Incorporating Basic Nutrition Science into Health Interventions for Cancer Prevention

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ABSTRACT Increasing evidence points to numerous dietary components that modify cancer incidence as well as the biological behavior of tumors. These inhibitory or stimulatory effects depend not only on the dietary component examined, but on a number of factors including the cellular DNA profile (nutrigenetic and nutrigenomic effects), protein formation and regulation (proteomic effect), and the effective delivery of the active intermediate at specific target sites (metabolomic effect). Unfortunately, the diet and cancer research domain is strewn with studies that were inadequately designed to monitor biological endpoints, used invalid biomarkers, or monitored irrelevant intakes or exposures. The scientific frontiers in health risk prediction and disease prevention strategies will greatly expand with the building of reliable nutrition and cancer biomarker databases that use modeling techniques to integrate information about intakes, effect biomarkers, and susceptibility biomarkers. Fundamental to this database will be the elucidation of the specific molecular sites of action (targets) for the specific dietary component. Clustering techniques that build on either genes or ratios of genetic expressions or their products will be needed to assess the merit of a particular dietary intervention. Models are already surfacing about how dietary-induced fluctuations in genes and their expression products can modify pathways associated with carcinogen activation and detoxification, alter rates of cellular proliferation, influence apoptosis, and modify angiogenesis. Embracing new genomic technologies offers exciting opportunities for advancing nutrition, especially those related to cancer prevention. We must effectively communicate, within a responsible bioethical framework, the potential value of knowledge about genes and gene products. J. Nutr. 133: 3820S–3826S, 2003.

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Advances in the molecular revolution and the advent of genomic and proteomic technologies are rapidly changing views about cellular events that relate to health and disease prevention (1–6). The human genome project has already documented that sequence variations are common and, most likely, important contributors to the variation in biological responses and outcomes. The genomics revolution has catalyzed the development of several new technologies that can be applied to evaluate more comprehensively the molecular changes occurring during the cancer process. These new technologies, which encompass genomics, proteomics, and nanotechnologies, provide exciting opportunities for simultaneously monitoring thousands of molecules involved in key pathways and evaluating the influence of foods and specific food constituents. As these opportunities are transformed into reality, the science of nutrition will be shaped by its ability to be integrated with molecular genetics, molecular biology, pathology, toxicology, physiology, and several other disciplines (including bioinformatics) to produce a broad-based molecular approach. This integration will not only allow for effective monitoring but should assist in identifying cellular disturbances that may be modified or corrected by dietary modification or the use of specific bioactive food components. These advances will surely transform the way nutrition and health issues are addressed as well as the delivery of messages to the general public and specific individuals.

The genomic era has already transformed views about experimentation by enabling researchers to more comprehensively examine extremely complex biological processes, including those associated with cancer. The complexity of the process influenced is highlighted by the potential involvement of pathways involved with carcinogen bioactivation, DNA repair, cell communication, cell signals, apoptosis, and angiogenesis (7,8). It is increasingly apparent that cells may contain dozens of genes that are abnormal in structure or copy number and that hundreds of genes may be differentially expressed depending on the environment or their phenotypic
characteristics. Genetic instability appears to be an early and essential event in tumor development that can ultimately influence a host of biological processes. This instability results in significant cell-to-cell genomic variation (genomic heterogeneity) and probably accounts for the uniqueness among cells within individual tumors (9). However, what remains unclear is which genetic change is most instrumental in transforming the normal cell into a neoplasm. What is becoming increasingly clear is that multiple mutations are needed to elicit the tumor. Although a number of familial cancer genes with high penetrance mutations have already been identified, the contribution of low penetrance genetic variants, or polymorphisms, to sporadic cancer risk and development remain unclear. Elucidation of differences in genomic perturbations between normal and neoplastic cells will assist not only in identifying new targets and potentially early or intermediate molecular biomarkers but also in identification of appropriate dietary intervention strategies to reduce the risk of developing cancer or changing the biological behavior of the neoplasm.

Oltvai and Barabasi (10) used a pyramid to portray the complexity of cellular processes. The base of the pyramid is composed of the various molecular components of the cell (i.e., genes, RNA, proteins, and metabolites) that serve as building blocks and organize themselves into small recurrent patterns called pathways in metabolism and motifs in genetic-regulatory networks. These pathways and motifs are seamlessly integrated to form functional modules or groups of nodes that are responsible for discrete cellular functions. These modules are intertwined in a hierarchical fashion and ultimately define a cell’s functional organization. Studies by Lee et al. (11) and Milo et al. (12) provide fundamental support for the cellular organization suggested by Oltvai and Barabasi’s complexity pyramid. Bioactive food components must be viewed in the context of their ability to influence cellular molecules; the effect that this has on motifs and pathways; and, ultimately, how they influence overall cellular processes and phenotypic characteristics (Fig. 1). The phenotypic uniqueness of cells may also influence the response to bioactive food components and thus the strategies used to modify molecules, motifs, and processes (Fig. 1). The integration of events represents a significant challenge for those involved with nutrition because the outcome will depend not only on the quantity and duration of exposure but on a host of cell, tissue, and organism events. The development of new and integrated maps such as those developed by the National Cancer Institute’s Cancer Genome Anatomy Project will help identify links between the different organizational events that may be influenced by the diet or dietary components (13,14).

**Nutritional preemption**

New approaches to prevention and treatment should arise as molecular information relating diet to cancer processes surfaces and will likely introduce a host of new terminologies. Terms such as nutritional genomics, nutrigenetics, and nutrigenomics are already beginning to creep into the literature and new terms are likely to follow (3,4,13,15). Because the goal of these approaches will ultimately be to prevent a carcinogenic event from taking place, we may be entering a new era of nutritional preemption. It could be argued that nutritional preemption has been the foundation of strategies for the prevention of essential nutrient deficiencies, but this has not been embraced as an overall strategy for reducing cancer burden. Although the science of nutrition undeniably has many significant advances to its credit, many uncertainties remain about who will be responsive to intervention strategies for disease risk reduction, especially related to cancer prevention. Several factors can influence the overall response to food components (Fig. 2). The genetic profile (nutrigenetic effect) can influence the response to bioactive food components by influencing absorption and metabolism and its target or site of action. Likewise, DNA methylation and other epigenetic events can regulate the response to food components by influencing the expression of genes. The responsiveness to food components also depends on the ability to lead to shifts in genetic expression profiles. Finally, alterations in the synthesis, degradation, and posttranslational modification of proteins can determine the response to foods and their components (Fig. 2).

**FIGURE 1** Nutrition, cellular processes, and phenotypic characteristics. The response to dietary component is dependent on a number of cellular intermediates that can influence genetic pathways, functional modules, and ultimately, phenotypic characteristics. Likewise, the phenotypic characteristics appear to influence the response to specific bioactive food components. The pyramid model for describing system biology is based on the publication by Oltvai and Barabasi (10).

**FIGURE 2** Interrelationships between bioactive food components and cellular processes. The response to bioactive food components is dependent upon genetic background (nutrigenetic effects) that can influence absorption and metabolism and its target or site of action. Likewise, the response to food components depends on DNA methylation and other epigenetic events. The ability of bioactive food components to influence gene expression patterns (nutrigenomic effects) is also a factor in determining the overall response. Finally, bioactive food components may influence protein synthesis, degradation, and posttranslational modifications.
**Variation in response across and within studies**

Numerous epidemiologic studies point to the likelihood that nutritional preemption may be a useful strategy to influence cancer risk at multiple sites (Fig. 3) (13,16,17). Much of this evidence suggests that the greatest protection coincides with greater fruit, vegetable, and grain consumption (13,17,18). Although it has been almost three decades since dietary habits were proposed to account for 60% of cancers in women and >40% in men (19), the foods and food components that provide the greatest protection remains largely obscure. Nevertheless, intriguing preclinical and epidemiologic studies provide evidence linking various bioactive food components with altered cancer risk and tumor behavior. The past decade has witnessed the publication of several articles that question the role of diet in the cancer process (20,21) and thus have raised concerns about what is physiologically important and the circumstances that may dictate the overall response (13,22). Whether preclinical studies truly reflect what occurs in humans or the background variation in humans due to environmental or genetic factors precludes detection of differences in response to diet is unclear. For example, whereas experiments conducted in vitro or with animal models provide rather compelling evidence that tea can be an effective agent against chemically induced tumorigenesis, affecting induction, tumor size, and metastases, epidemiologic findings are far less compelling (23). The real question is about which series of studies reflect reality. Maybe both are providing important clues to the puzzle and thus the totality of the information must be continually evaluated to determine who will benefit maximally from intervention rather than to try to determine whether all will be equally influenced.

Lycopene is a good example of the controversy that exists within the published literature. Although considerable variability exists in the literature about the potential protective effects of lycopene against prostate cancer (24), five studies support a 30–40% reduction in risk that is accompanied by high tomato or lycopene consumption. However, another seven studies did not support a preemptive relationship (24). The reasons for these inconsistencies are not clear but may relate to the quantity or duration of exposure to lycopene or to genetic differences among subjects in the studies. Increasingly, genetics is being recognized to have an intimate involvement in directing the cancer process and thus is a likely modifier of the response to diet. Evidence for the nutrient-gene interactions come from a variety of studies, including those involving the BHE/Cdb rat, which is a recognized model for mitochondrial diabetes due to a mutation in the ATPase 6 gene. Interestingly, these rats also require more dietary vitamin A to optimize mitochondrial function than do normal Sprague-Dawley rats (25). In humans, hepatic genes appear to influence the response to dietary lipids (26). Overall, the importance of nutrigenetics in explaining the response to foods can be significant. However, as indicated below, it is only one factor establishing the overall response or need for intervention. Nevertheless, a greater research focus on the interrelationships between bioactive food components and genetic pathways linked with cancer, and vice versa, offers hope for untangling the current conundrum.

**Numerous bioactive food components are likely involved**

The interrelationship between the diet and the development and progression of cancer has been a topic of conversation for decades. Which dietary components account for these interrelations has continued to mystify scientists worldwide. Part of the confusion arises from the complexity of the diet and from the fact that numerous essential and nonessential components may modify one or more steps in the cancer process (13). Dietary components with a likely influence on the cancer process are not limited to plants because zoochemicals arising from the consumption of animal products can provide compounds such as conjugated linoleic acid and n-3 fatty acids, which may also influence cancer (27). Likewise, compounds arising from mushrooms (fungochemicals) have been proposed to have anticancer properties (28). Even the microorganisms residing within the gastrointestinal tract may play a key role by forming compounds (bacteriochemicals) that may increase or decrease cancer (29).

The magnitude of the problem in understanding the role of the diet is further illustrated by the fact that thousands of compounds are consumed in the foods ingested every day. The dearth of information about the biological response to specific components is particularly troubling and is limiting the ability to unravel which bioactive components are most important in physiological processes, including those involving normal and neoplastic cells. For example, although it is estimated that humans may be exposed to >5000 flavonoids, only a few have been examined for their anticarcinogenic effects. Overgeneralizations about classes or groups of compounds may lead to false impressions about which are key factors influencing the cancer process and which factors do not have to be considered. Clearly, absolute intake, duration of exposure, and speciation are fundamental to the ability of any bioactive food component to bring about a response. There is reason to believe that in many cases the response in humans will be similar to that observed in models, but the literature is not plentiful with data documenting this with biomarkers for cancer risk or tumor behavior. To move this area forward, additional attention is needed to determine the critical intake and duration required to bring about a desired and physiological change in cancer incidence and tumor behavior.

The complexity of the diet makes simple recommendations extremely challenging (4). Foods are not simply purified elements acting on single molecular targets but are complex mixtures of molecules that likely modulate a host of genetic pathways. Recommending intakes of foods or components above and beyond those needed to provide adequacy requires scientific knowledge and regulatory scrutiny to ensure their efficacy and safety. Designing a diet to improve physiological health is a laudable goal but is not without major challenges and uncertainties. It remains to be established that altering one or more cellular events will truly influence cancer risk or behavior and whether this has any ultimate influence on overall health. Many unanswered questions remain; a greater un-

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**FIGURE 3** Bioactive food components can influence genomic and proteomic events associated with several cancer processes.
understanding of the temporal relationship for gene-nutrient interactions and how short- and long-term exposures influence this relationship will assist in clarifying the overall importance of dietary change.

Single-nucleotide polymorphisms and nutritional effects

Technologies that provide a genome-wide view offer an unprecedented opportunity to scrutinize the molecular biology of the cell and provide insights into intervention strategies for prevention or treatment. Single-nucleotide polymorphisms are the most common type of genetic variation. Because of their distribution across the genome, single-nucleotide polymorphisms are viewed by many as ideal markers for large-scale genome-wide association studies to discover genes in common complex diseases, such as cancer (30,31). Epidemiologic studies have shown that relatives of lung cancer cases are at a twofold increased risk of developing the disease (32), and although part of this is likely to be attributable to familial nongenetic factors, there is support for an inherited predisposition. Part of this susceptibility may be related to interindividual variation in genes encoding DNA repair proteins, cell cycle control proteins, and metabolic enzymes responsible for the bioactivation and detoxification of carcinogens (31). The identification of susceptibility factors that predispose individuals to cancer at other sites will not only provide insight into the etiology of the malignancy but provide targets for future interventions, including those associated with dietary change. In 1999, Vineis et al. (33) provided important insights into how metabolic polymorphisms likely influenced the interrelationship between diet and cancer. Since then new and exciting information has accumulated that points to candidate genes involved in a range of functions including carcinogen metabolism, DNA repair, steroid hormone metabolism, signal transduction, and cell cycle control possibly being involved in the response to dietary components.

The prevalence of these polymorphisms is increasingly being recognized as a significant variable that may influence the results and interpretation of otherwise solidly designed studies. Linkages between polymorphisms in genes associated with drug metabolism and dietary habits are becoming more apparent; these linkages are important for explaining alterations in the initiation phase of carcinogenesis as well as interactions with drugs (34). A low prevalence of polymorphisms in genes coding for activation (phase I) enzymes CYP1A1 (0.07) and CYP2E1 (0.02) was observed in a sample of subjects involved with the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study. There was also a high prevalence in genes coding for detoxification (phase II) enzymes GSTM1 (0.40) and NQO1 (0.20) (35). What effect these or other polymorphisms had on the outcome of the study remains unclear.

Recent epidemiologic, preclinical, and intervention studies suggest an association between low selenium levels and the development of cancers at several sites (36). Recently, human cellular glutathione peroxidase 1 was found not only to be a selenium-dependent enzyme that protects against oxidative damage and its peroxidase activity but to be linked to cancer risk in the lung and breast (37,38). By analyzing the frequency of a polymorphism within the glutathione peroxidase 1 gene resulting in a leucine or proline at codon 198, Hu and Diamond (38) determined that the leucine-containing allele was more frequently associated with breast cancer than was the proline-containing allele (odds ratio = 1.9; P < 0.05). Their studies also suggest that the leucine-containing allele is less responsive to selenium supplementation than is the proline-containing allele. It is unclear whether individuals with the leucine allele account for a large proportion of the protection seen when selenium yeast supplements were provided in the large intervention trial conducted by Clark et al. (39).

Rodent models offer opportunities for identifying targets

Recent developments with mouse strains containing cancer-related genes that are overexpressed or inactivated provided investigators with new models for studying the carcinogenesis process and testing preventive strategies. For example, a mutation of the p53 tumor suppressor gene is one of the most frequently observed genetic lesions in human cancer, accounting for ~50% of all human tumors examined to date. Hursting et al. (40) observed in p53-knockout (p53−/−) mice that energy restriction (60% of the control intake of carbohydrate energy) increased the latency of spontaneous tumor development by ~75%, decreased serum insulin-like growth factor-1 and leptin levels, and significantly slowed thymocyte cell cycle traverse and induced apoptosis in immature thymocytes. Still other research demonstrates the effect of the tumor suppressor gene p21 in determining the response to a diet high in fat and low in vitamin D and calcium and how the allele from each parent can influence the size of the response in terms of longevity (41). Collectively, both animal and human studies provide evidence that genetic background can profoundly influence the way that bioactive food components are absorbed, are metabolized, and influence molecular targets.

Unquestionably, more information is needed to examine how genetic profiles influence the ability of specific dietary components to bring about phenotypic changes. Understanding the dynamic interactions between food components and genetic pathways leading to cancer is the basis of a recent request for application (RFA 03-001) and its soon-to-be-released reissuance. It is believed that enhanced emphasis on genetic pathways and molecular targets will energize the nutrition community to explore sites of action of many bioactive food components across various tissues.

Credentialing gene expression patterns

New microarray technologies that permit parallel analysis of expression patterns of literally thousands of genes in a single experiment, have created an exciting new frontier for the nutrition and health care community. The use of cDNA and oligonucleotide microarrays, or chips, is emerging as a powerful new technology for high throughput examination of gene expression. As microarray technologies emerge, there is widespread belief that they will significantly enhance the ability to explore genetic changes associated with cancer etiology and development and ultimately lead to the discovery of new biomarkers for diagnosis and prognosis prediction and new nutrition intervention strategies. A host of studies are appearing in the literature that demonstrate the nutrigenomic effects of bioactive food components that result in marked increases and suppression in the expression of multiple genes (42–44).

Despite the growing interest in a number of food components for their ability to preempt cancer development, only limited information is available on the molecular mechanism of their action. Additional research is desperately needed to deal with the temporal effects of foods and their components on gene expression patterns across multiple tissues. Recently, Dong et al. (42) found that many genes were influenced by the addition of selenium to synchronized cells in culture. These genes were
clustered into 12 distinct patterns of modulation. Such an approach may assist other investigators to gain valuable insights into the biological effects of food components. Complimenting these in vitro studies in animal models and in humans is fundamental to future developments in nutrigenomics.

Unfortunately, conclusions are far too often established on the basis of a limited number of observations using relatively few chips. It is becoming increasingly apparent that the variation in gene expression profiles requires repeated analysis of each experimental condition to establish conclusions. As the pressure to identify small changes in gene expression grows, it will become increasingly necessary to examine even greater numbers of samples for the variation in response to bioactive food components. The vast amount of gene expression data that will be generated from these multiple samples requires a robust database system that will facilitate efficient data storage, retrieval, secure access, data dissemination, and integrated data analyses. It is important to establish whether commonality in response across tissues occurs or whether there is tissue specificity. A recent National Institutes of Health announcement (CA 03-027) is aimed at supporting research to determine whether bioactive food components alter gene expression across various tissues and whether there is consistency in response among animal models and what occurs in humans.

DNA methylation and dietary intakes

Epigenetic events constitute an important mechanism by which gene function is selectively activated or inactivated (45). Because epigenetic events are susceptible to change, they offer possible explanations of how environmental factors, including diet, may modify cancer risk and tumor behavior. Abnormal methylation patterns are a nearly universal finding in cancer; changes in DNA methylation have been observed in many sites including colon, stomach, uterine cervix, prostate, thyroid, and breast. Site-specific alterations in DNA methylation were also observed in cancer and appear to have a significant role in gene regulation and cancer development. It is likely that dietary factors may influence the methylation process in four different ways (46). First, dietary factors may influence the supply of methyl groups available for the formation of S-adenosylmethionine. Thus, dietary factors such as folate, choline, vitamin B-6, and vitamin B-12 may limit the availability of methyl groups for methylation of DNA or other cellular components. Second, dietary factors may modify the use of methyl groups by processes including shifts in DNA methyltransferase activity. Although several dietary factors appear to influence the methyltransferase reaction, many dietary components have not been adequately examined (46). A third plausible mechanism, which has not been as thoroughly examined, is related to the ability of dietary components to influence DNA demethylation activity. Finally, DNA methylation patterns may influence the response to bioactive food components by influencing their ability to interact with molecular targets. Because methylation patterns appear to influence the response to drugs (47), it would not be surprising if this also influences the response to various dietary components. Again, such findings point to the need for a better understanding of how bioactive food components may influence processes differently in normal and neoplastic conditions. It is not at all clear that preventive strategies with bioactive food components will be identical to those used for therapy.

Posttranslational events

As single-cell organisms have evolved into complex life forms, food components have continued to play a role in influencing directly or indirectly, through hormonal regulation, the expression of genes encoding proteins involved in energy metabolism, cell growth, and cell differentiation. The essential and nonessential food components govern the tissue content and activity of numerous proteins by functioning as regulators of gene transcription, nuclear RNA processing, mRNA degradation, and mRNA translation as well as by functioning as posttranslational modifiers of proteins (48,49). One dietary constituent that has a strong influence on cell differentiation, growth, and metabolism is fat (50). The fatty acid component of dietary lipid influences hormonal signaling events by modifying membrane lipid composition, and fatty acids have a very strong direct influence on the molecular events that govern gene expression. However, shifts in posttranslational events are not only influenced by fatty acids and energy but by a host of bioactive components. Recent studies by Knowles and Milner (51) show that hyperphosphorylation of selected proteins is likely key to the antiproliferative properties attributed to garlic and its allyl sulfur components. It is likely that other food components may also operate by influencing phosphorylation, thiolation, or glycosylation or shifting other posttranslational regulatory events; few compounds have been adequately examined.

More is not always better

Increasing evidence shows that an enhanced intake of a number of bioactive food components retards the cancer process, but it is obvious that additions to the diet are not always protective. Recent evidence by Calle et al. (52) suggests that men with a body-mass index (BMI, weight in kilograms divided by the square of height in meters) of ≥40 had death rates from all cancers combined that were 52% higher than those of their normal-weight counterparts with a BMI of 18.5–24.9. Overweight women (BMI ≥40) had a 62% higher rate than their leaner counterparts with a BMI of 18.5–24.9. In both men and women, body mass index was also significantly associated with higher rates of death due to cancer of the esophagus, colon and rectum, liver, gallbladder, pancreas, and kidney; non-Hodgkin’s lymphoma; and multiple myeloma. Significant trends of increasing risk with higher BMI were observed for death from cancers of the stomach and prostate in men and for death from cancers of the breast, uterus, cervix, and ovary in women. On the basis of associations observed in this study, Calle et al. (52) estimated that current patterns of overweight and obesity in the United States might account for 14% of all deaths from cancer in men and 20% of those in women.

Energy restriction is one of the most consistent modifiers of chemically induced cancer in animal models (33). Reduced energy intake is generally associated with lower rates of cell proliferation during both the premalignant and malignant stages of the cancer process. Jiang et al. (54) reported that not only did energy restriction lead to a reduction in plasma insulin-like growth factor-I and corticosterone but also reduced the levels of phosphorylated retinoblastoma, elongation factor E2F-1, and activity of cyclin-dependent kinases 2 and 4 in carcinoma induced by 1-methyl-1-nitrosourea. Their data also demonstrate the transitory nature of energy restriction because refeeding led to a rapid reversal of these changes.
Nutrition nanotechnologies

Considerable progress has been made in the development of new biology techniques since the discovery of the structure of DNA and the implementation of a polymerase chain reaction methodology. However, several of these technologies have not been adequately embraced by the nutrition community. Nanotechnology must be viewed as an emerging technology that can extend the limits of molecular detection and diagnosis to the nanoscale and create interesting possibilities for assessing the nutritional status of individuals. Mammalian cells are typically ~10,000–20,000 nm in diameter. Therefore nanoscale devices (having at least one dimension <100 nm) can enter cells and the organelles within to interact with DNA and proteins. Biological tests that incorporate nanoscale particles as tags or labels have the potential to allow for monitoring that is more rapid, sensitive, and flexible (55). These technologies coupled with artificial organelles or cells could provide valuable insights into how bioactive food components influence cellular characteristics such as oxidative stress (56) or verification of shifts in site-directed mutagenesis products (57). Recently, polycrylamide-based, ratiometric, spherical, optical nanosensors (polycrylamide probes encapsulated by biologically localized embedding (PEBBLE)) have been fabricated to allow for real-time glucose imaging in intact biological systems. The use of such technologies may assist in unraveling issues surrounding insulin resistance and cancer risk (24). Likewise, nanotechnologies may provide a sensitive method for detecting species of biologically active components arising from the diet. For example, Lin et al. (58) developed an acid extraction protocol coupled to an internally standardized gas chromatography with mass-selective detection assay to monitor total folate in an incredible small amount of blood. More attention to such methodologies may provide important clues that will shed valuable information on shifts in metabolism that occur during the early stages of cancer and after the intake of specific foods or components.

Proteomics

Proteomics is rapidly becoming a major focus as researchers attempt to understand the vast amount of genomic information. Unfortunately the complexity of proteins makes identifying and understanding these gene function products inherently difficult. The challenge of studying proteins is forcing the development of new technologies for systematic and comprehensive analysis of protein structure and function. Researchers are addressing the challenge of parallel expression of components and as an indicator or biomarker for the effectiveness of the intervention. Energy restriction is already recognized to lead to significant shifts in protein profiles (60). Clearly vast possibilities exist for using this new technology to address fundamental questions about nutrition and cancer prevention and therapy.

Establish data bases and bioinformatics

Bioinformatics is a rapidly emerging field of biomedical research. A flood of large-scale genomic and postgenomic data means that many of the challenges in biomedical research are now challenges in computational biology. Postgenomic informatics, powered by high throughput technologies and genomics-scale data bases, is likely to transform biomedical enterprise, including nutritional science, forever. The informatic revolution will likely change the very nature of how we investigate the preemptive effects of bioactive food components. The use of integrative biochip informatics technologies, including multivariate data projection, gene-metabolic pathway mapping, automated biomolecular annotation, text mining of factual and literature data bases, and the integrated management of biomolecular data bases are on the forefront of bioinformatics (61). It is disappointing that few articles highlight the opportunities for using bioinformatics to unravel key nutrition and cancer questions. Undeniably this is an area that deserves special attention for nutritionist and other health professionals.

The sequencing of the human genome coupled with technological advances are providing a fundamental opportunity to transform nutrition and cancer research. In conjunction with novel techniques, a genome-wide annotation of function in cellular models as influenced by bioactive food components is a real possibility. Overalying data derived from whole genome sequence, expression analysis, and functional analysis will facilitate the identification of causal genes in cancer and significantly streamline the bioactive food component-target validation process. Several parallel technological advances in nanotechnology should provide more sensitive indicators of nutritional status and result in the development of expedient and powerful platforms for elucidating intervention strategies. Thus, the future of nutrition and cancer research likely resides in being able to identify molecular targets for food components, convince consumers that this genetic information will assist in appropriate and tailored recommendations, and show that this information can be managed ethically and responsibly. Although there are many challenges to understanding the role of nutrition in the cancer process, the rewards are unmistakable.

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