Nutrigenetics, Nutrigenomics, Epigenomics, Oh My!

California Dietitians in Integrative & Functional Medicine
November 4, 2017

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Assistant Professor, USC Keck School of Medicine and Leonard Davis School of Gerontology
Learning Objectives

By the end of the presentation participants will be able to:

1. Define nutrigenetics, nutrigenomics and epigenomics and their application to nutrition practice.
2. Locate genetic testing resources and understand cost and use.
3. Weigh the pros and cons of direct to consumer genetic testing (legal, ethical, confidentiality).
4. Discuss how consumer nutrigenomic data can potentially be applied, in select situations, to clinical dietetics practice for personalized diet planning.
Start with the end in mind ..........
What if ..........

Epigenetics & Personal Health: Can We Control Our Own Future? | Matt Riemann | TEDxVeniceBeach 2015

https://www.youtube.com/watch?v=BZ3o5X2j3kY

Rosie the Maid Jetson’s
Apple Smart Watch
- BP
- Heart
- Steps, laps
- Calories
- Pulse Oximeter

Diabetes patch and pump

Early Adopters are Onboard

APP for Estimating Longevity

Inside Tracker FNCE 2017
What if…. We could wear a sensor that told us what we needed to eat each day, each meal? Would we take more responsibility for our health? What information would we need to direct such a device? Are were there?
Genetic Testing is here –
Ancestry, Health, Disease, Medications
• Gerontology – Study of the aging process
• Healthspan vs. Lifespan – live longer, healthier
• Health influences- genetics (family history), environment (chemicals, stress, sleep, food), disease exposure (viral, bacterial), accident/injury
• Prevention and early intervention- add to toolkit
• Genetic testing for common diagnoses – Alzheimer’s (APOE4), Breast Cancer (BRCA)
Definitions

Epigenetics - the study of gene activity during the development of complex organisms. *Epigenetic* can be used to describe anything other than DNA sequence that influences the development of an organism. Variance in phenotype without change in DNA sequence.

**Genome** – genetic material of an organism

**Genomics** – The study of genes and their function

**Phenome** – set of all phenotypes expressed by a cell, tissue, organ, or organism, examples of human phenotypic traits are skin color, eye color, height, taste variation, personality characteristics.

**SNP** – Single nucleotide polymorphism - phenotypic expression may be influenced by environmental influences, mutation, and genetic variation
Definitions

Nutrigenetics - Impact of genetic differences between individuals on the response to dietary intake and the ultimate influence on health status and disease risk.

Nutrigenomics - The interactions between dietary components and the genome and the resulting changes in proteins and other metabolites that affect gene expression.

Epigenomics - the study of the complete set of epigenetic modifications on the genetic material of a cell, known as the epigenome.

Omic - informally, related to a field of study in biology. Example – proteomics, metabolomics, genomics.
Epigenetic mechanisms are affected by development in utero and in childhood, environmental chemicals, drugs and pharmaceuticals, aging, and diet. DNA methylation is what occurs when methyl groups can tag DNA and activate or repress genes. Histones are proteins around which DNA can wind for compaction and gene regulation. All of these factors and processes can have an effect on people’s health possibly resulting in cancer, autoimmune disease, mental disorders, or diabetes among other illnesses. National Institutes of Health
The **Agouti gene**, makes mice fat & yellow when not silenced, when silenced in pups of vitamin-dosed mothers results in a healthy brown mouse. (discovered 1994)

Epigenetic mechanisms include chromatin folding and attachment to the nuclear matrix, packaging of DNA around nucleosomes, covalent modifications of histone tails (e.g. acetylation, methylation, phosphorylation), and DNA methylation. The influence of regulatory small RNAs and micro RNAs on gene transcription is also increasingly recognized as a key mechanism of epigenetic gene regulation. Culprits: bisphenol A, deficiency of methyl-related nutrients include folate, methionine, Vitamin B12 and Vitamin B6
Nutritional Genomics in Practice: Where Do We Begin?

RUTH M. DEBUSK, PhD, RD; COLLEEN P. FOGARTY, MS, RD; JOSÉ M. ORDOVAS, PhD; KENNETH S. KORNMAN, PhD, DDS

Editor's note: This is the first in a series of articles on nutritional genomics. The series will appear periodically in the Journal, and is designed to address the educational, professional, and practical needs of the dietetics professional in this rapidly changing arena. Dr DeBusk and colleagues make the case for advancing application of genomics to clinical practice, improve therapeutic outcomes, and significantly expand career and economic opportunities for practitioners. The future of dietetics is unquestionably intertwined with nutritional genomics.

Position of the Academy of Nutrition and Dietetics: Nutritional Genomics

**ABSTRACT**

It is the position of the Academy of Nutrition and Dietetics that nutritional genomics provides insight into how diet and genotype interactions affect phenotype. The practical application of nutritional genomics for complex chronic disease is an emerging science and the use of nutrigenetic testing to provide dietary advice is not ready for routine dietetics practice. Registered dietitian nutritionists need basic competency in genetics as a foundation for understanding nutritional genomics; proficiency requires advanced knowledge and skills. Unlike single-gene defects in which a mutation in a single gene results in a specific disorder, most chronic diseases, such as cardiovascular disease, diabetes, and cancer are multigenetic and multifactorial and therefore genetic mutations are only partially predictive of disease risk. Family history, biochemical parameters, and the presence of risk factors in individuals are relevant tools for personalizing dietary interventions. Direct-to-consumer genetic testing is not closely regulated in the United States and may not be accompanied by access to health care practitioners. Applying nutritional genomics in clinical practice through the use of genetic testing requires that registered dietitian nutritionists understand, interpret, and communicate complex test results in which the actual risk of developing a disease may not be known. The practical application of nutritional genomics in dietetics practice will require an evidence-based approach to validate that personalized recommendations result in health benefits to individuals and do not cause harm.


**POSITION STATEMENT**

It is the position of the Academy of Nutrition and Dietetics that nutritional genomics provides insight into how diet and genotype interactions affect phenotype. The practical application of nutritional genomics for complex chronic disease is an emerging science and the use of nutrigenetic testing to provide dietary advice is not ready for routine dietetics practice. Registered dietitian nutritionists need basic competency in genetics as a foundation for understanding nutritional genomics; proficiency requires advanced knowledge and skills.
How Much do we Need?
Start with Direct to Consumer Tests for Genetic & SNP Analysis:

- 23 and Me $199, includes ancestry and health info.
- Ancestry.com $99 (less on Father’s day, $79) only provides ancestry matching, raw data can be downloaded.
- Promethease.com, used raw genetic data compared to NIH research, defining SNP risk $5-10.
- SNPedia - a Wiki investigating human genetics. Information about the effects of variations in DNA, citing peer-reviewed scientific publications.
- Disease-Specific Companies defining risk for specific conditions, look at only limited SNPs, often need to be reviewed by MD.
- Full genome evaluation (~ $1,000)
23 & Me

• Educator resources for classroom teaching
• Discount on test kits for students
• Consumer friendly navigation and results
• FDA limits what they can share without MD involvement, gradually new information
• Can tell you carrier status for Genetically inherited conditions
Patrick Kreutzer 100%

- European 100%

See all 31 tested populations

European 100%

- Northwestern European 92.7%
  - British & Irish 39.6%
  - French & German 34.1%
  - Scandinavian 1.9%
  - Broadly Northwestern European 17.0%

- Southern European 4.2%
  - Iberian 1.8%
  - Italian 1.1%
  - Sardinian 0.3%
  - Broadly Southern European 1.0%

- Eastern European 1.0%

- Broadly European 2.1%
Carrier Status Reports

These reports tell you about variants that may not affect your health, but could affect the health of your future family. For the conditions included in these reports, a person can be a carrier even if they don’t have a personal or family history of the disease.

View Carrier Status Tutorial

About "Variant not detected" ♩

You may see “Variant not detected” for many reports. What does that mean?

If you see "Variant not detected" for a Carrier Status report, it means you’re not a carrier of the tested variant(s). Keep in mind that while our Carrier Status reports cover many variants, they don’t include all possible variants associated with each condition. So it’s still possible to be a carrier of a variant not included in our test. Learn more.

- ARSACS
  Variant not detected

- Agenesis of the Corpus Callosum with Peripheral Neuropathy
  Variant not detected

- Autosomal Recessive Polycystic Kidney Disease
  Variant not detected
Healthy Habits for Your Genetics

We looked at 23andMe research participants with a genetic weight predisposition like yours and found certain lifestyle factors that were associated with the biggest weight differences.

These habits made the biggest difference in people with your genetics:

1. **Limiting red meat**
   - Associated with weighing up to **12.1% less**
   - People at a healthy weight ate red meat less than 2 times per week, on average.
   - People who never ate red meat weighed up to 12.1% less than those who ate red meat every day.

2. **Avoiding fast food**
   - Associated with weighing up to **11.3% less**
   - People at a healthy weight ate fast food less than once per week, on average.
   - People who never ate fast food weighed up to 11.3% less than those who ate fast food almost every day or more.

3. **Sleeping a healthy amount**
   - Associated with weighing up to **11.1% less**
Ancestry.com
• Look for ancestors and create family tree
• Download raw Data
### AncestryDNA raw data download

This file was generated by AncestryDNA at: 09/21/2016 17:09:47 MDT

Data was collected using AncestryDNA array version: V1.0

Data is formatted using AncestryDNA converter version: V1.0

Below is a text version of your DNA file from Ancestry.com DNA, LLC. This information is for your personal use and is intended for genealogical research only. It is not intended for medical or health purposes. The exported data is subject to the AncestryDNA terms and conditions, but please be aware that the downloaded data will no longer be protected by our security measures. When you download your raw DNA data, you assume all risk of storing, securing and protecting your data. For more information, see AncestryDNA FAQs.

Genetic data is provided below as five TAB delimited columns. Each line corresponds to a SNP. Column one provides the SNP identifier (rsID where possible). Columns two and three contain the chromosome and basepair position of the SNP using human reference build 37.1 coordinates. Columns four and five contain the two alleles observed at this SNP (genotype). The genotype is reported on the forward (+) strand with respect to the human reference.

<table>
<thead>
<tr>
<th>rsid</th>
<th>chromosome</th>
<th>position</th>
<th>allele1</th>
<th>allele2</th>
</tr>
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<tbody>
<tr>
<td>rs4477212</td>
<td>1</td>
<td>82154</td>
<td>T</td>
<td>T</td>
</tr>
<tr>
<td>rs3131972</td>
<td>1</td>
<td>752721</td>
<td>A</td>
<td>G</td>
</tr>
<tr>
<td>rs12562034</td>
<td>1</td>
<td>768448</td>
<td>G</td>
<td>G</td>
</tr>
<tr>
<td>rs11240777</td>
<td>1</td>
<td>798959</td>
<td>A</td>
<td>G</td>
</tr>
</tbody>
</table>
Promethease is a literature retrieval system that builds a personal DNA report based on connecting a file of DNA genotypes to the scientific findings cited in SNPedia.

Biomedical researchers, healthcare practitioners and customers of DNA testing services (such as 23andMe, Ancestry.com, FamilyTreeDNA, Genos, etc.) use Promethease to retrieve information published about their DNA variations. Most reports cost $5 and are produced in under 10 minutes. Much larger data files (such as imputed full genomes from dna.land) cost $10 and have increased runtime.

Your report will remain anonymous, but here are some sample reports
- 23andMe Sample1
- 23andMe Sample2
- Ancestry.com Sample1
- Ancestry.com Sample2
- Ancestry.com Sample3 (older platform)
- Ancestry.com Sample4 (older platform)
- FamilyTreeDNA Sample1
- FamilyTreeDNA Sample2
- Genos Sample1
rs762551(A;C)
Carrier of one CYP1A2*1F allele; Slow Caffeine Metabolizer. One copy of the slow caffeine metaboliser SNP, and one copy of the fast version. This makes you more strongly affected by drinking coffee, as caffeine is broken down slower in the liver. Supposedly this increases the risk of heart attacks, although other studies show caffeine is generally good for the heart. It also makes caffeine more effective at preventing Breast Cancer, Alzheimer's Disease, and Parkinson's disease. Too much caffeine will shrink your breasts.

rs762551, also known as -164A>C or -163C>A, is a SNP encoding the CYP1A2*1F allele of the CYP1A2 gene. For historic reasons, the rs762551(C) allele is considered the wild-type, even though it is the rarer allele in most populations. The rs762551(A) allele is the “fast metabolizer” allele known as CYP1A2*1F; the (C) allele is by comparison a slower metabolizer of certain substrates (including caffeine). In terms of genotypes, only rs762551(A;A) individuals are considered fast metabolizers. Individuals who are rs762551(A;C) heterozygotes or rs762551(C;C) homozygotes are both considered slow metabolizers. The CYP1A2 gene encodes a member of the cytochrome p450 family of proteins, which metabolize nutrients and drugs. One well known substrate of CYP1A2 is caffeine; individuals who are carry one or more CYP1A2*1C alleles are “slow” caffeine metabolizers, whereas carriers of the variant CYP1A2*1F are “fast” caffeine metabolizers. The same amount of caffeine will therefore tend to have more stimulating effect on CYP1A2 slow metabolizers than on CYP1A2 fast metabolizers. A study of healthy premenopausal non-hormone using women concluded that drinkers of 3 or more cups of...
Medications

ra2032583(T:T)

7x less likely to respond to certain antidepressants. This version of a blood brain barrier protein blocks many common antidepressants from entering the brain, including: amitriptyline (Elavil), citalopram (Celexa), paroxetine (Paxil), and venlafaxine (Effexor). That makes those antidepressants 7 times less effective.

ra2032583 is a SNP in the ABCB1 gene (also known as the MDR1 gene), which encodes a protein that transports certain molecules across the blood-brain barrier. SNPs in ABCB1 may thus influence the intracerebral concentrations of certain drugs and thus their efficacy or potential for adverse side effects. ra2032583 is one of 9 SNPs found within a tight linkage block ($\chi^2 = 0.8$) such that the minor allele at any one of them predicts (with ~80% accuracy) that the other SNPs will also be the minor allele. The list of the 9 SNPs is shown below. When treated for depression with substrates of the protein encoded by ABCB1, carriers of one or two minor alleles at these ABCB1 SNPs have been reported to respond better than non-carriers. The antidepressant drugs that are known to be substrates include:

- more info
SNPedia is a wiki investigating human genetics. We share information about the effects of variations in DNA, citing peer-reviewed scientific publications. It is used by Promethease to create a personal report linking your DNA variations to the information published about them. Please see the SNPedia:FAQ for answers to common questions.

BROWSE

- genes
- genosets
- genotypes
- medicines
- medical conditions
- topics
rs6983267 is a SNP on chromosome 8q24, associated with increased risk for several [PMID 19047180] cancers, particularly prostate cancer. In studies dividing the 8q24 region, this SNP falls in region 3. This SNP has also been reported to influence the cancer-risk decreasing effect of aspirin.

In a study of over 3,600 Caucasians with prostate cancer, rs6983267 is one of five SNPs used (with family history as a sixth factor) to cumulatively predict overall risk. On their own, the rs9883267 (G,G) and (G,T) risk genotypes yield an odds ratio for developing prostate cancer of 1.37 (CI: 1.18-1.59, p=3.4e-10) and may account for 22.2% of population attributable risk. [10.1056/NEJMoa075819]

The increased risk of developing prostate cancer associated with rs6983267 now appears to be independent of the risk associated with its close neighbor, rs1447295. The odds ratio for heterozygotes is estimated to be 1.26 (CI: 1.13 - 1.41), and for homozygotes, 1.58 (CI: 1.40 - 1.78), compared to the homozygote rs6983267(T,T) genotype. [PMID 17401383]

[1] The rs1447295 location could be responsible for about seven percent of prostate cancer cases in white men of north European descent. Thus, taken together with rs8983267, these two genetic changes could account for as much as one quarter of prostate cancer cases in white men. The increased risk conferred by these loci was observed for all age groups studied.

Cancer related according to this [blog]

We estimate that the population attributable risk of the new locus, marked by rs6983267, is higher than the locus marked by rs1447295 (21% vs. 9%) [PMID 17826875]

In a study of 1,563 patients of European ancestry, this SNP was designated as the representative of a prostate cancer risk region termed "locus 2", with an odds ratio of 1.70 (CI: 1.35-2.07) for carriers of a risk genotype. Two other regions of chromosome 8q24 were also studied [PMID 17925536]
myBRCA

A simple screening test to help you understand your risk for hereditary breast and ovarian cancer. Order now for $199.
What do you get?

A Report
A report with your results

Genetic Counseling
A complimentary call with one of our genetic counselors to review your results upon request (currently applies to US only)

Valuable Insights
Insights to help you and your doctor determine the most appropriate breast and ovarian cancer prevention strategies based on your risk

How to get started

1. Order the test
Order the test on our website and we will get in touch with your doctor for their approval

2. Receive a kit
We’ll mail you a saliva collection kit to easily collect your sample

3. Sample is processed
Once we receive your sample, we process it at our CLIA lab and provide results within 6-6 weeks

4. Your report is ready
We let you and your doctor know that your results are ready on our secure site
Information for Healthcare Professionals

Nutrigenomics Inc. is a biotechnology company founded by some of the global leaders in nutrigenomics research. We are dedicated to empowering healthcare professionals and their patients with comprehensive, reliable, cutting-edge genomic information with the ultimate goal of improving health through personal nutrition. Our nutrigenomics test kit enables healthcare professionals to counsel individuals according to their DNA, which creates an avenue to personalized nutrition. Nutrigenomics provides you with a new and powerful technology to add to your portfolio of skills as a healthcare professional.

Join the exciting era of genomics and personalized nutrition by making Nutrigenomics a part of your practice today.

Become an authorized provider of Nutrigenomics®

Register Now
Download Brochure
The answer may be in your genes

In 480 BC, Hippocrates noted that “positive health requires knowledge of man’s primary constitution”. This was just an ancient way of saying that we cannot achieve optimum health without knowing about our genes. We now know that specific variations in our genes can explain how we will respond to the foods, beverages and supplements we consume.

Learn how your genes can affect:

- Cardio-metabolic Health
- Nutrient Metabolism
- Weight Management
- Food Intolerances
- Eating Habits
- Physical Activity
- Injury Risk

USC Leonard Davis
School of Gerontology

University of Southern California
## Summary of Results

### Nutrient Metabolism

<table>
<thead>
<tr>
<th>Dietary Component</th>
<th>Gene, rs Number</th>
<th>Risk Variant</th>
<th>Your Variant</th>
<th>Your Risk</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin A</td>
<td>BCMO1, rs11645428</td>
<td>GG</td>
<td>AA</td>
<td>Typical</td>
<td>Meet the RDA for vitamin A daily.</td>
</tr>
<tr>
<td>Vitamin B₁₂</td>
<td>FUT2, rs601338</td>
<td>GG or GA</td>
<td>GA</td>
<td>Elevated</td>
<td>Focus on consuming bioavailable sources of vitamin B₁₂.</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>GSTT1, rs2266633</td>
<td>Del</td>
<td>Ins</td>
<td>Typical</td>
<td>Meet the RDA for vitamin C daily.</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>CYP2R1, rs10741667</td>
<td>Algorithm</td>
<td>AA</td>
<td>Elevated</td>
<td>Consume 1000 IU (25 mcg) vitamin D daily.</td>
</tr>
<tr>
<td></td>
<td>GC, rs2282679</td>
<td></td>
<td>GG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin E</td>
<td>F5, rs6025</td>
<td>CT or TT</td>
<td>CC</td>
<td>Typical</td>
<td>Meet the RDA for vitamin E daily.</td>
</tr>
<tr>
<td>Folate</td>
<td>MTHFR, rs1801133</td>
<td>CT or TT</td>
<td>CC</td>
<td>Typical</td>
<td>Meet the RDA for folate daily.</td>
</tr>
<tr>
<td>Iron Overload</td>
<td>SLC17A1, rs17342717</td>
<td>Algorithm</td>
<td>CC</td>
<td>Typical</td>
<td>Follow the recommendations provided in the Low Iron Status section.</td>
</tr>
<tr>
<td></td>
<td>HFE rs1800562</td>
<td></td>
<td>GG</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
GERO 518 Topics in Clinical Nutrition – Assignments

- Confidentiality Waiver Completed (required by University)
- Each student completes 23 and Me or Ancestry saliva test; analyzes their data using Promethease
- Student writes reflection on use of genetic data in understanding disease and the role of nutrition
- Student completes literature review and presents abstract of findings and PPT presentation to class
Genetics and Diet

- Cardiovascular disease
- Inflammatory disorders
- Immune health and cancer
- Blood sugar regulation
- Bone mineralization
- Weight management
- Chronic diseases
Each student will select a SNP of interest from their Promethease report (or will select from the list provided by the professor) where nutrition potentially plays a role in SNP activation or protective non-activation (e.g., folate metabolism, diabetes, obesity, macular degeneration, caffeine, heart disease). Prior approval for the SNP research topic from the professor is required before beginning research (due date assigned SNP approval is October 7, 2016). Students will conduct a literature review for their defined SNP and will evaluate the evidence presented in the literature, focus on the strengths of the evidence. Once the research review is completed you will make nutrition recommendations, as if you were preparing to counsel a patient in practice with the SNP. Students will present a summary of their research to the class. Presentations will be scheduled the day of the class final exam in place of a final exam. Distance students will record and post their presentation with Youtube or a video link in Blackboard for all students to review. Literature review spread sheet and research abstract will be uploaded into blackboard through Turnitin. Powerpoint presentation will be posted in Blackboard by the deadline scheduled.
1. Perilipin1 (PLIN1) Meal Timing and Weight Loss
2. Type 1 Diabetes & Celiac Disease [rs3184504 (T,T)]
3. MTHFR C677T Folate & Depression and Colorectal Cancer
4. MDRI/ABCB1 Cancer Risk
5. NAT2/C282T Chemical Detoxification & Cancer Risk
6. rs2282679 Low Vitamin D Levels and Colorectal Cancer Risk
7. CTEP (rs5882) Aging, Longevity and Alzheimer’s Disease
8. TAS2R38 ((rs10246939, rs1726866, rs713598) Taste Perception
9. FUT2 gene and Vitamin B12 Status (rs602662, rs601338)
10. FTO (rs9939609) Obesity and Type 2 Diabetes and Physical Activity; Ghrelin and Obesity
11. Caffeine Metabolism CYP1A2 (rs762551)
12. AGT Gene and M235T (rs699) and Hypertension (HTN)
TAS2R38: Taste 2 Receptor Member 38

Combination of 3 SNPs: rs10246939, rs1726866, and rs713598

Located on Chromosome 7q

3 Main Combinations of Alleles and Amino Acids
- Homozygous Dominant: Taster (PAV/PAV)
  - Proline-Alanine-Valine
- Heterozygous: Taster (PAV/AVI)
- Homozygous Recessive: Non-taster (AVI/AVI)
  - Alanine-Valine-Isoleucine
Genotype vs. Phenotype

Common bitter compounds: quinine, phenylthiocarbamide (PTC), or propylthiouracil (PROP)
- Ex: Celery, Broccoli, Brussels sprouts, Kale, Cabbage, other dark cruciferous vegetables, coffee, and dark beers

Changes in taste affect Vegetable consumption, Sugar, Fat, and Alcohol intake.
Findings about Tasters

- UK study comparing Broccoli and White Cabbage v. Spinach and Courgette: Tasters and Non-tasters agreed the GREEN vegetables were visually more appealing, but TASTERS were more sensitive to the broccoli and cabbage.
  - Consumed LESS vegetables than Non-Tasters using a FFQ

- “Taster” Men >66 yrs. were found with more Colonic Polyps
  - “Taster” men also had higher BMI’s and reported less intake of vegetables [compared to Non-Tasters]
Supertasters and tasters experience more negative sensations such as bitterness, irritation, and sulfur odors.

Suppressing the positive sensations of flavors such as sweetness.

Potentially impeding on the nutritional balance of one’s diet.

Basson et al. (2005)
"A Spoonful of Sugar Helps the Medicine Go Down🎶🎶"
Taster children had increased preference of Sucrose ($p=0.01$)
  - Homozygous Tasters preferred sweeter cereals & sweeter beverages
  - Supported by 2 other studies 10 years later

Preference of Sugar switches to Sodium at adolescence

Higher sugar intake=link to increased insulin resistance?

Higher sodium intake= link to Hypertension?
Findings about Non-Tasters

- Elevated concentrations of Surfactant Protein D (SLD) and Mannan Binding Lectin (MBL)
  - Linked to increased Obesity and Inflammation

- Consumed more alcohol annually
  - AVI/AVI: 285.16+/−55.82 drinks/yr
  - PAV/AVI: 180.49+/−29.32 drinks/yr
  - PAV/PAV: 132.90+/−21.98 drinks/yr

- [Hispanic Non-Tasters] Increased BMI’s and Increased caloric consumption

- Preferred Higher Fat Foods (texture)
Non-tasters living in a healthy environment consumed more **vegetables** than tasters in a similar environment.

Non-tasters reported an average of 300 kcal/d higher intake than tasters.

Non-taster’s preferred/ reported higher intake of:
- Spinach & Raw Broccoli
- Cheddar Cheese, Whole Milk, & High Fat Meats
- Thiamine, Folate, & B6

Tasters preferred more Sweets and Sugar.
Non-Taster Mothers perceived their Taster Children as “more emotional” compared to the other children.

PAV/PAV children were reported as “more active”.

PAV/AVI Tasters with Alexithymia \( (\text{inability to express emotion and understand bodily sensations}) \) had a decreased response to PROP (compared to PAV/AVI w/o Alexithymia).

- May be prone to eating disorders or disordered eating, and “Picky-eating”
Recommendations

- TASTE PREFERENCES (phenotypic expression) CAN CHANGE

- Intervene at a young age!
  - If child is a Taster- teach them to prefer less sugar (and salt) and continuously expose them to “bitter” vegetables
  - If child is a Non-Taster- Expose to “healthy” fats instead of “bad” fats

- If older patient
  - Understand their taste preferences and work around them
Nutrigenomics
RS762551 – Caffeine Metabolism

Maria Schellenberger, MS, RDN
GERO 518, Spring 2016

Maria Schellenberger
4/28/2016
Rs762551 AKA -164A>C or -163C>A

Location: CYP1A2 Gene
Chromosome: 15
Position: 74749576

3 Genetic Variations
- AA (50%) – fast caffeine metabolism
- AC (40%) – slow caffeine metabolism
- CC (10%) – slow caffeine metabolism
Metabolic Action

- CYP1A2 encodes cytochrome P450 1A2 which metabolizes caffeine and other drugs.
- Cytochrome P450 1A2 is responsible for metabolizing between 90-95% of caffeine in the body.
- Caffeine is metabolized into Paraxanthine, theobromine, and Theophylline.
- Caffeine has a half life of 3-7 hours
- Rate of caffeine metabolism can also be altered by other chemicals: nicotine, contraceptives and hormones during pregnancy.

The vast majority of caffeine is metabolized by cytochrome P450, and the inducibility of this enzyme is varied by the Rs762551 SNP.

Caffeine appears to offer protective effects against Parkinson’s disease, but not in all individuals.

Caffeine is known to raise BP, but not for all.

Caffeine may decrease the risk of cancers.
Nutrition Studies

**Parkinson’s Disease**
- 4 studies
- 3 studies – caffeine consumption is inversely related to PD risk
- 2 studies – no relationship with caffeine consumption and CYP1A2 variations
- 2 studies – slow metabolizers have added protection from PD with increased caffeine consumption

Conclusions: Moderate evidence that slow caffeine metabolizers experience increased benefits from caffeine at preventing PD. However, not all studies found this effect.

**Hypertension/ Myocardial Infarction**
- 2 studies on hypertension, 1 study on MI
- Hypertension – 2 studies found fast-metabolizers consuming caffeine are at decreased risk for hypertension compared to slow-metabolizers.
- Myocardial Infarction – slow-metabolizers had an increased risk of MI with increased caffeine consumption
- Myocardial Infarction – fast-metabolizers appeared to have protective effect against MI by consuming caffeine
<table>
<thead>
<tr>
<th>Impaired Fasting Glucose</th>
<th>Bone Mineral Density</th>
<th>Ergogenic Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 1 study</td>
<td>• 1 study</td>
<td>• 1 study</td>
</tr>
<tr>
<td>• Slow metabolizers with high caffeine consumption have 178% increased risk of impaired fasting glucose</td>
<td>• Higher caffeine intake is associated with decreased bone mineral density</td>
<td>• Fast metabolizers – 4.9% decrease in race time</td>
</tr>
<tr>
<td>• Fast metabolizers with high caffeine consumption had 71% increased risk of impaired fasting glucose</td>
<td>• Fast caffeine metabolizers with high caffeine consumption are at increased risk for low bone mineral density</td>
<td>• Slow metabolizers – 1.8% decrease in race time</td>
</tr>
</tbody>
</table>

Conclusion: Moderate evidence that slow metabolizers may benefit from reducing caffeine intake

Conclusion: Moderate evidence that fast metabolizers may be at increased risk of low bone mineral density with caffeine consumption

Conclusion: Fast metabolizers may benefit from stronger ergogenic effects of caffeine which may help improve performance.

*This study was small (n=36) and only involved professional cyclists*
Nutrition Interventions

Caffeine Sources
- Coffee, Soft Drinks, Energy Drinks
- Chocolate, Dietary Supplements, Medications

Fast Metabolizers
- Caffeine consumption may prevent hypertension
- Stronger ergogenic effect of caffeine, may help with performance
- Higher risk for low bone mineral density

Slow Metabolizers
- Slight protective effect at preventing Parkinson’s disease
- Higher risk of hypertension and MI
- Higher risk for impaired fasting glucose

Clinical Nutrition Application
RDN and MD

While Risk is UNCLEAR for many SNPs – General Guidelines Can be Given

Good News

- Healthy kidney function
- Fast metabolizer of caffeine, less stimulated
- Decrease risk for post-operative nausea
- No alcohol flush, body is able to break down acetaldehyde
General Concerns

**Cardiometabolic**
- Slight risk for cardiovascular disease
- Slight risk for hypertension, atrial fibrillation, and/or ischemic stroke
- Slight risk for Type 2 diabetes

**Oncogenic**
Increase risk for prostate cancer
Risk for lung cancer if a smoker

**Other**
Poor ability to metabolize folate, missing adequate amount of enzyme, so poor absorption
Slight increase risk for Alzheimer's disease (APOe 3 + 4)
Clinical Nutrition Recommendations

• Review genetic data with your primary physician
• Regularly review laboratory data including lipid panel, hsCRP, HgA1C; Recommend a target of total cholesterol below 180; Recommend a target HgbA1c below 5.2 – consider various diet and exercise approaches.
• Monitor blood pressure, treat as needed – recommend a target of systolic blood pressure of 120 mm HG)
• Mediterranean Diet: Minimize meat and dairy, increase plant-based foods; include Olive Oil, nuts, regular fish intake.
• Increase intake of natural phytochemicals (berries, vegetables, other fruits)
• Reduce stress through yoga, meditation, music
• Optimize sleep
• Exercise at least 30-60 minutes per day
Dear Colleague,

The International Society of Nutrigenetics/Nutrigenomics (ISNN) was established in 2005, under the Presidency of Artemis P. Simopoulos, MD (USA).

It is the purpose of the Society to increase the understanding of the role of genetic variation and individual dietary response, and the role of nutrients in gene expression generally. This purpose is pursued through research and education of professionals and the general public.

The Aims of the Society shall be achieved through:

a. promoting research on the role of genetic variation and dietary response and the role of nutrients in gene expression;

b. defining the relationship between genes and nutrients from basic biology to clinical states. This encompasses the areas of (1) genetic variation and dietary response, (2) nutrients in gene expression, and (3) the role of genes in the determination of nutritional requirements;

c. establishing a Network of Centers on Genetics, Nutrition and Health worldwide;

d. encouraging the development of programs for genetics and nutrition in departments of nutrition and genetics, and in schools of public health and medicine;

e. serving as a clearing-house for the media in disseminating facts regarding the role of genetic variation and dietary response and the role of nutrients in gene expression.
International Society of Nutrigenomics and Nutrigenetics (ISNN)
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Next Steps

• Spit
• Explore
• Learn
• Apply – in addition to existing assessment measures
• Exercise caution

POSITION STATEMENT
It is the position of the Academy of Nutrition and Dietetics that nutritional genomics provides insight into how diet and genotype interactions affect phenotype. The practical application of nutritional genomics for complex chronic disease is an emerging science and the use of nutrigenetic testing to provide dietary advice is not ready for routine dietetics practice. Registered dietitian nutritionists need basic competency in genetics as a foundation for understanding nutritional genomics; proficiency requires advanced knowledge and skills.

2014
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