Nutrition and Genomics

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- **Nutritional genomics, or nutrigenomics,** is the study of how foods affect the expression of genetic information in an individual and how an individual's genetic makeup metabolizes and responds to nutrients and bioactives.
- Not all individuals respond similarly to food.
- That food alters expression of genetic information and that genotypic differences result in different metabolic profiles are concepts central to nutritional genomics and provide the critical link between diet and health.
- In other words, the need to understand nutritional influence on the genome and the genome's influence on metabolism led to the concept of nutritional genomics.
- The notation that interactions between dietary factors and genes (or their variants) can promote health or cause disease is perhaps best captured by the term "nutrigenomics" (a contraction of nutritional genomics).

- **Nutrition-Gene Interaction**

1. Direct interactions

Nutrients, sometimes after interacting with a receptor, behave as transcription factors that can bind to DNA and acutely induce gene expression.

2. Epigenetic interactions

Nutrients can alter the structure of DNA so that gene expression is chronically altered.

3. Genetic variation

Common genetic variations such as single-nucleotide polymorphisms (SNPs) can alter the expression or functionality of genes.

Transcription-factor pathways mediating nutrient-gene interaction

Nutrient	Compound	Transcription factor
Macronutrients		
Fats	Fatty acids Cholesterol	PPARs, SREBPs, LXR, HNF4, ChREBP SREBPs, LXRs, FXR
Carbohydrates	Glucose	USFs, SREBPs, ChREBP
Proteins	Amino acids	C/EBPs
Micronutrients		
Vitamins	Vitamin A Vitamin D Vitamin E	RAR, RXR VDR PXR
Minerals	Calcium Iron Zinc	Calcineurin/NF-ATs IRP1, IRP2 MTF1
Other food components		
	Flavonoids Xenobiotics	ER, NFκB, AP1 CAR, PXR

Nutrient Absorption
Nutrient Utilization
Food/Nutrient
Tolerance
Nutrient Requirement

Food/Nutrient

Nutrigenomics

Nutritional Genomics

Nutrigenetics

Genome Evolution/Selection
Genome Mutation Rate
in-utero Genome Viability
Genome Programming
Gene Expression

Genetic Variation

Nutrigenomics vs. Nutrigenetics

Nutrigenomics

- "Nutrigenomics refers to the application of genomics in nutritional research enabling associations to be made between specific nutrients and genetic factors, e.g. the way in which food or food ingredients influence gene."

Nutrigenetics

- "Nutrigenetics is the study of individual differences at the genetic level influencing response to diet. These individual differences may be at the level of single nucleotide polymorphisms rather than at the gene."

Nutrigenomics

- "Nutrigenomics attempts to study the genome-wide influences of nutrition…[and] aims to identify the genes that influence the risk of diet-related diseases on a genome-wide scale, and to understand the mechanisms that underlie these genetic predispositions."

Nutrigenetics

- "Nutrigenetics examines the effect of genetic variation on the interaction between diet and disease or on nutrient requirements. Genetics has a pivotal role in determining an individual's risk of developing a certain disease."

Nutrigenomics

- "Nutrigenomics describes the use of functional genomic tools to probe a biological system following a nutritional stimulus that will permit an increased understanding of how nutritional molecules affect metabolic pathways and homeostatic control."

- "Nutrigenomics focuses on the effect of nutrients on the genome, proteome, and metabolome."

Nutrigenetics

- "Nutrigenetics embodies the science of identifying and characterizing gene variants associated with differential responses to nutrients, and relating this variation to disease states."

- "Nutrigenetics examines the effect of genetic variation on the interaction between diet and exercise. This includes…gene variants associated with, or responsible for, differential responses to nutrients."

Nutrigenomics

- **Nutrigenomics adhere to the following percepts:**
- Poor nutrition can be a risk factor for diseases;
- Common dietary chemicals can act on the fish genome, either directly or indirectly to alter gene expression and/or gene structure;
- The degree to which diet influences the balance between health and disease depends on an individual's genetic makeup;
- Some diet-regulated genes (and their common variants) play a role in the onset, incidence, progression, and/or severity of chronic diseases, and
- Dietary intervention based on knowledge of nutritional requirement, nutritional status, and genotype can be used to prevent, mitigate, or cure chronic disease.
- Genomic analysis reveals that humans are 99.9% identical at the DNA level. This implies that the remaining 0.1% of the human genome (or about 3 million single nucleotide polymorphisms (SNPs) is responsible for all the morphological, physiological, biochemical and molecular differences between any two individuals and susceptibility to disease.

Nutrigenomics …..

- Common genetic variation in the form of SNPs in enzyme-encoding genes (or their promoters) can affect reaction rates in metabolic pathways that in turn, can create individual differences in the way we absorb, metabolize, store and utilize nutrients.
- SNPs are the most common variation in the primary sequence of DNA.
- SNPs are defined as nucleotide base pair differences in the primary sequence of DNA and can be single base pair insertions, deletions, or substitutions of one base pair for another.
- SNPs contribute to susceptibility for common disease and developmental anomalies and polymorphic alleles have been identified that increase the risk of common disorders including neural tube defects, cardiovascular disease, cancers, hypertension, and obesity.

Nutrigenomics …..

- The initial successes of nutrigenomics have revealed that indeed the natural variation in the genome is responsible for significant variations in response to diets.
- Therefore, the optimal diet for one individual in a population will not be the same for every individual in that population.
- As we learn more about the health-promoting dietary chemicals we eat and how they interact with nutrient-regulated and disease-associated genes, we should be able to achieve optimal health and wellness earlier, maintain it longer, and at a lower cost.
- Just as pharmacogenomics has led to the development of “personalized drugs,” so will nutrigenomics open the way for “personalized nutrition”.

Nutritional Regulation of Gene Expression …..

- From the stand-point of nutritional influences on gene expression, processes are envisioned in which dietary conditions, through either direct interaction of specific nutrients with transcription factors or mRNA binding proteins, or, more commonly, through indirect means (e.g., hormones or signaling systems), produce changes that define phenotypic expression.

- Classic experiments demonstrated that polyribosome formation depended on the presence of essential amino acids in the diet.

Disease – Inherited Risk, Not Inevitable Outcome

- However, if genes alone determine the size, shape and function of organisms, how can we explain the fact that the average height of adult Japanese men and women has increased nearly six inches since WW II?
- The genes have not changed. What has changed is the nutrition of Japanese.
- Nutritional environment combined with genetic inheritance yields the "phenotype" of the individual that is observable size, shape and function.
- **Phenotype**: The entire physical, biochemical and physiological makeup of an individual as determined both genetically and environmentally, as opposed to genotype.

Can Food Improve the Expression of Genes?

- One meal does not make a difference in the expression of genes but over the course of many years dietary choices can influence gene expression in such a way as to modify phenotype, enhancing or diminishing cellular function.
- This does not mean that food changes genes in any way. The message remains intact, embedded in the nucleus of cells in every organ of body.
- **What does change is the way the message from genes is expressed.**
- The effect of the nutrients ingested on the expression of messages within genes is like the effect of hydroxyurea on sickel cell anemia.
- Both substances are capable of waking up the sleeping message in the genome for the production of fetal hemoglobin.

How does diet Improve the Expression….

- By using a substance that modifies genetic expression, it is possible to alter the course of a genetically determined illness.
- Genetic messages can either be put to sleep or awakened as a consequence of alterations in diet. Putting to sleep the messages that result in increased risk of disease and awakening those messages enhance health.
- Administering hydroxyurea to an individual who carries the genetic message for the production of sickle hemoglobin awakens the message to produce the normal fetal hemoglobin that dilutes the sickel hemoglobin, preventing it from crystallizing.
- This nutritional intervention is a classic example of the genetic nutritioneering approach.

How diet Influences Genetic Expression

- The understanding that diet can modify gene expression achieved a new level of acceptance due to the pioneering work of Michael Brown & Joseph Goldstein on cholesterol and its relationship to heart disease.
- They found that there is a basic defect (genetic trail) that leads to high incidence of heart disease, which is associated with very high blood cholesterol levels.
- Affected individuals have elevated blood levels of the “bad” LDL cholesterol. Over time, cholesterol is deposited in arteries, resulting in plaque and a narrowing of the arteries which leads to heart disease.

Phytochemicals and Gene Expression

- Phytochemicals are plant-derived substances that can modify gene expression or physiological functions in individuals who consume them.
- One example of the power of phytochemicals is the recent report that the flavonoid **naringenin**, which is found in grapefruit but not in orange, lemon or lime, can assist the costly prescription drug **cyclosporin** in preventing organ transplant rejection after surgery.
- Naringenin suppresses the gene expression for a detoxifying enzymes in the liver that eliminates the drug cyclosporin from the body. By inhibiting the expression of this enzyme, naringenin helps patients get more benefit from cyclosporin by preventing its detoxification, thereby slowing its elimination from the body.
- A number of biologically active substances in foods help regulate gene expression.

Vitamins, Minerals and Gene Expression

- Vitamin B6 (pyridoxine), vitamin B12 (cobalamin) and folic acid play important roles in modulating gene activity through their ability to mask certain portions of the gene that should not be expressed in adults. Through this masking effect, messages related to the risk of both heart disease and cancer can be put to sleep.
- The essential trace mineral zinc is important in modulating gene expression as well.
- Zinc is a pivotal nutrient in supporting immune system function and it helps regulate the way that the genetic message is translated into protein synthesis in the cell.
- One of the first signs of zinc inadequacy is the loss of taste or smell.
- Individuals whose gene expression is modified as a consequence of zinc insufficiency frequently have a poor sense of taste or smell.

Foods and Gene Expression

- Genes affect response to the food eaten on several levels. They influence the way to absorb, metabolize and excrete nutrients.
- They partially control other factors such as taste and smell, and how quickly or slowly a meal is digested.