The role of nutrigenomics and metabolomics in public health-cancer research paper...

Science, Genetics

Introduction

Most of the world's chronic diseases are preventable by long term dietary behavior. Out of the ten major causes of deaths for Americans, diet is a contributing factor to at least five of them. These diseases are such as cardiovascular diseases, cancer and diabetes. A report by the Joint World Health Organization on diet made in 2003 revealed that, most of the world's chronic diseases can be prevented by regular physical exercise and maintenance of a healthy weight. This finding is valid up to date. According to this report, a person's genome determined their susceptibility to disease while external factors such as a person's diet determined which susceptible people were more likely to get ill.

" Genome" refers to the entire sequence of the DNA of an organism. As much as the gene has four bases, their sequence has a great effect on an individual's health and alteration of the sequence can have adverse effects. Among the fundamental areas in genomics is transcriptomics which concerns the transcription of DNA to RNA and Proteomics, the translation of RNA to proteins. Proteins can alter the cellular structure as well as metabolites which determine a person's phenotype eventually .

Metabolomics is the screening of metabolites found in living organisms. Under metabolomics, metabolome profiles can be compared to determine the differences of different groups; healthy verses diseased and wild versed genetically modified. Metabolomics has been in a clinical study for the past decade, in metabolomics profiling, thanks to bioinformatics and developed technology (Gonzalez-Vallinas et al., 2013). This has led to the development of study of the effect of interaction of genes and bioactive food components,

Nutrigenomics. It is through this study that nutritionists have determined how eating behaviors have varied health results across different people. Diet alters the development of disease and its severity. It is also capable of altering gene expression and the result of genetic polymorphisms .

The Role of Nutrigenomics, and Metabolomics in Public Health

The discovery of personalized responsiveness to food has triggered in-depth research on how the interaction of food with genes affects a person’s phenotype; Nutrigenomics/ Nutritional Genomics. Genomic technologies used in nutrition have had profound implications on the advancement of health policies. For example, phenylketonuria (PKU) is a metabolic disease in which an enzyme required to process essential amino acid is absent. The result is mental retardation. A diet devoid of phenylalanine has been the globally accepted standard of care for this disease.

Metabolomics has evolutionalized nutritional research by looking deeper into nutritional value of food beyond the general classification into carbohydrates, proteins and vitamins among others. A big proportion of the food metabolome consists of phytochemicals some of which include lycopene in tomatoes and ioflavones found in soy, and polyphenols found in fruits. This has led to the identification of food-specific biomarkers. Examples of biomarkers include phenylacetylglutamine and glycine for a vegetarian diet usually measured using urine samples. Chlorogenic acid is also a biomarker for a diet that includes coffee and hippuric acid for tea. To determine these biomarkers, different metabolic approaches are used to carry out tests on urine or serum.

The biomarkers could be short term, medium term or long term. EPA, DHA and oleic acid provide short term biomarkers of relative intake of fat, but not the total fat. Red blood cells are believed to have the potential to be more long term than oleic acid, EPHA and DHA. Sodium and nitrogen are also ideal biomarkers for salt and proteins respectively. However, they have to be carried out on 24-hour urine samples for accuracy. These biomarkers reveal a person’s diet exposure. As metabolites interact with genes, enzymes and proteins, they affect cell metabolism through three mechanisms:

- “ Dietary metabolites can act as signaling messengers”. For instance, metabolites can modify nucleic acids such as DNA, proteins such as histones as well as enzymes. By so doing, the metabolites modulate the gene expression in an organism and reprogram an organism’s genetic code. These epigenetic modulations are determined by the presence of subcellular compartmentalization and the concentration of certain metabolites such as acetyl CoA. Certain diet patterns such as fasting and low carbohydrate intake can cause enzyme modulation.
- Dietary metabolites regulate energy metabolism pathways.
- Metabolites are constituents of major macromolecules such as oligosaccharides and DNA. Therefore, they determine the chemical and physical properties of thee macromolecules. Therefore, diet, which affects metabolites, affects these macromolecules and other body organs .

How Nutrition is connected to Cancer

Development of lung, prostate, liver and colorectal cancer is to a great extent linked to diet. However, the patterns differ. This is attributed to the

difference in diet requirement and consequences depending on the individuals' genome and epigenetic events. Nutrigenomics has shown promise of containing and reducing vulnerability to cancer and other opportunistic diet-related diseases. The therapeutic effect of fruits, wine and vegetables, are attributed to phenolic compounds .

Phenolic compounds are responsible for down regulating and up regulating the expression of proinflammatory mediators. They are, therefore, antioxidants and possess anti-inflammatory therapy (Gonzalez-Vallinas et al., 2013). Alcohol affects miRNA expression and how it is an important factor in alcohol liver disease. Alcohol alters the balance of miRNAs by increasing some and reducing some all of which have varying consequences. For instance, alcohol leads to over expression of miR-212 which induces hyperpermiability of the gut by 50% .

The Role of Metabolomics in Diagnosis and Management of Colorectal Cancer

Colorectal cancer (CRC) contributes a great deal to cancer related deaths worldwide. Early imaging of CRC is, therefore, necessary. Metabolomics provides for noninvasive procedures of screening disturbances in metabolisim that are associated with tumor formation. Deeper understanding of the metabolome will not only bring out the sites that require regulation but also help in identifying cancer bio-markers, both surrogate and intermediate . These marker metabolites will make it possibly to know the critical pathways of metabolism in CRC which will be useful in diagnosis of CRC, provide guidance on therapy required and determine the response this will have on CRC. Metabolomics proves to be potentially useful

in early detection of CRC thus increasing chances of successful interventions.

Metabolomics is more accurate in terms of sensitivity and analysis than other “ omics” because of its ability to give results by the use of just a few metabolites, unlike the use of endless miRNA molecules. Metabolomics has helped in the clinical experiments of CRC in easy discovery of molecular target, choice of therapy, biomarker discovery and biomarker validation (Zhang et al., 2013). Samples of serum from colon cancer patients were collected to analyze metabolic alterations. The results revealed a significant number of disease-related alterations in the amino acid profile. This revealed the diagnostic power of metabolomics and its influence in prognostic assessment. Metabolites are critical indicators of pathological processes taking place in the body, normal biological processes and the potential response to clinical therapeutic interventions.

The Genomic Effects of Dietary Components

Nutrient-gene interactions are divided into three major groups:

- Direct interactions: Nutrients after contact with a receptor could bind to DNA thus inducing gene expression
- Epigenetic Interactions: Nutrients can alter the DNA structure leaving the gene severely altered.
- Genetic Variations: Single Nucleotide Polymorphisms (SNPs) have the capacity to alter gene expression.

Clinical studies reveal that the patterns of DNA methylation are partly related to bioactive food components which counteract cancer. These

nutrients are such as vitamin B(12), methionine, choline and vitamin B(6). The effect of diet affects on gene expression is mediated by methylation of DNA. DNA methylation is an epigenetic mechanism that is involved in transcriptional control. It is through DNA methylation that cellular functions are maintained. Alterations in patterns of methylation could alter development. For instance, aberrant methylation is commonly found in tumor cells and hypermethylation has been found to inactivate tumor suppressor genes (Zhang et al., 2011).

How to Prevent and Control of Cancer

The role of micro RNAs in carcinogenesis as well as their potential to be modified by bioactive components found in the diet has been under study for some years now. Their modification is subject to adverse effects because of the important role they play in a number of biological events such as controlling the proliferation of cells, apoptosis, the differentiation of cells and their dysregulation in relation to diseases such as cancer. Various tumor sites have been observed to have certain miRNA expression patterns in them which differ from normal tissues . Studies have also revealed the different microRNA expressions determine pathogenesis of liver cancer and an individual’s susceptibility to liver carcinogenesis, all determined by dietary components.

The level of miRNAs influences tumor progression as well as invasiveness and the possibility of drug resistance . Only recently have studies shown that compounds that influence cell growth or differentiation also modulate miRNA expression. This study has also revealed the dietary components that

counteract cancer through modulation of miRNA expression, thus showing how diet influences carcinogenesis brought about by miRNA (Zhang et al., 2011). The dietary components found to have cancer protective effects are such as folate, curcumin and retinoids, all of which modulate miRNA expression. Micro RNAs are expected to serve as the biomarkers of prevention of cancer, early diagnosis of a disease and nutritional status. Single nucleotide polymorphisms (SNPs) such as inherited polymorphisms in BRCAI have been found to influence susceptibility to breast cancer and women with a low intake of vegetables are considered vulnerable (Zhang et al., 2011).

The Challenges Facing “ OMICS”

Advanced technology such as microarrays, nanotechnologies, and RNA interference has made clear how specific components of bioactive food affect individual phenotypes. This creates necessity to research further on the “ omics” of nutrition. Bioactive food, essential and non-essential have been found to be responsible for the modification of several cellular processes that are directly involved with disease prevention and health in general. This includes hormonal balance, cell signaling, cell cycle control and apoptosis among others. The challenge lies in “ which process” is significant enough to bring a phenotypic change. “ Omics” provides a new insight to the importance of nutrition in prevention of diseases. Selineum supplementation is linked to prevention of cancer in human beings. However, study has it that genetic disparities among individuals are also a critical factor in determining the effect that such a supplement will have on them.

Conclusion

The nutritional value of our diet influences our vulnerability to carcinogenesis, development or inhibition of cancer as well as its regulation. Although the field of miRNA has developed over the past few years, ambiguity remains in the secondary targets and effects as well as the exact dietary proportions required in bringing the biological effects. Motabolimics has shown great promise in future detection and treatment of cancer. This is through the ability to use metabolites to diagnose cancer on time, determine its severity and give the accurate medication. This is expected to increase the number of cancer survivors and provide more accurate results to people who go for check up in an attempt to avoid cancer.

Diet is a determining factor in metabolism; the processes involved; complications and outcome of the entire process. That is why choosing the right diet in correct quantities is important in the prevention of cancer, specifically colorectal and prostrate cancers which have become leading cancer killers worldwide. It has become clear that the effects that diet has on our genome could last a lifetime and even pass on to other generations. This cycle can only be broken by careful and consistent eating habits (Gonzalez-Vallinas et al., 2013).

Dietary and caloric restrictions have proved to reduce chances of breast cancer by close to 80%. Consumption of some dietary components such as those in alcohol has been found to cause gut leakage. This explains why alcoholics have increased chances of obesity. Nutrigenomics and metabolomics are premature fields that are critical in maintaining healthy individuals across the globe by reducing chances of contracting diseases and

mortality. Most important is its goal to enable personalized dietary prescriptions based on an individual’s genotype.

References

Astarita, G., & Langridge, J. (2013). An emerging role for metabolomics and nutrition science. Journal of Nutregenetics and Nutrogenomics , 6:(4-5), 181-200.

Cifuentes, A. (2013). Foodomics: Advanced mass spectrometry in modern food science and nutrition. New York, NY : John Wiley & Sons.

González-Vallinas, M., González-Castejón, M., Rodríguez-Casado, A., & Ramírez de Molina, A. (2013). Dietary phytochemicals in cancer prevention and therapy: A complementary approach with promising perspectives. Nutrition Reviews , 71 (9), 585-599.

Romagnolo, D. F., & Milner, J. A. (2012). Opportunities and challenges for nutritional proteomics in cancer prevention. The Journal of Nutrition , 142 (7), 1360S-1369S.

Zhang, A., H., S., Yan, G., Wang, P., Han, Y., & Wang, X. (2013). Metabolomics in diagnosis and biomarker discovery of colorectal cancer. Cancer Letters , 345 (1), 17-20.

Zhang, F., Morabia, A., Carroll, J., Gonzalez, K., Fulda, K., Kaur, M., et al. (2011). Dietary patterns are associated with levels of global genomic DNA methylation in a cancer-free population. The Journal of Nutrition , 141 (6), 1165-1171.