslational modifications,
and other chromatin alterations or nutritional epi-
genetics, and (c) nutrient induced changes in gene
expression or nutritional transcriptomics.

**NUTRIENTS AND SINGLE
NUCLEOTIDE POLYMORPHISMS
(SNPS)-NUTRIGENETICS**

Vitamin D is a fat soluble vitamin that is found in
food and can be formed in a person’s skin in response
to sunlight. In the presence of adequate ultraviolet
light (UVB) in the wavelength range of 290–315 nm, a
dietary intake of vitamin D may not be needed. Since
adequate exposure to UVB is not always possible for
a variety of reasons, a dietary source of vitamin D
is needed to avoid skeletal diseases that weaken
bones, such as rickets and osteomalacia. There is
evidence that vitamin D adequacy may play a role
in immune function and the regulation of cell growth
and differentiation, and therefore vitamin D may be a
factor in the development of cancer [15]. The vitamin D
receptor (VDR), a nuclear hormone receptor, is known
to mediate the biological actions of 1,25-dihydroxyvi-
tamin D3 (1,25(OH)2 D3), which is the physiologically
active form of vitamin D, by regulating a variety of
target genes involved in cell proliferation and differen-
tiation. There are several known VDR polymorphisms,
but only a few have been shown to exhibit functional
consequences [16] or impact the response to various
dietary components and disease risk [17, 18]. One
particular VDR polymorphism is Fok1 which results in
a VDR protein that is three amino acids longer than the
protein produced from individuals carrying the non-
variant F allele. Individuals with the Ff or ff genotype
were reported to have a 51% and 84% greater risk of
developing colorectal cancer, respectively [18]. Those
consuming a low calcium or low fat diet were found to
have more than doubled the risk of colorectal cancer
when they carried the ff compared to the FF genotype.
Moreover, once the inadequacy of the diet was elimi-
nated the effect of genotype disappeared [18]. Thus
in certain cancers, this polymorphism may serve as a
predictive marker for those who will benefit most from
ensuring adequate nutrient intakes. To complicate
the picture even more, the Fok1 F allele has also been
found to protect against prostate cancer only among
men who get sufficient exposure to vitamin D [17].

Additional VDR polymorphisms have been studied
in connection with many types of cancer, including
bladder, breast, and melanoma, and there is also
evidence that environmental exposures can modify
these relationships [19]. However, many of these
relationships are not consistent from study to study.
The occurrence of multiple VDR gene polymorphisms
raises questions about the importance of single SNPs
in accounting for variation and which dietary-allele
interactions are the most important determinants of
phenotype. Furthermore, multiple variables, includ-
ing diet, race, and sunlight exposure can influence
the relationship between VDR and disease risk [18,
19, 20]. Future studies are needed to expand the un-
derstanding of the molecular and cellular significance
of various polymorphisms, including copy number
variations [21], and their utility in population studies
to detect susceptibility under a variety of environmental
conditions.

An interesting example that highlights fruits and
vegetables, which contain several dietary compo-
ents, concerns manganese superoxide dismutase
(MnSOD), which is a mitochondrial enzyme that plays
a key role detoxification of reactive oxygen species.
A polymorphism (a valine to alanine substitution) in
the mitochondrial targeting sequence, thought to
alter transport of the enzyme into mitochondria, has
been associated with increased risk for breast cancer
[22]. This association has been found to be more
pronounced among women with low intake of fruits
and vegetables. The relationship between MnSOD,
genotype, prediagnostic levels of plasma antioxidants,
and prostate cancer risk has also been evaluated [23].
Plasma levels of selenium, lycopene, and α-tocopherol
were each inversely associated with risk of prostate
cancer, however the associations of prostate cancer
risk with the combined status of lycopene, α-tocophe-
rol, and selenium (antioxidant score) and the MnSOD
polymorphism modified the relation to prostate
cancer risk. The interaction between the combined anti-
odioxidant score and MnSOD polymorphism was stronger
than those for antioxidants assessed individually.
In stratified analyses by the genotype, among men
homozygous for the variant A allele, high (versus low)
antioxidant score was associated with significantly
reduced risk of total prostate cancer. While there is
evidence that some diseases are associated with a
SNP, the majority of the chronic diseases are thought
to have multigenic roots. Thus, examining a single SNP
may not provide sufficient detail to predict risk and/or
appropriate intervention strategies. For the MnSOD
elementary, further studies are needed that consider ad-
ditional genetic polymorphisms- perhaps in the same
gene or other genes- that influence detoxification of
reactive oxidant species.

One additional example of the interrelationship
between SNPs and food components illustrates how
reported discrepancies in the response to disease
outcome may arise from failure to account for several
polymorphisms or genetic differences. A recent case-
control study explored the joint effects of environmen-
tal factors coanalyzed with combinations of six single
nucleotide polymorphisms located in cytochrome P450 genes (c.-163A > C and c. 1548T > C in CYP1A2, g.-1293G > C and g. - 1053C > T in CYP2E1, c. 1294C > G in CYP1B1, and c. 430C > T in CYP2C9) on colorectal cancer risk [24]. In this study, red meat intake was associated with increased risk of cancer, but there were no associations between single SNPs and colorectal cancer as well as single SNPs, red meat intake, and colorectal cancer. However, 3 allelic variant combinations were associated with a significant increase in colorectal cancer risk in interaction with an excessive red meat consumption suggesting an exacerbation of the procarcinogenic effect of red meat in a subpopulation of susceptible individuals.

While there is more and more evidence that the frequency of functional polymorphisms may influence the response to a variety of dietary components, we need to validate and verify these findings [14]. Most findings are associated with single observations in an epidemiological context and therefore need to be substantiated for their relevance and physiological significance in other settings. Additionally, attention needs to be given to the interaction of multiple genes in order to understand what is occurring within cells and ultimately being expressed in terms of cancer development and prevention. This point has been highlighted by Ulrich and collaborators [25] for the example of polymorphisms in folate-metabolizing enzymes that may be linked to cancer risk. These investigators promote the use of a pathway-based approach to data analysis to help discern the independent and combined effects of dietary intakes and genetic variability in folate metabolism. Cost restraints may explain why molecular epidemiological studies have considered only a limited number of polymorphisms that may confer disease susceptibility. The use of haplotypes, which are a set of closely linked genetic markers present on one chromosome which tend to be inherited together, may offer a cost-effective solution for screening large populations. The importance of utilizing haplotypes versus SNPs to examine the VDR gene has been reported [26]. In this example, two subjects (A and B) have identical genotypes at three polymorphisms in the VDR (the Cdx2, the Fok1, and the Bsm–Apa–Taq3UTR polymorphisms) but only differ in their particular combinations of alleles on chromosomes (i. e., their haplotypes). The result for subject B is that less “high-activity” VDR proteins (i.e., having the “F” allele) are expressed, which is expected to lower responses to vitamin D. Interestingly, if only one of the polymorphisms was tested, this difference would not have been detected. Moreover, if only the three individual polymorphisms were analyzed and the haplotypes not taken into account, these effects would also not have been noticed. Thus, not controlling for the underlying complexities in VDR polymorphisms, i.e., by not analyzing multiple polymorphisms and analyzing their haplotypes, can also help to explain contradictory results from in vitro and in vivo functional experiments.

**NUTRITIONAL EPIGENOMICS**

Epigenetics is an emerging frontier of science that involves the study of changes in the regulation of gene activity and expression that are not dependent on gene sequence. Epigenetic regulatory processes are critical components for normal development, organogenesis, tissue formation, differentiation and aging. Evidence continues to support the hypothesis that epigenetic abnormalities are causative factors in cancer, genetic disorders and pediatric syndromes as well as contributing factors in autoimmune diseases and aging [27, 28].

At least four distinct mechanisms are intricately related to epigenetics: DNA methylation, histone modifications, microRNAs as well as other noncoding regulatory RNA, and the emerging evidence concerning chromatin remodeling factors [28]. Abnormal DNA methylation patterns are a nearly universal finding in cancer, as changes in DNA methylation have been observed in many cancer tissues, specifically colon, stomach, uterine cervix, prostate, thyroid, and breast tissues [29, 30]. A common observation in cancer cells is global DNA hypomethylation which is associated with chromosomal instability [31]. Site-specific alterations in DNA methylation are thought to play a significant role in gene regulation and tumor behavior.

For example, cancer cells often have region-specific hypermethylation which is frequently associated with gene silencing of tumor suppressor genes [32] and region-specific hypomethylation has also been observed and is associated with increased oncogene expression [31]. The relationship between aberrant hypermethylation and hypomethylation on the expression of genes and their relationship to disease risk remains an area of active investigation.

It is increasingly apparent that histone posttranslational modifications are important in chromatin structure and dynamics and influence cancer. For example, a switch from inactive to active chromatin is often accompanied by histone hyperacetylation of critical sites in gene regulatory regions. Histone acetylation is regulated by several enzymatic activities with the capacity to either transfer acetyl groups or to induce histone deacetylation, which is associated with gene silencing. In addition to the loss of monoacetylation and trimethylation of histone H4 as a common hallmark of human tumor cells [33], an imbalance of histone acetyltransferase (HAT) and histone deacetylase (HDAC) activities also exists in cancer cells [34].

There is a growing and relatively unrecognized field of study whereby small RNAs have been shown to suppress gene expression at the transcriptional level (i.e., through targeting epigenetic changes to gene promoter loci) [35]. The majority of work to date on non-coding RNA, however, has centered on the role of small RNAs in modulating post-transcriptional silencing (i.e., the targeted degradation of mRNAs) and many investigators consider this an epigenetic mechanism. MicroRNAs (miRNAs), for example, are small RNA molecules, ~22 nucleotides long that
can negatively control their target gene expression posttranscriptionally. Accumulated findings during recent years have established a crucial role for these small RNA in cancer, which has led to the suggestion that dysregulation in the expression of miRNAs may contribute to cancer initiation and progression [36]. Most of studies concerning miRNAs and cancer have been based on expression analyses of tumor cells in comparison with normal cells, with little understanding of mechanistic signals upstream or downstream of miRNA expression.

Because epigenetic marks can be modified, they offer another explanation for how environmental factors, including diet, can influence biological processes and phenotypes. Several dietary components have been reported to influence DNA methylation patterns, including folate, choline, methionine, selenium, and retinoic acid [29]. A classic example for the impact of diet in DNA methylation and cancer is the finding that dietary methyl deficiency (of folate, choline, and methionine) in a rat model has been shown to alter hepatic DNA methylation patterns and induce hepatocarcinogenesis in the absence of a carcinogen [37]. Food components have the capacity to influence DNA methylation in at least four different ways [29]. First, dietary factors are important in providing and regulating the supply of methyl groups available for the formation of S-adenosylmethionine (SAM), the universal methyl donor. Second, dietary factors may modify the utilization of methyl groups by processes including shifts in DNA methyltransferase activity. A third plausible mechanism relates to DNA demethylation activity, which has yet to be fully elucidated. Finally, DNA methylation patterns may influence the response to nutrients by regulating genes (through silencing or activating marks) which influence absorption, metabolism or the site of action for the bioactive food component. It should also be noted that histone methylation may be similarly effected by food components.

A good example for the role of diet in DNA methylation which impacts phenotype has been found using the agouti model. Dietary supplementation with methyl donors (i.e., choline, betaine, folic acid) to maternal diets led to a shift in coat color in offspring from yellow to an agouti coat, which is traditionally associated with a lower risk of cancer, diabetes, obesity and prolonged life [38, 39]. Along with the shift in coat color, investigators examined CpG methylation of the agouti locus with methyl supplementation compared to non-supplemented animals [39]. They found that the coat color changes were directly linked to alterations in DNA methylation with a distribution shift toward increased CpG methylation at the A\textsuperscript{\text{agouti}} locus with methyl supplementation. More recently, dietary genistein supplementation during pregnancy has been found to change the coat color of the offspring in this model and this change was also associated with changes in DNA methylation [40]. The genistein-induced hypermethylation persisted into adulthood, decreasing ectopic agouti expression and protecting offspring from obesity. Approximately 23% of genistein supplemented offspring were characterized as normal adult weight compared to only 10% of unsupplemented offspring. While humans do not have the long term repeat upstream of the agouti gene found in these mice, these studies serve as a proof-of-principal that diet can influence epigenetic events and lead to phenotypic change.

In utero or neonatal exposure to bisphenol A (BPA), a high-production volume chemical used in the manufacture of polycarbonate plastic, is associated with higher body weight, increased breast and prostate cancer, and altered reproductive function. A recent study shows that maternal exposure to this endocrine active compound shifted the coat color distribution of A\textsuperscript{v} mouse offspring toward yellow by decreasing CpG methylation in the agouti locus [41]. Moreover, maternal nutritional supplementation of the BPA diet with either methyl donors or genistein resulted in a control coat color distribution and negated the DNA hypomethylating effect of BPA. Thus, early developmental exposure to a xenobiotic chemical such as BPA can change offspring phenotype by stably altering the epigenome, an effect that can be counteracted by maternal dietary supplements. These types of studies also suggest that in utero exposure to dietary components may not only influence embryonic development but may also have profound and long-term health consequences.

Another good example for the impact of diet on epigenetics concerns histone modification. Recent investigations suggest that several dietary factors, including butyrate (formed in the colon from the fermentation of dietary fiber), diallyl disulfide (present in garlic and other Allium vegetables), and sulforaphane (found in cruciferous vegetables) have the ability to inhibit type I and II HDAC enzymes [42]. These dietary compounds have been associated with cancer prevention in various preclinical and clinical studies. The inhibition of HDAC activity by these dietary constituents may be associated with their cancer protective effects as they have been shown to inhibit cell proliferation and stimulate apoptosis in a manner similar to other HDAC inhibitors.

Dashwood and colleagues identified and characterized the ability of sulforaphane (SFN) to inhibit histone deacetylase (HDAC) in human colon cancer cells and prostate epithelial cells [43, 44]. The HDAC inhibition was associated with global increases in histone acetylation, enhanced interactions of acetylated histones with the promoter regions of the P21 and BAX genes, and elevated expression of p21\textsuperscript{Cip1/Waf1} and BAX proteins. More recently these investigators tested whether SFN might inhibit HDAC activity in vivo [45]. When consumed in the diet, SFN retarded the growth of human PC-3 prostate cancer cells in nude mice. In addition, SFN inhibited HDAC activity in the xenografts, as well as the prostates and mononuclear blood cells (MBC) of these animals, and there was a trend towards increased global histone acetylation in the xenografts, prostates, and MBC. In healthy human subjects, a single dose of 68 g
BroccoSprouts inhibited HDAC activity significantly in peripheral blood mononuclear cells (PBMC) 3 and 6 h following consumption. In addition, there was strong induction of histone H3 and H4 acetylation associated with HDAC inhibition at 3 and 6 h, and whereas HDAC activities returned to normal by 24 h, the apparent histone hyperacetylation was evident for at least 48 h. These findings provide evidence that one mechanism through which SFN may act as a cancer chemopreventive agent in vivo is through the inhibition of HDAC activity. Moreover, the data suggest that HDAC activity in PBMC may be used as a biomarker for assessing exposure to novel dietary HDAC inhibitors in human subjects. Whether dietary agents act as weak ligands for HDAC to regulate genes (such as P21 and BAX) that affect how normal cells respond to external stimuli such as oxidative stress and toxic insults, requires further investigation. It remains to be determined whether HDAC inhibition in healthy individuals influences cancer prevention and whether there are susceptible periods during the lifespan for such protection.

**NUTRITIONAL TRANSCRIPTOMICS**

Modulation of genomic and epigenomic processes do not entirely account for the influence that dietary factors can have on phenotype since changes in the rate of transcription of genes (transcriptomics) can also be exceedingly important [46]. Several bioactive food components have been reported to be important regulators of gene expression patterns both in vitro and in vivo. Vitamins, minerals, macronutrients, and various phytochemicals have been reported to significantly influence gene transcription and translation in a concentration and time dependent manner [14, 47]. These changes may be key links to the ability of food components to influence one or more biological processes including cellular energetics, cell growth, apoptosis, and differentiation, all of which are important in regulating cancer risk and consequences.

Transcriptomics allows for genome-wide monitoring of the simultaneous expression of tens of thousands of genes as well as a comparison of relative expression between these genes. Microarray technologies provide an important tool to discover gene expression changes that are linked to cellular processes, however such responses may be cell type specific and may vary between healthy and neoplastic conditions, as well as during cancer progression. Studies using animal models are beginning to identify specific sites of action of bioactive food components via transcriptomic approaches. For example, the nuclear factor E2 p45-related factor 2 (Nrf2) and the Kelch domain-containing partner Keap1 are modified by sulforaphane and allyl sulfur compounds [48, 49]. Gene expression profiles from wild-type and Nrf2-deficient mice fed sulforaphane have revealed several novel downstream events and thus more clues about the true biological response to this food component. The up-regulation of glutathione s-transferase, nicotinamide adenine dinucleotide phosphate:quinone reductase, gamma-glutamylcysteine synthetase, and epoxide hydrolase has been identified via transcriptomics, which may help explain the ability of sulforaphane to influence multiple processes including those involving xenobiotic metabolizing enzymes, antioxidants, and biosynthetic enzymes of the glutathione and glucuronidation conjugation pathways [50].

Mammals are known to adapt to excess exposure to foods and their components through shifts in absorption, metabolism or excretion. Thus, the quantity and duration of exposure must be considered when evaluating the response of gene expression patterns. Over-interpretation of the physiological significance of a gene expression pattern is possible because microarray technologies provide only a single snapshot in time. While mRNA microarray technology continues to provide a powerful tool for examining potential sites of action of food components, their usefulness for population studies remains uncertain. In this regard, transcriptomic technologies have been used to examine the relationship between diet and prostate cancer among native Japanese and second-generation Japanese-American men as a function of consumption of animal fat and soy [51]. This technology was able to discriminate between benign and cancer tissue as well as identify detectable differences associated with body mass and metabolism between Japanese-born men and second-generation or third-generation American-born Japanese men [51]. To date, relatively few human studies have used transcriptomics to characterize the response to specific dietary components and thus it is hard to make firm conclusions about the utility of this technology. Nevertheless, a recent study illustrates the potential of gene expression profiling to study the effects of a dietary intervention with either high protein or carbohydrate breakfast cereals in healthy individuals. Using blood leukocytes as a source of mRNA, these investigators found that, within a few hours after consumption, the high carbohydrate breakfast resulted in differential expression of glycogen metabolism genes, whereas consumption of the high protein breakfast resulted in differential expression of genes involved in protein biosynthesis [52]. Another recent study suggests the feasibility of using gene expression changes in human prostate epithelium as a measure of response to a dietary intervention [53]. The investigators found significant gene expression changes in human prostate epithelium following a six-week, low-fat/low-glycemic load diet. Future studies of this nature may give insight into the molecular mechanisms underlying the associations of diet and obesity with the development or progression of prostate cancer. Much of the current evidence, however, suggests that mRNA abundance is not always proportional to protein activity and thus cannot substitute for functional and ecological analyses of candidate genes [46]. While the transcriptional profile can be useful in predicting metabolic stress, simpler indicators may suffice. It is possible that more select gene expression microarrays may be useful if targeted to some cellular process. At
this point, however, it seems wise to evaluate carefully the costs and benefits of transcriptomics technologies before including this research approach into large population studies.

CONCLUSIONS

One current working definition for nutritional genomics or “nutrigenomics” is the study of how genes interact with dietary components to alter phenotype. In this view, nutritional genomics encompasses variation in genetic influences on the diet due to gene polymorphisms (nutrigenetics), nutrient induced changes in DNA methylation, histone posttranslational modifications, and other chromatin alterations (nutritional epigenetics), and nutrient induced changes in gene expression or (nutritional transcriptomics). Nutritional genomics will likely impact public health paradigms, including public health recommendations, as well as provide insight about prevention and/or modification of preneoplastic phenotypes in apparently healthy individuals. Thus, in contrast to disease and drug applications of genomics technologies, the goal in nutrigenomics also concerns the ability to distinguish existing disease from absence of disease. To add to the numerous challenges, many of the early nutrigenetic studies assumed that single nucleotide polymorphisms were the main source of human variability, but increasing evidence suggests the importance of more subtle gene regulatory mechanisms, including copy number variants as well as the need to consider adaptation responses and compensatory mechanisms in signaling pathways. There is also a significant bioinformatics challenge with regard to analyzing the results from each of the nutrigenomic approaches. A single gene expression microarray experiment can generate an enormous amount of data. The challenge is to extract useful biological insights from these data. With more robust technologies, DNA methylation patterns and other epigenetic marks may have greater utility in the future as biomarkers in population and case-control studies to determine if differences exist between certain exposed groups or between cases and control. Such studies have the potential to assist in understanding the pathogenesis of cancer and/or maintenance of health as well as support the importance of epigenetic control on gene expression and the impact of dietary influences on epigenetic control. Unraveling the effects of dietary factors on genes and their encoded proteins as well as identifying genetic influences on absorption, metabolism and excretion of these bioactive food components is essential for identifying those who will and will not benefit from intervention strategies.

REFERENCES


ПИТАНИЕ И ГЕНОМИКА: ПРОФИЛАКТИКА РАКА

Данные исследования свидетельствуют о том, что питание в существенной степени может определить риск развития опухолевого процесса. В то же время необходимы дальнейшие исследования взаимосвязи между диетой и геномом для возможности определить чувствительность организма к диетическому лечению. Задачами этой области знаний (“nutrigenomics”) является то, каким образом ответ на биоактивные компоненты пищи зависит от индивидуальных генетических особенностей, вызванных введением таковых изменений в метилировании ДНК, посттрансляционные модификации гистонов и другие изменения хроматина или изменения экспрессии генов. Такие подходы к изучению питания помогут выяснить, каким образом генетические вариации, эпигенетические события и регуляция экспрессии генов изменяют потребности организма и его реакцию на компоненты диеты. Выяснение взаимосвязей между генами и элементами диеты помогут идентифицировать модифицируемые молекулярные мишени для профилактики рака, задержки развития опухолевого процесса и устранения симптоматики рака и других хронических заболеваний.

Ключевые слова: питание, эпигенетика, экспрессия гена.