

# We Really Are What We Eat

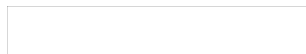
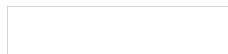
*How Nutrition “codes” your genes . . .*

*Susan Buckley RD  
Nutrition Manager  
South Denver Cardiology Associates*




## Nutrigenomics

- Wouldn't it be wonderful if we could prevent devastating diseases from developing just by changing our diets?
- *Nutrigenomics*
- Blend of Nutrition and Genomics
- The study of genetics with food and nutrition research
- How foods affect the metabolic pathways that alter gene expression



## Nutrigenomics

- You can't choose your family or the genetic risk they pass on to you. . .
- But you CAN choose your diet
- Diet may prove to be enough to mitigate the bad effect of genes, researchers are reporting
- Genetics loads the  gun – lifestyle pulls the trigger!!

## Nutrigenomics

- In 1990 the Human Genome Project (HGP) was initiated as a worldwide effort to clone, map and sequence the entire human genome
- Completed in 2003
- Challenge now is to understand how individual genes function, how they are regulated, and how the encoded proteins interact with and influence each other to cause disease or maintain health

## Nutrigenomics

- HGP is making it possible to identify the genetic factors that influence a person's susceptibility to diseases associated with diet
- Knowledge of the interactions between genotype, diet, lifestyle and environment will ultimately yield *personalized nutritional recommendations*



## Nutrigenomics

- Genes evolve *in response* to many types of environmental stimuli including:
  - Nutrition
  - Exercise
  - Stress
  - Environmental Toxins



## Nutrigenomics

- The basic definition of evolution is a change in the gene pool of a population of organisms over time.
- All of evolution is based on genetic change.
- The foundation of evolution is not just working DNA but *changing* DNA.
- DNA changes in response to the environment – diet, lifestyle

## Nutrigenomics

- Genes are genes, but they can be turned “on” and “off” allowing or preventing the gene from being used to make a particular protein
- Proteins are the building blocks of life
- Proteins are “information” on how your body operates
- The foods you eat, the water you drink, the exercise you get, the toxins you ingest can all affect how your genes get turned on and off.

## Nutrigenomics

- Nutrients can modify the *expression of genes and proteins*
- Progression from a healthy to a chronic disease state may occur due to changes in *gene expression*

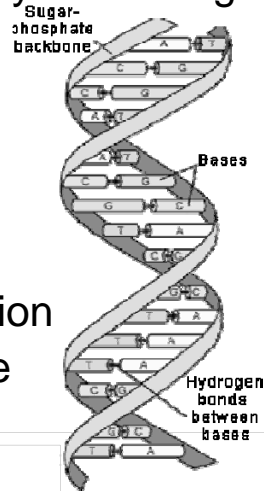


## Nutrigenomics

- Dietary chemicals are regularly ingested and are involved in the regulation of gene expression
- A subset of genes regulated by diet is involved in the initiation, progression and severity of disease
- Diet has a major influence on the incidence and severity of chronic diseases, as we know from research

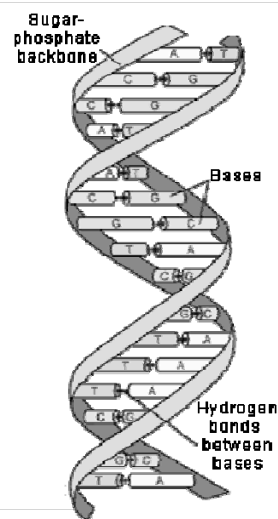
## Nutrigenomics

- Polymorphism – the quality of existing in several different forms
- DNA sequence
- (A, T, G and C)
- Single nucleotide polymorphisms (SNPs) is a single base substitution within the DNA sequence



## Nutrigenomics

- SNPs can result from:
- Genetic predisposition
- Environmental influences
- Combination of both



## Nutrigenomics

- SNPs – Single nucleotide polymorphisms – a single base substitution within the DNA sequence (A, T, G and C) can have multiple effects
- Can influence the sequence, number or level of expression of genes
- Some are associated with a specific disease state
- If SNPs are associated with disease, they can serve as markers and be diagnostically useful

## Nutrigenomics

- The human population is characterized by genome diversity due to these polymorphisms
- All humans are 99.9% identical at the gene sequence level
- The 0.1% variation in sequence produces differences in phenotype the "outward, physical manifestation" of the organism: body size and shape, or chemical differences like plasma glucose, lipids, etc  
Genotype - is the internally coded, inheritable information, or your genes

## Nutrigenomics

- Individual requirements for different nutrients can vary on the basis of a person's genotype
- A diet that may be optimal for one person could predispose another to disease
- Everyone responds differently to diet
- Genetic background can alter nutrient requirements and influence how nutrients are assimilated, metabolized and stored in the body

## Nutrigenomics

- Vitamin and mineral needs vary by individual
- Sodium increases blood pressure in some people and not in others
- The ability of fiber to reduce cholesterol is also subject to genetic influence



## Nutrigenomics

- One of the largest gene-diet interaction studies ever conducted on cardiovascular disease published just this month in PLoS Medicine
- Researchers discovered that the gene that is the strongest marker for heart disease can actually be modified by generous amounts of fruit and raw vegetables

## Nutrigenomics

- Researchers at Canada's McGill and McMaster Universities analyzed data from the INTERHEART and FINRISK studies (over 27,000 people) found that a diet high in raw vegetables and fruits reduced the risk of cardiovascular disease related to the chromosome 9p21 region
- 9p21 carriers are at increased risk of early heart attack or AAA – about 30% increased
- Diets high in raw fruits and vegetables decreased that risk back down to 0% - the same as the general population

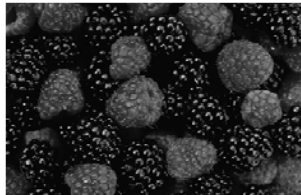
## Nutrigenomics

- The strongest interaction was with raw vegetable intake
- Overall diet high in raw vegetables, fruits and berries was inversely associated with cardiovascular disease compared with the diets lowest in those foods



## Nutrigenomics

- The goal of nutrigenomics will be to identify genes that can be targeted by nutritional intervention to **PREVENT** diseases from developing



## Nutrigenomics

- **Lactose intolerance** – the lactase hydrolase gene allows adults to digest milk/milk products
- **PKU – phenylketonuria** – a recessive disorder characterized by a deficiency in the phenylalanine hydroxylase enzyme which results in the accumulation of phenylalanine, an essential amino acid, in the blood, which increases the risk of neurologic damage and can result in mental retardation
- **Galactosemia** – rare recessive defect of the enzyme galactose-1-phosphate uridylyltransferase (GALT). The lack of GALT results in accumulation of galactose in the blood, which increases risk of mental retardation

## Nutrigenomics

- Research on long-term effects of maternal care on a child's development shows effects all the way into adulthood
- Nutritional programming in utero has a major impact on the development of chronic illness later in life
- Extensive human epidemiologic data have indicated that prenatal and early postnatal nutrition influences adult susceptibility to diet-related chronic diseases including cardiovascular disease, type 2 diabetes, obesity and cancer

## Nutrigenomics

- What a woman eats when she is pregnant can influence her child's genetics in ways that have long-lasting effects on their weight, finds research published in the journal *Diabetes*.
- The study showed that maternal **diet** is linked to epigenetic changes in people and that these changes are related to body fat in children years later.
- Epigenetic – over, above,
- around genetics or environment



## Nutrigenomics

- The moms who ate **diets** lower in vegetables, fruits, grains and other carbohydrates were more likely to have babies with subtle changes in their DNA markers that dictate how genes are read and expressed.
- These children were more likely to be heavier and have higher body fat at age nine. The findings reinforce how important it is for women of childbearing age and pregnant women to eat a balanced, nutritious **diet**, the researchers conclude.

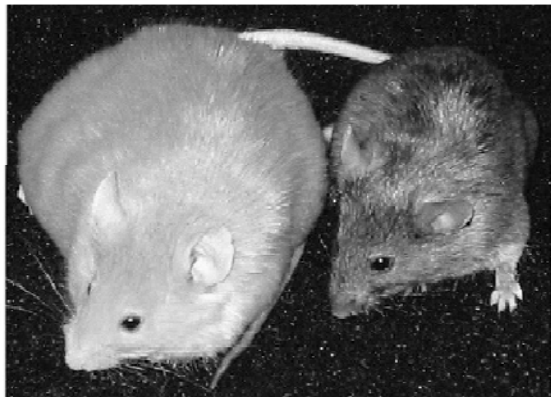
## Nutrigenomics

- Experiments in mice show just how important a mother's diet is in shaping the epigenome of her offspring. Both mice and people have a gene called agouti.
- When a mouse's agouti gene is completely unmethylated it has a yellow coat color, is obese and prone to diabetes and cancer.
- When the agouti gene is methylated (as it is in normal mice) the coat color is brown and the mouse has a low disease risk.

## Nutrigenomics

- Fat yellow mice and skinny brown are genetically identical. You can think of the fat yellow mice as looking different because they have an epigenetic "mutation."
- When researchers fed pregnant yellow mice a methyl-rich diet, most of the resulting pups were brown and healthy and stayed that way for life.
- These results indicate that an individual's adult health is heavily influenced by early prenatal factors. In other words, our health is not only determined by what we eat, but also what our parents ate.

**These Two Mice are Genetically Identical and the Same Age**



While pregnant, both of their mothers were fed Bisphenol A (BPA) but **DIFFERENT DIETS**:

<p>The mother of this mouse received a <b>normal mouse diet</b></p>	<p>The mother of this mouse received a diet <b>supplemented</b> with choline, folic acid, betaine and vitamin B12</p>
---	---

## Nutrigenomics

- **5 principles of Nutrigenomics**
- 1. Common dietary chemicals act on the human genome, either directly or indirectly, to alter gene expression or structure
- 2. Under certain circumstances and in some people, diet can be a serious risk factor for many diseases
- 3. Some diet-regulated genes are likely to play a role in the onset, incidence, progression, and/or severity of chronic diseases

## Nutrigenomics

- 4. The degree to which diet influences the balance between healthy and disease states may depend on a person's genetic makeup
- 5. Dietary intervention based on knowledge of nutritional requirements, nutritional status, and genotype (i.e. "individualized nutrition") can be used to prevent, mitigate or cure chronic diseases

## Nutrigenomics

- At some point in the near future, you will walk into your doctors/dietitian's office with your DNA profile and he/she will design an effective dietary regime for the prevention and management of complex chronic diseases



## Nutrigenomics

- Many chronic diseases – obesity, cancer, diabetes and cardiovascular disease come about from the interaction of multiple genetic factors and environmental factors like diet
- However, the nutritional requirements needed to PREVENT disease may be different from the requirements needed to maintain or improve health

## Cardiovascular Disease

- One of the most common inherited disorders with nutritional implications is familial hypercholesterolemia caused by mutations in the LDL receptor gene
- This mutation leads to impaired clearance of LDL which elevates cholesterol levels
- Could explain why some people have a family history of sudden premature death

## Cardiovascular Disease

- Epidemiologic studies and long-term outcome trials have established a clear link between lipids (fats) and development of CVD
- Several genetic links
- Genes responsible for lipid metabolism that determine levels of LDL cholesterol
- Genes effecting folate metabolism that elevate levels of homocysteine



## Cardiovascular Disease

- Lipoprotein lipase is an enzyme responsible for the breakdown of triglycerides
- Dysfunctional lipoprotein lipase has been associated with various disease states
- Several genes involved in the disruption of normal function of lipoprotein lipase – contribute to the premature development of coronary heart disease
- Triglycerides are increased and HDL levels are decreased

### Apo E Review of Literature<sup>†</sup>

It is necessary to monitor your patients' therapeutic responses and modify your treatments accordingly.

		Apo E2		Apo E3		Apo E4	
Genotype		2/2	2/3	3/3	2/4	3/4	4/4
Population Frequency		1%	10%	62%	2%	20%	5%
Dietary Contribution	<b>Soluble Fiber<sup>1</sup></b>	↓↓LDL		↓LDL		↓LDL	
	<b>Fish Oil<sup>2</sup></b>	↓↓TG ↓small dense LDL ↑HDL		↓TG ↓small dense LDL ↑HDL		↓TG ↓↓small dense LDL ↓HDL may ↑LDL	
	<b>Plant Sterols<sup>3</sup></b>	↓LDL ↓Apo B		↓LDL ↓Apo B		↓LDL ↓Apo B	
	<b>Soy Protein<sup>4</sup></b>	↓Apo B		↓Apo B		↓Apo B	
Dietary Fat and Alcohol Effects	<b>Low Fat Diet<sup>5,6</sup></b>	↓LDL ↑small dense LDL		↓↓LDL ↔ small dense LDL		↓↓↓LDL ↓small dense LDL	
	<b>Moderate Fat Diet<sup>6</sup></b>	↔LDL ↔ small dense LDL		↓LDL ↓ small dense LDL		↓LDL ↑↑small dense LDL	
	<b>Moderate Alcohol<sup>7</sup></b>	↑HDL ↓LDL		↑HDL		↓HDL ↑LDL	

**Legend:** ↓ decreases    ↑ increases    ↔ no change    ↓↓ significantly decreases    ↑↑ significantly increases

**References:**  
 1. a) Am J Clin Nutr. 1997 Sep;66(3):584-90 b) Metabolism 1993;42:585-93  
 2. Arterioscler Thromb Vasc Biol. 2000 Aug;20(8):1990-7  
 3. Nutrition 2002 Jul-Aug;18(7-8):561-5  
 4. Nutr Metab Cardiovasc Dis 2000 Dec;10(6):315-22  
 5. Am J Clin Nutr 2003;77:1098-111  
 6. J Nutr. 2004 134:2517-2522  
 7. a) Am J Clin Nutr. 2001 Apr;73(4):736-45 b) Obes Res 2003 Oct;11(10):1200-6  
 c) Atherosclerosis 2004 Mar;173(1):79-87 d) J Neural Trans 2003 Apr;110(4):401-11  
 e) Proc Nutri Soc 2004(63):5-10 f) Arterioscler Thromb Vasc Biol. 2002 May 12;22(5):824-31

## Cardiovascular Disease

- The effects of these polymorphisms can be offset by exercise and a low-calorie diet
- The National Cholesterol Education Program recommends specific therapeutic guidelines to decrease risk of CVD
- First line of therapy – therapeutic lifestyle change: changes in diet, physical activity, coupled with no smoking and weight loss if applicable

## Cardiovascular Disease

- The second line of therapy is medication
- People respond differently to these interventions
- Varying degree of response stem from genetic differences
- Some patients cannot achieve the recommended lipid levels by *lifestyle changes alone*

## Cardiovascular Disease

- Certain genes may be more susceptible to influence from nutrients
- These are called candidate genes
- Several candidate genes have been identified and may alter individual sensitivity to developing coronary heart disease
- Apolipoprotein AI and lipoprotein lipase which help to remove cholesterol from the arteries, are susceptible to dietary interventions and may curb the onset of coronary heart disease

## Cardiovascular Disease

- Adding to the understanding of how olive oil benefits the heart, scientists have recently found that the polyphenols in extra virgin olive oil can promote heart health on a molecular level.
- A study published in the July 2010 issue of the *Journal of the Federation of American Societies for Experimental Biology* (FASEB) reported that olive oil can alter genes in a heart-healthy way.



## Cardiovascular Disease

- **Researchers from the Cardiovascular Risk and Nutrition Research Group** in Barcelona, Spain, conducted a study involving three groups of healthy individuals.
- One group consumed a Mediterranean diet that included extra virgin olive oil with high levels of polyphenols
- A second group consumed olive oil with low levels of polyphenols
- A third group consumed their usual diet.
- After three months, the group that consumed the olive oil with the highest level of polyphenols had significant reduction in the expression of atherosclerosis-related genes. This explains for the first time one reason for the heart healthy benefit of olive oil.

## Clinical Recommendations

- Low-fat, low-carbohydrate diet to reduce weight, especially diet low in saturated fats
- Consume EVOO
- High-fiber diet
- Increase physical activity
- Stop Smoking



## Hypertension

- Increased levels of circulating angiotensinogen are associated with increased blood pressure
- A SNP affects the angiotensinogen gene
- Some people who follow the DASH diet show dramatically reduced blood pressure
- However, the same diet is less effective in other people, possibly due to gene variation

## Clinical Recommendations

- DASH diet – Dietary Approaches to Stop Hypertension
- Diet high in vegetables, fruits, magnesium, calcium, potassium
- Reduce sodium to less than 2,000 mg a day
- Increase exercise to 30 min/day at 4-5 days per week



## Diabetes

- Type 2 diabetes – high blood sugars and often dyslipidemia
- Diets high in fats and calories and sugars along with an inactive lifestyle have been shown to play a huge role in the onset of disease
- Many genes involved in the development of this disease
- They appear to be VERY responsive to dietary interventions

## Diabetes

- Some people can completely control their diabetes through lifestyle changes alone
- Increasing activity
- Reducing calorie/carbohydrate intake
- Changing the environment (diet, exercise) can **alter gene expression**
- Some people are less responsive to lifestyle changes – most likely due to genes
- May need medication *in addition of lifestyle*

## Clinical Recommendations

- Balanced diet rich in fiber: 30-40 grams per day (legumes/oats/vegetables/fruits)
- 40% carbohydrates from vegetables, fruits, whole grains, beans/legumes
- Lean proteins
- 30% good fats from olive oil, avocado, nuts, seeds
- Medication if needed

## Cancer

- Cancer is cell division out of control
- Develops from interaction between internal factors (genetic, hormonal) and external factors (cigarette smoking, chemical exposure, diet and lifestyle choices)
- Carcinogenesis is a multistep process that begins the cancer process
- Experimental evidence shows that dietary constituents can alter carcinogenesis

## Cancer

- Cancer is now considered a chronic disease of the genome that may be influenced at many stages by nutritional and metabolic factors
- This interaction can affect not only prevention, but also **progression of cancer**
- Estimated that up to 80% of colon, breast, and prostate and 1/3 of all types of cancer may be influenced by diet and associated lifestyle factors
- Mutation of BRACA1 or BRAC2 increase risk of breast cancer in women

## Clinical Recommendations

- Reduction in refined carbohydrates, red meat and saturated fats in diet
- Addition of olive oil – monounsaturated fats may help to regulate initiation of cancer
- Addition of omega 3 fats (fish) could help reduce colon and breast cancer
- Genetic testing for breast and colon cancer

## Obesity

- During last several decades – increase in prevalence of obesity
- Increased risk of diabetes, cardiovascular disease, and certain cancers
- Our genes have not changed that much in the last several decades
- Obesigenic society – abundance of food, lack of physical activity most likely cause

## Obesity

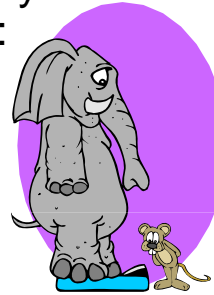
- However, despite obesigenic society – large variation in susceptibility to obesity
- Genetic susceptibility to obesity is the result of multiple genes that interact with one another and the environment
- Having adequate fat was at one time an evolutionary advantage
- Due to evolutionary pressures, combinations of genes were selected that favored accumulation of fat

## Obesity

- Now we have such an abundance of food that genes that were once beneficial for our survival now contribute to obesity and disease
- Tendency of populations to gain weight under conditions of abundance may be considered a normal physiologic response to our obesigenic society

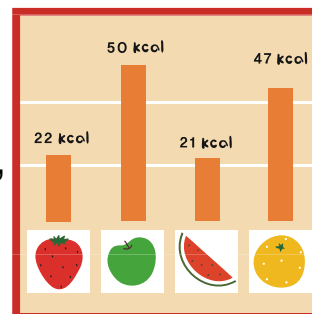
## Obesity

- Genetics may also play a role
- Regulation of food intake may be affected by genes encoding:
- Taste receptors
- Insulin
- Leptin
- Ghrelin
- Some genes SLOW metabolism



## Clinical Recommendations

- Low-fat, low-carbohydrate diet
- Limit saturated fats
- High fiber
- Diet high in vegetables, fruits, whole grains
- Increased activity



## Micronutrients

- Approx 40 micronutrients are required by the human diet
- Suboptimal intake of specific micronutrients has been associated with **cardiovascular disease**: B vitamins, Vitamin E, Carotenoids
- **Cancer**: folate, carotenoids
- **Neural tube defects**: folate
- **Bone mass**: vitamin D


## Micronutrients

- Vitamins B6, B12 and folate deficiencies are associated with increased homocysteine levels
- Deficiencies in vitamins B12, folic acid, B6, niacin, C, and E can damage DNA by causing breaks in the single and double strands
- The high incidence of most cancers may be because majority of US population does not eat the recommended daily amount of fruits and vegetables, which are rich in these nutrients

## Phytochemicals

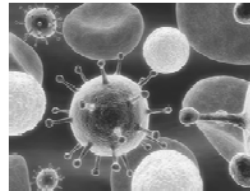
- Phytochemicals are compounds found in fruits, vegetables, whole grains and other plant foods
- An increase in phytochemical consumption has been linked to a *reduction in chronic disease*
- They have been shown to affect all stages of cancer formation by acting as ***cancer-blocking agents***

## Probiotics and Prebiotics

- Human beings, like all animals, play host to many types and high numbers of microbes on our skin, in our mouths, in women's vaginal tracts, and all the way through our gastrointestinal tract.
- 
- It has been estimated that there are more microbes associated with the human body (about  $10^{14}$ , or 100,000,000,000,000 bacterial cells) than there are human cells in it (about  $10^{13}$ ) !!!!!!!

## Probiotics

- The microflora or bacteria population of the large intestine is acquired shortly after birth
  - It's composition is dependent on mother's diet
  - We all have our own specific balance of microflora in our guts
- This can be altered by our diet



## Probiotics

- Research suggests that the consumption of probiotic cultures may decrease cancer risk.
- Researchers testing the effect of the consumption of fermented milks and probiotic bacteria have found:
- A reduction in the incidence of chemically induced tumors in rats.
- A reduction of the activity of fecal enzymes thought to play a role in colon cancer in human and animal subjects.
- Prevention of damage to DNA in certain colonic cells.
- Enhancement of immune system functioning.

## Conclusions

- Diet and specific nutrients can affect gene function
- Genes are turned on and off by what we eat
- Genes are important for determining function, but nutrition modifies the extent to which different genes are expressed
- Nutrition may account for 50% or more of the risk for disease and, depending on the person, may be as important, or more important, than other environmental factors

## Conclusions

- Although many diseases and other threats to health are independent of nutrition, nutrition can influence the outcome of these diseases and the extent to which they affect health
- The interaction between nutrition and the human genome determines gene expression and the metabolic response
- This interaction ultimately affects health status or predisposition to disease, or both

## Conclusions

- The challenge will be to identify nutrient-influenced molecular pathways and determine the downstream effects of specific nutrients
- A complete understanding of the links between nutrition and the genome will enable us to grasp the influence of nutrition on human health and help us understand that

WE REALLY ARE WHAT WE EAT!!!

## We Really Are What We Eat!!



## Resources

- [It's Not Just Your Genes!](#) by Ruth DeBusk and Yael Joffe (Paperback - 2006)
- [www.epigeneating.com](http://www.epigeneating.com)



•Let's Get  
Cooking!

