Nutrigenomics: An Emerging Clinical Tool?

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CAUTION

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Core Knowledge and Competencies for the Registered Dietitian (6/1/2022)

KRDN 3.5. Describe concepts of nutritional genomics and how they relate to medical nutrition therapy, health and disease.

CDRnet.org

Partial History Genomics

- 1999 – beginning of research using Systems Biology
- June 2000 – US and UK complete entire Human Genome Sequence the Human Genome Project (HGP). Cost $ 100 million. (Today $ 1,000)
- 2002 first GWAS published myocardial infarction. Landmark GWA 2005 study investigating patients with age-related macular degeneration (2 SNPs with significantly altered allele frequency compared to healthy controls)
- 2014 - Precision Medicine – President Obama – look at genetic variants across genome in diverse populations (race, culture)
- 2015 – US Proposes analyzing DNA from 1 million people (All of Us Study). $ 215 million
  - $130 M – 1 million people study, $70 M Ntl. Cancer Institute, $10 M FDA database for regulatory structure, $5 M Health Info. Tech. develop privacy stds. and secure exchange of data.
- 2017 – US FDA approved 23 and Me to provide general recs. for health based on SNP data

SYSTEMS BIOLOGY

Moore, 2020

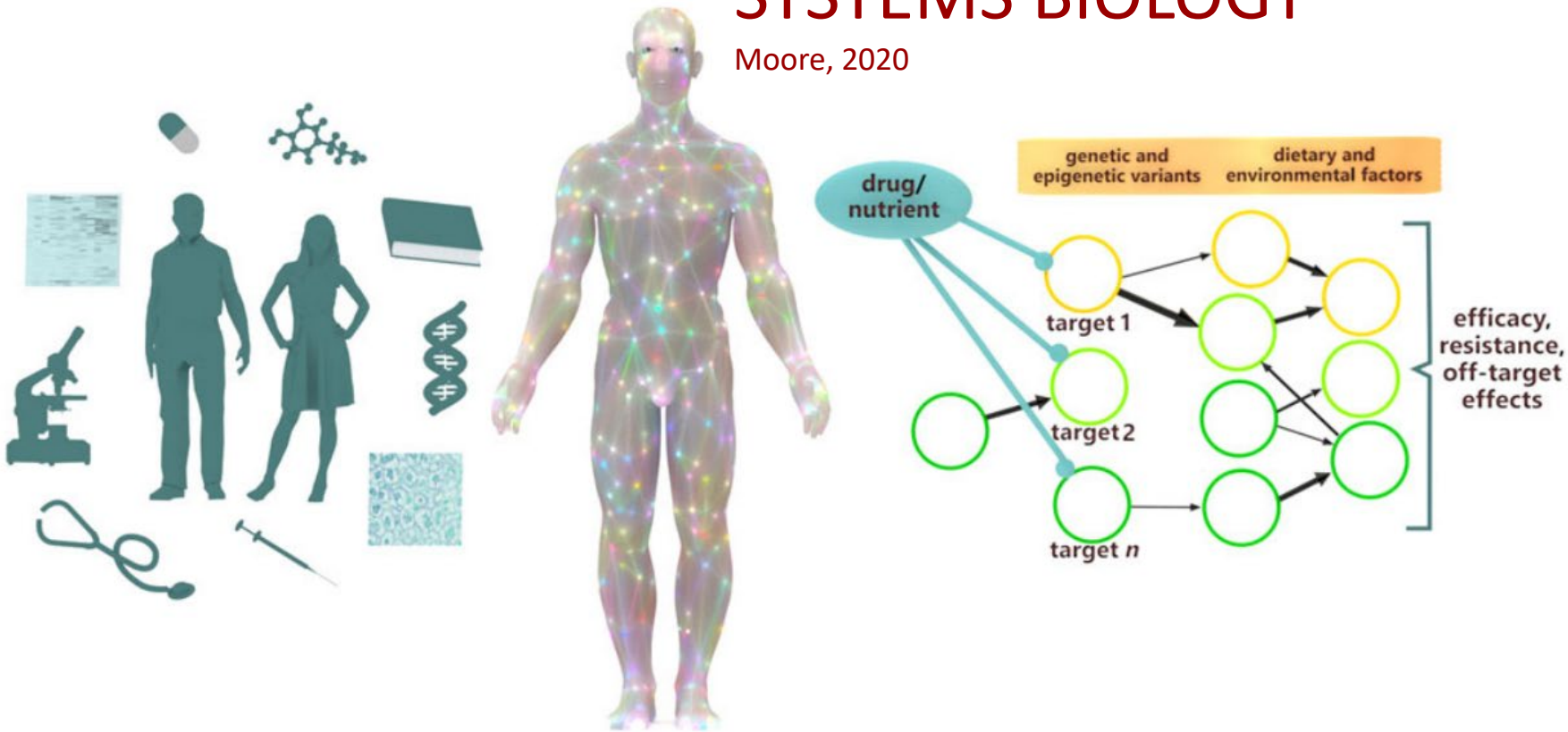
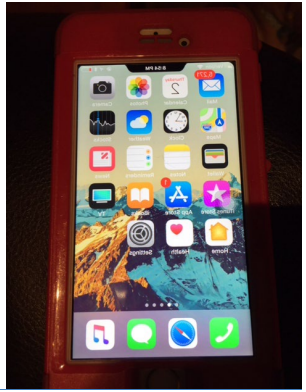


Fig. 2. (Colour online) Systems approaches integrate genetic, clinical and 'omic' data into *in silico* models. Simulations aim to understand network dynamics and predict the response to dietary or pharmaceutical intervention accounting for an individual's genetics, lifestyle, life stage, health and/or disease state. Reprinted with permission[48].

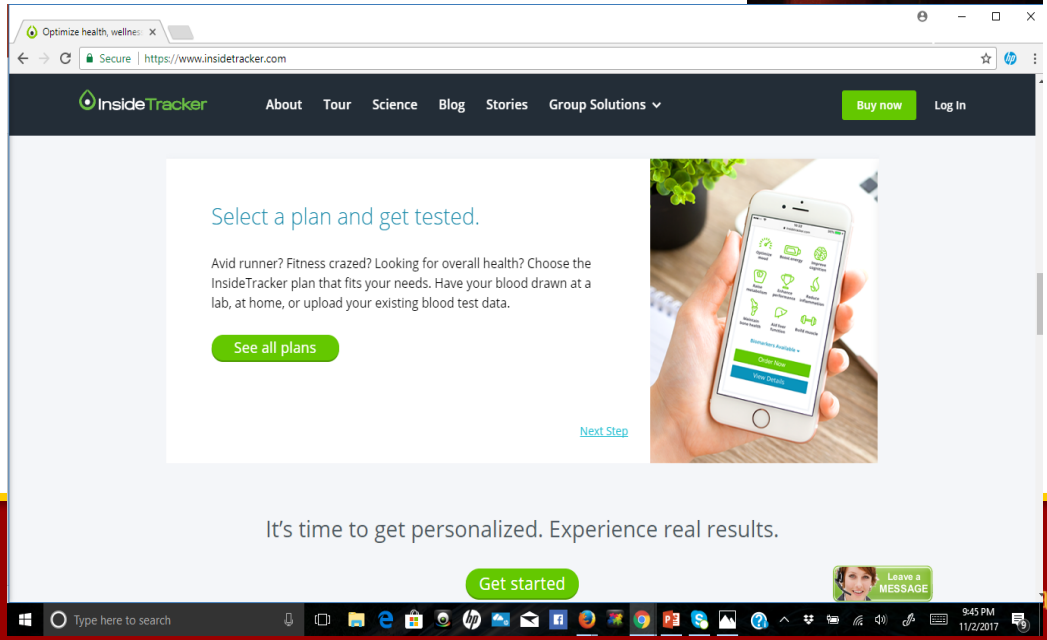
Early Adopters are Onboard

Diabetes patch and pump

APP for Estimating Longevity



Insidetracker.com

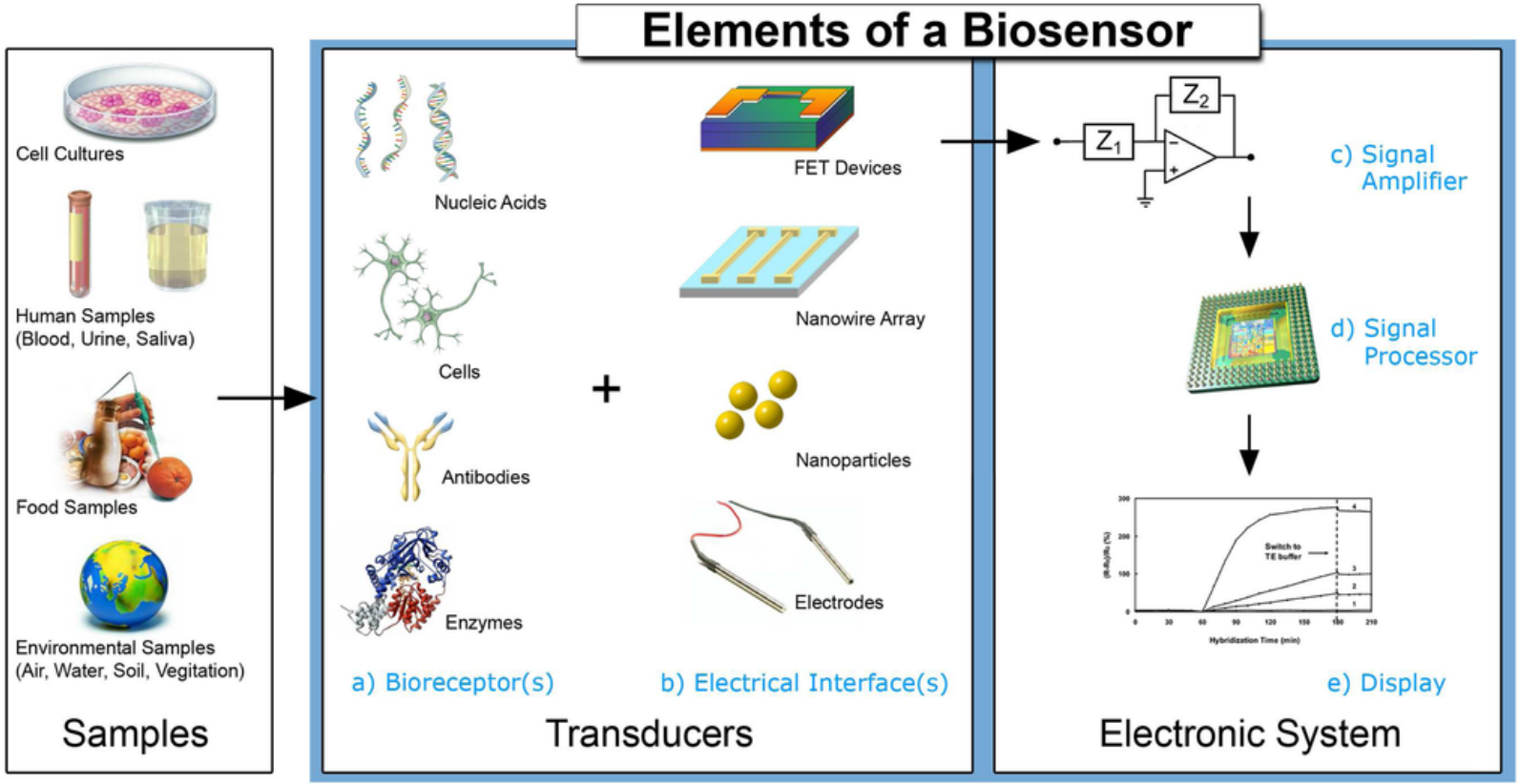


Apple Smart Watch

- BP
- Heart
- Steps, laps
- Calories
- Pulse Oximeter

USC Leonard Davis School of Gerontology

Elements of a Biosensor



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?

Samsung Health App

Samsung Health provides core features to keep up your body fit and healthy. It will record and analyze your daily activities and habits to help maintain successful diet and lead healthy lifestyle.
Whether you walk or run, hike or bike, play indoor or outdoor sports, you can add and track the various physical exercises and activities in a single step using the various built-in trackers. You can also record your step count activity using Pedometer.

Samsung Health helps to create a balanced lifestyle pattern by recording a variety of information like your food, caffeine and water intake details. Provide your daily snacks, food, water and caffeine intake and track your diet and weight on the go while staying comfortable using the sleep & stress tracker.

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Manage health and environmental records such as heart rate, blood pressure, blood glucose levels, stress, weight & SpO_2 using built-in sensors and third party devices.

April 2005, Vol. 105, #4, pg.589

Review

Continuing Education Questionnaire, page 666
Meets Learning Need Codes 2000, 2050, 3000, and 6000

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, an*

cal practice, improve therapeutic outcomes, and significantly expand career and economic opportunities for practitioners. The future of dietetics is unquestionably intertwined with nutritional genomics.

J Am Diet Assoc. 2005;105:589-598

FROM THE ACADEMY

Position Paper

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.

J Acad Nutr Diet. 2014;114:299-312.

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.

Feb. 2014, Vol. 114, #2, pg.299

FROM THE ACADEMY
Evidence Analysis Center

Effect of Incorporating Genetic Testing Results into Nutrition Counseling and Care on Dietary Intake: An Evidence Analysis Center Systematic Review—Part I

Katie Robinson, PhD, MPH, RD, LD; Mary Rozga, PhD, RDN; Andrea Braakhuis, PhD, MND, RD; Amy Ellis, PhD, MPH, RDN, LD; Cathriona R. Monnard, PhD, RDN; Rachel Sinley, PhD, MPH, RD; Amanda Wanner, MLIS, AHIP; Ashley J. Vargas, PhD, MPH, RDN, FAND

ABSTRACT

Consumer interest in personalized nutrition based on nutrigenetic testing is growing. Recently, multiple, randomized controlled trials have sought to understand whether incorporating genetic information into dietary counseling alters dietary outcomes. The objective of this systematic review was to examine how incorporating genetic information into nutrition counseling and care, compared to an alternative intervention or control group, impacts dietary outcomes. This is the first of a 2-part systematic review series. Part II reports anthropometric, biochemical, and disease-specific outcomes. Peer-reviewed randomized controlled trials were identified through a systematic literature search of multiple databases, screened for eligibility, and critically reviewed and synthesized. Conclusion statements were graded to determine quality of evidence for each dietary outcome reported. Reported outcomes include intake of total energy and macronutrients, micronutrients, foods, food groups, food components (added sugar, caffeine, and alcohol), and composite diet scores. Ten articles representing 8 unique randomized controlled trials met inclusion criteria. Of 15 conclusion statements (evidence grades: Weak to Moderate), 13 concluded there was no significant effect of incorporating genetic information into nutrition counseling/care on dietary outcomes. Limited data suggested that carriers of higher-risk gene variants were more likely than carriers of low-risk gene variants to significantly reduce intake of sodium and alcohol in response to nutrition counseling that incorporated genetic results. Included studies differed in quality, selected genetic variants, timing and intensity of intervention, sample size, dietary assessment tools, and population characteristics. Therefore, strong conclusions could not be drawn. Collaboration between the Academy of Nutrition

Effect of Incorporating Genetic Testing Results into Nutrition Counseling and Care on Health Outcomes: An Evidence Analysis Center Systematic Review—Part II

Amy Ellis, PhD, MPH, RDN, LD; Mary Rozga, PhD, RDN; Andrea Braakhuis, PhD, MND, RD; Cathriona R. Monnard, PhD, RDN; Katie Robinson, PhD, MPH, RD, LD; Rachel Sinley, PhD, MPH, RD; Amanda Wanner, MLIS, AHIP; Ashley J. Vargas, PhD, MPH, RDN, FAND

ABSTRACT

In recent years, literature examining implementation of nutritional genomics into clinical practice has increased, including publication of several randomized controlled trials (RCTs). This systematic review addressed the following question: In children and adults, what is the effect of incorporating results of genetic testing into nutrition counseling and care compared with an alternative intervention or control group, on nutrition-related health outcomes? A literature search of MEDLINE, Embase, PsycINFO, CINAHL, and other databases was conducted for peer-reviewed RCTs published from January 2008 until December 2018. An international workgroup consisting of registered dietitian nutritionists, systematic review methodologists, and evidence analysts screened and reviewed articles, summarized data, conducted meta-analyses, and graded conclusion statements. The second in a two-part series, this article specifically summarizes evidence from RCTs that examined health outcomes (ie, quality of life, disease incidence and prevention of disease progression, or mortality), intermediate health outcomes (ie, anthropometric measures, body composition, or relevant laboratory measures routinely collected in practice), and adverse events as reported by study authors. Analysis of 11 articles from nine RCTs resulted in 16 graded conclusion statements. Among participants with nonalcoholic fatty liver disease, a diet tailored to genotype resulted in a greater reduction of percent body fat compared with a customary diet for nonalcoholic fatty liver disease. However, meta-analyses for the outcomes of total cholesterol, low-density lipoprotein cholesterol, body mass index, and weight yielded null results. Heterogeneity between studies and low certainty of evidence precluded development of strong conclusions about the incorporation of genetic information into nutrition practice. Although there are still relatively few well-designed RCTs to inform integration of genetic information into the Nutrition Care Process, the field of nutritional genomics is evolving rapidly, and gaps in the literature identified by this systematic review can inform future studies.

J Acad Nutr Diet. 2020;■(■):■-■.

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.

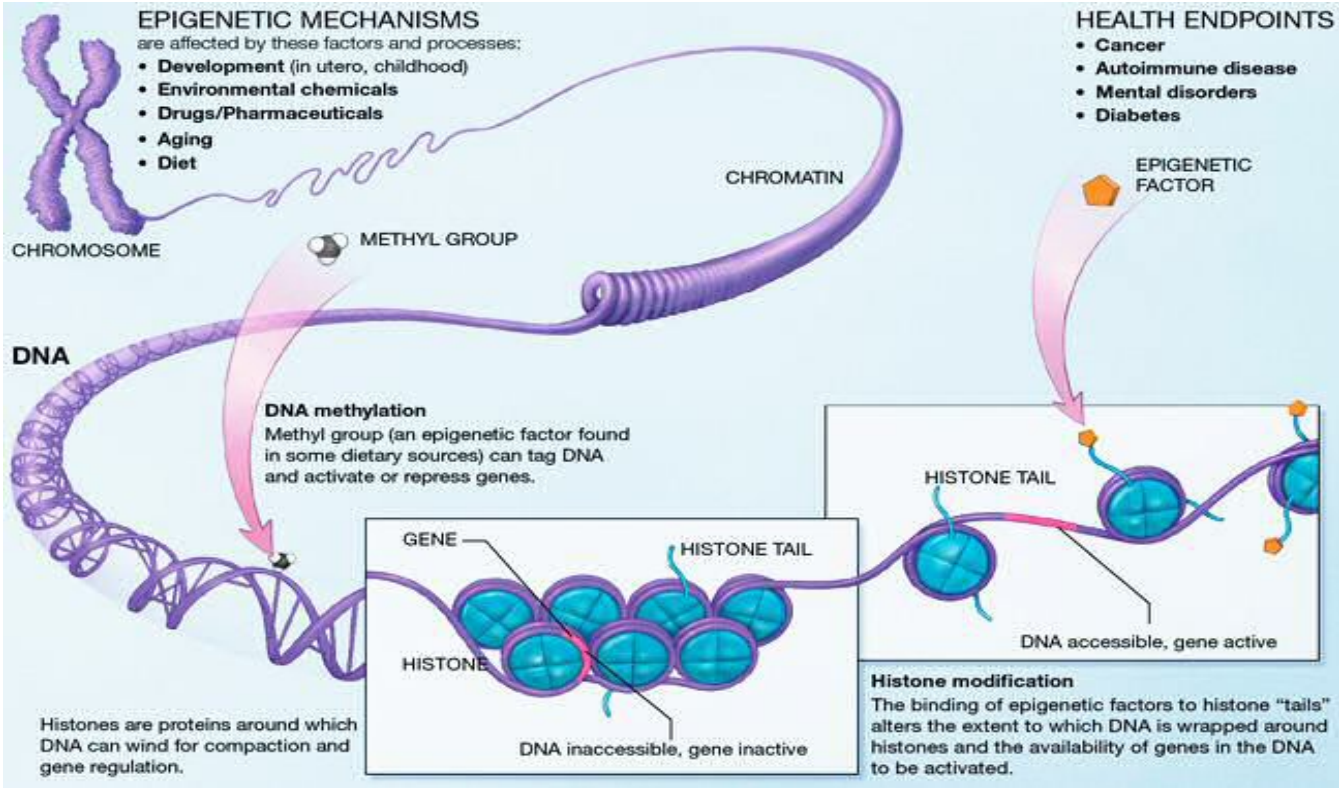
Genome – The sum of all genetic material of an organism, includes genes

Genomics – The study of genomes, composition, organization 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

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.



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)

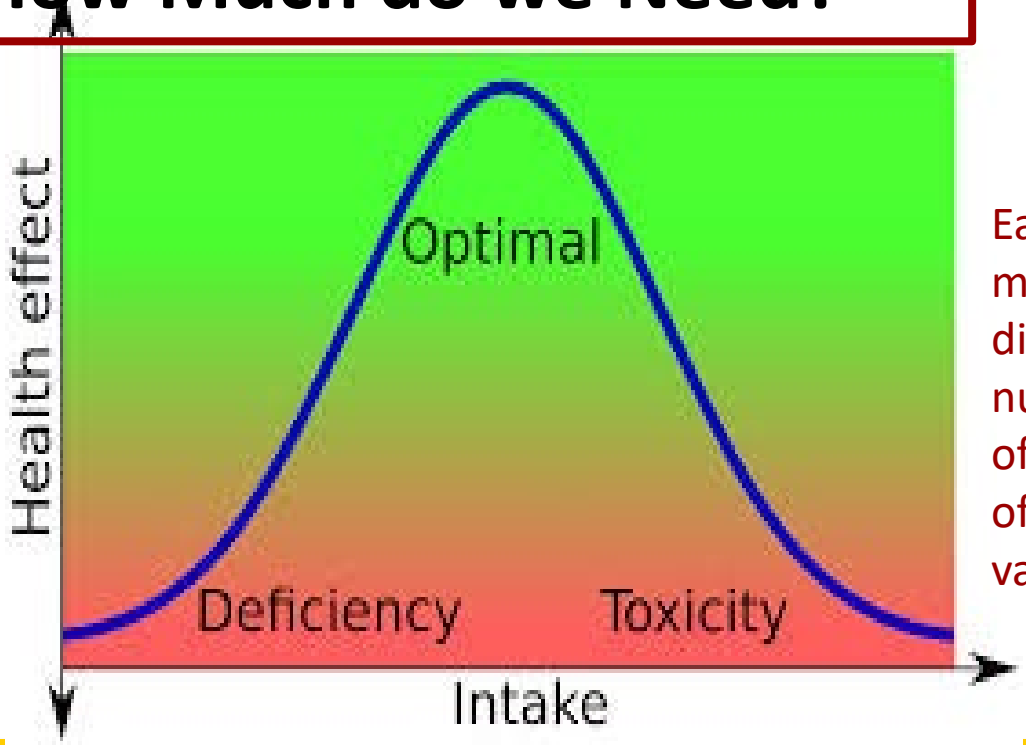
Epigenetic mechanisms include chromatin folding and attachment to the nuclear matrix, packaging of DNA around nucleosomes, covalent modifications of histone tails (e.g. acetylation, methylation, phosphorylation), and DNA methylation. The influence of regulatory small RNAs and micro RNAs on gene transcription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

Mouse given folic acid & choline before, during and after pregnancy gives birth to thin, brown pups. Agouti Gene is silenced.

How Much do we Need?

rs1801133(C;T)
1 copy of C677T allele of MTHFR = 65% efficiency in processing folic acid *

*may require L-5-MTHF supplement, not synthetic Folic Acid

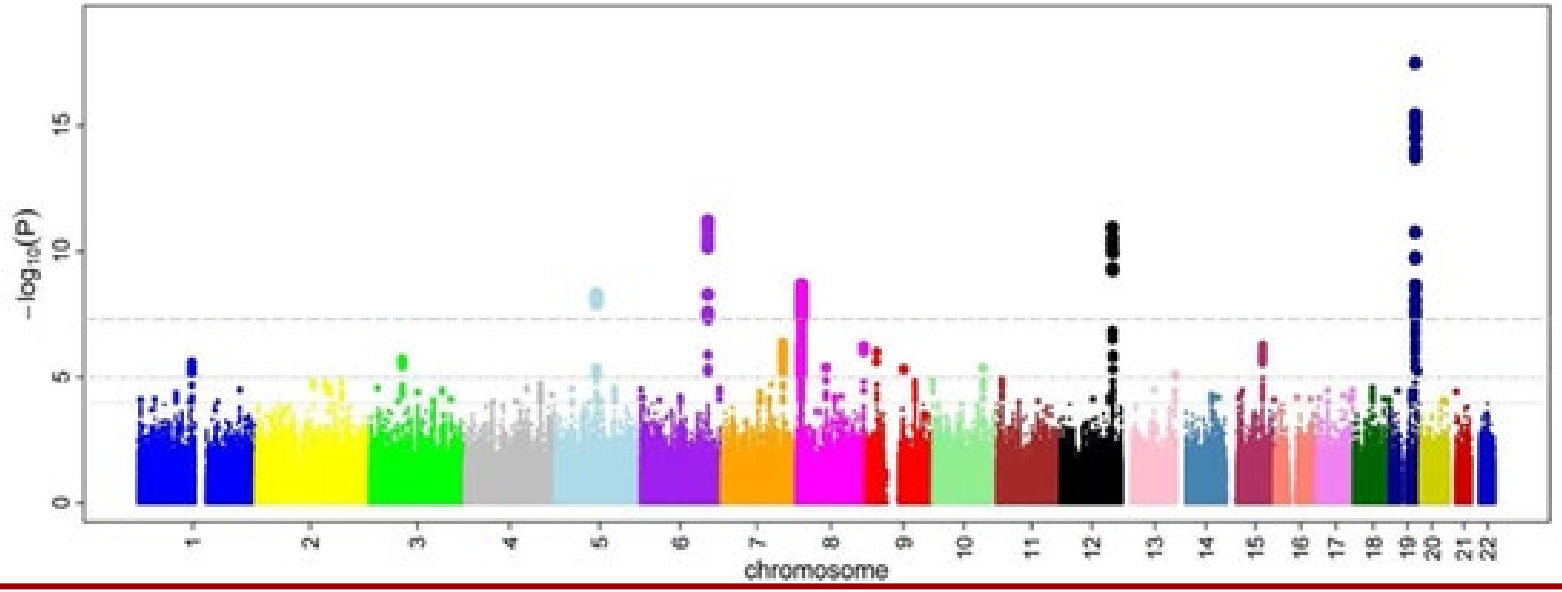


Each individual may require a different level of nutrients because of their unique set of genetic variations

Genome Wide Association Study (GWAS)

- **GWAS** is an observational study of a genome-wide set of genetic variants in different individuals to see if any variant is associated with a trait.
- GWAS typically focus on associations between SNPs or traits like major human diseases. Each person gives a sample of DNA, from which millions of genetic variants are read using SNP arrays. If one type of the variant (one allele) is more frequent in people with the disease, the variant is said to be *associated* with the disease. The associated SNPs are then considered to mark a region of the human genome that may influence the risk of disease.
- GWAS studies investigate the entire genome, in contrast to methods that specifically test a small number of pre-specified genetic regions. GWA studies identify SNPs and other variants in DNA associated with a disease, but they cannot on their own specify which genes are causal.
- The first successful GWAS was published in 2005. It investigated patients with age-related macular degeneration and found two SNPs with significantly altered allele frequency compared to healthy controls.

GWAS



GENOME WIDE ASSOCIATION STUIDES

An illustration of a Manhattan plot showing several strongly associated risk loci. Each dot represents a SNP, with the X-axis showing genomic location and Y-axis showing the level of association. This example looks at microcirculation, the highest point indicates genetic variants that more often are found in individuals with constrictions in small blood vessels.

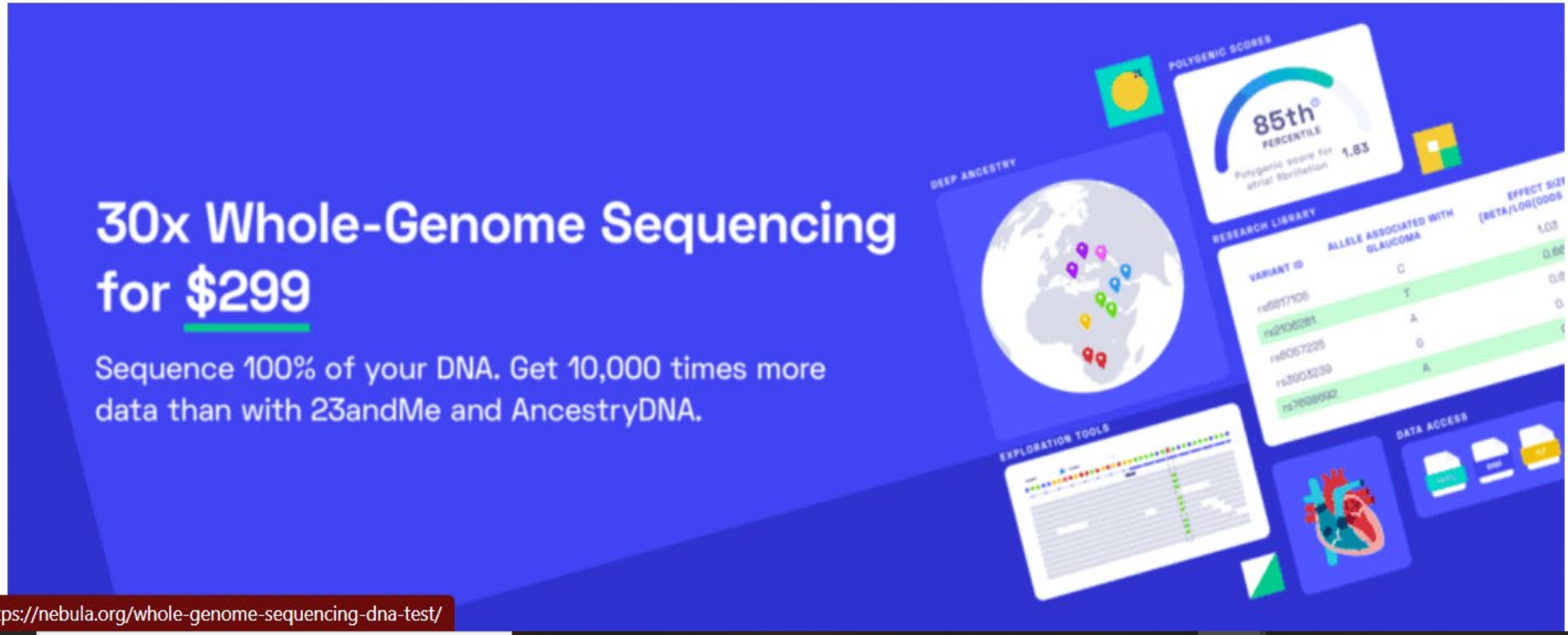
Ikram MK, Sim X, Xueling S, Jensen RA, Cotch MF, Hewitt AW, et al. (October 2010). McCarthy MI, ed. Four novel loci (19q13, 6q24, 12q24, and 5q14) influence the microcirculation in vivo. PLoS Genetics. 6 (10): e1001184.

Direct to Consumer & MD ordered tests for genetic variants

- 23 and Me $ 199 (ancestry and health), $99 ancestry only
- Ancestry.com $ 99; Family Tree DNA $ 99
- Disease-Specific Companies defining risk for specific conditions, look at only limited SNPs, which often need to be reviewed by MD
- Whole exome eval. 31 million data points $700 vs. 23&Me Gene Array 700,000 data points
- **SNPedia** - a Wiki investigating human genetics. Information about the effects of variations in DNA, citing peer-reviewed scientific publications.
- **ClinVar** - Aggregates information about genomic variation and its relationship to human health.

30x Whole-Genome Sequencing is here!

News / By Nebula Genomics



Genetic Testing is here – Ancestry, Health, Disease, Medications

olor tests are physician-ordered. Either your own doctor or an
dent physician will review your purchase and determine whether
tic testing is appropriate. The cost will be refunded if the physician
decides that testing is not appropriate.

SAMPLE DNA TESTING INFORMATION NUTRITION

https://www.dnaweekly.com/blog/best-nutrition-dna-tests/#more-tests

What information will a personalized nutrition DNA test tell me?

A personalized nutrition test will provide you with several important pieces of information for devising your optimal diet:

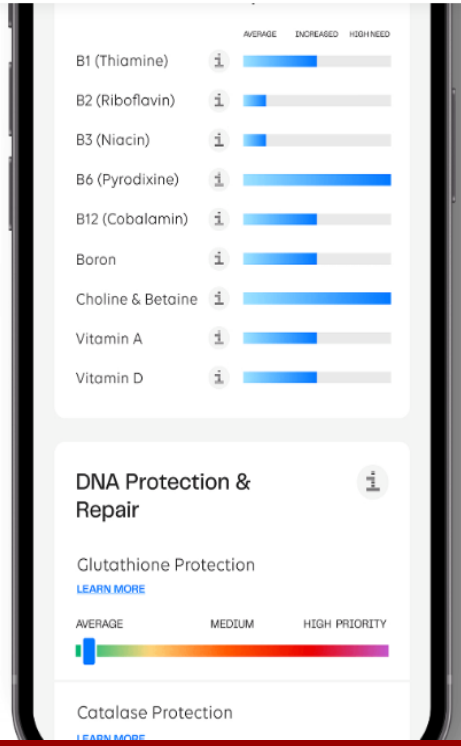
- The right portions of fat, carbohydrates, and proteins to include in your meals
- A detailed nutrient report that details predispositions to vitamin deficiencies and suggests ideal amounts of micronutrients
- A substance metabolism report that shows how well you will metabolize caffeine, alcohol, and other substances
- A food sensitivity report that identifies lactose intolerance, cilantro aversion, bitter taste, and other things

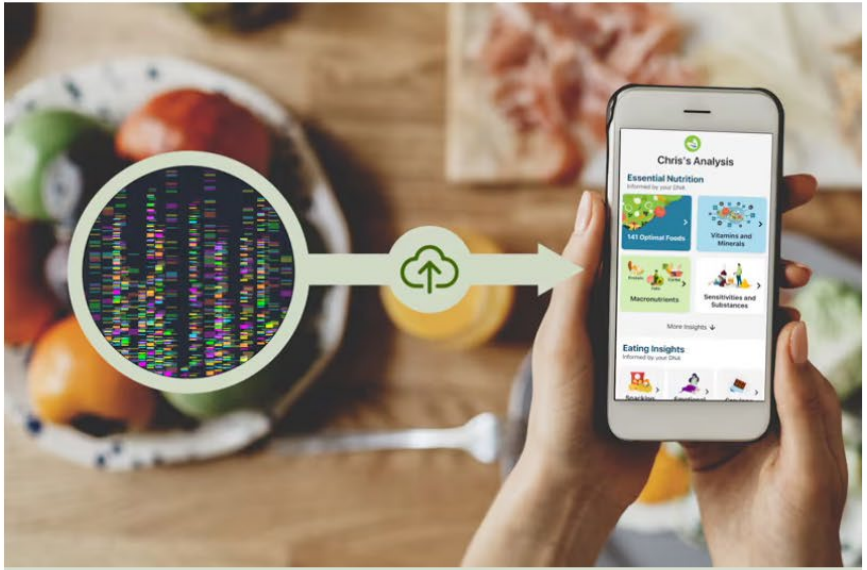
We'll help you remove the guesswork

Experience the most advanced nutrigenomic test available, covering 100 clinically relevant genes for a "whole body" analysis. Take control of your health today.

$359

BUY NOW





Results delivered in 24 hours

$ 159.00

Upload Your Existing DNA Data

Already have your DNA data from 23andMe or AncestryDNA?

Results delivered in 4-6 weeks

$ 179.00

Order a DNA Collection Kit

New to DNA testing? Order our easy-to-use DNA Collection Kit,

Chat wit

Upload your own DNA, provide recs. for vit/supplement, talk with an RDN

Information for Healthcare Professionals

Nutrigenomix 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 Nutrigenomix test kit enables healthcare professionals to counsel individuals according to their DNA, which creates an avenue to personalized nutrition. Nutrigenomix 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 Nutrigenomix a part of your practice today.

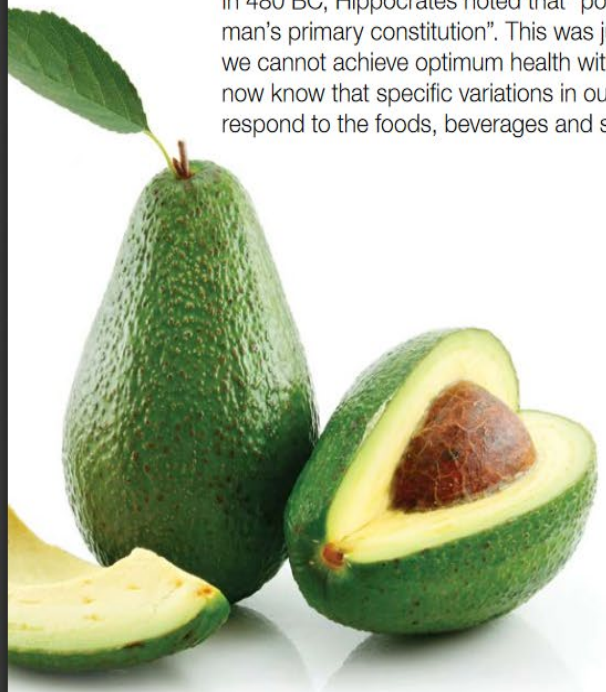
Become an authorized provider of Nutrigenomix®

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

NUTRIGENOMI

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Clinic Locator

What is your location?

California, USA

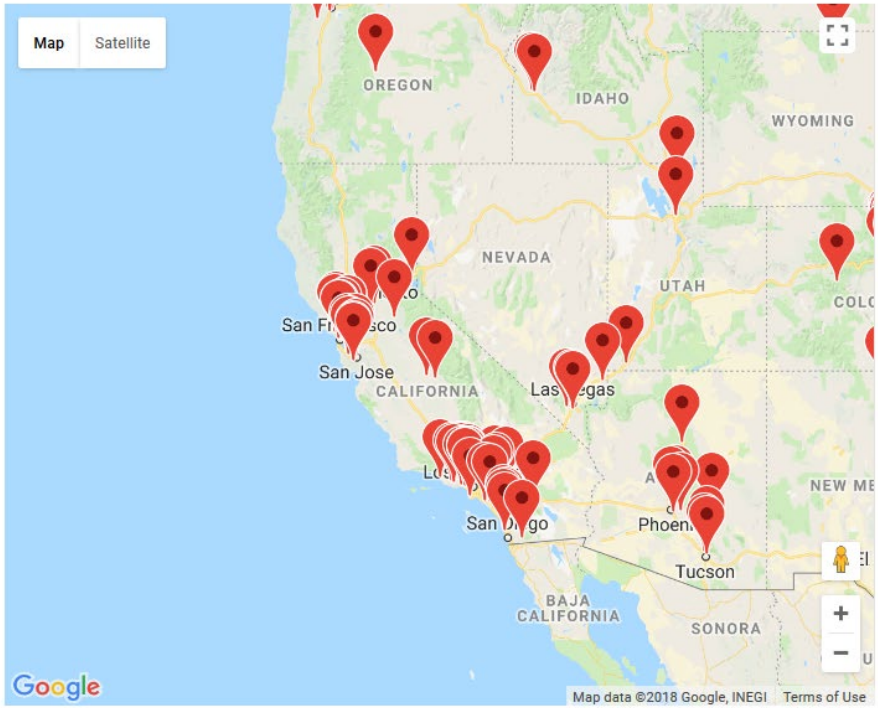
Walsh Nutrition
Canada
More information

Nutrition by Cristen
2851 Serena Ave
Clovis, CA 93619
United States
More information

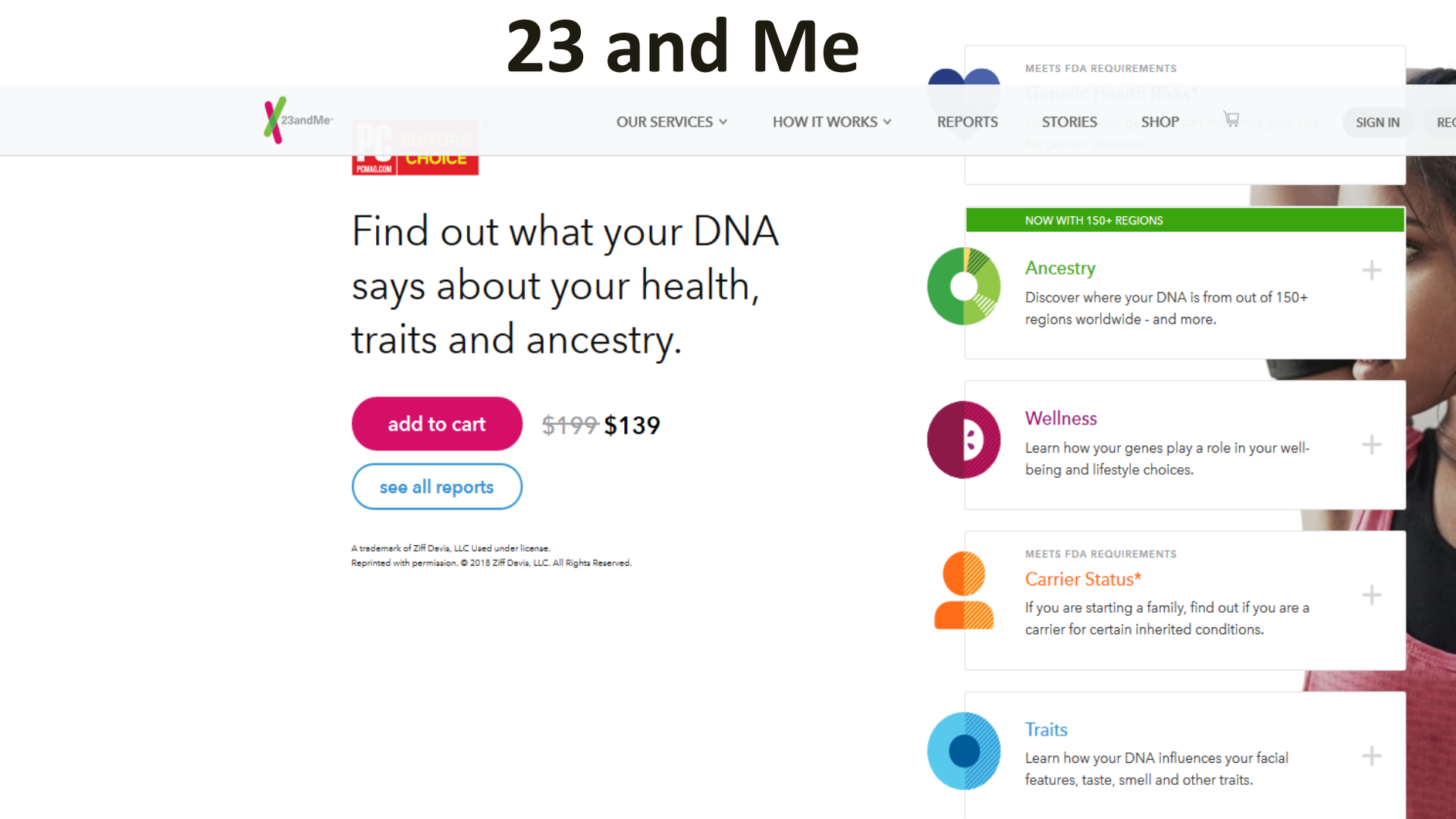
MissBrittRD
PO Box 87
Mokelumne Hill, CA 95245
United States
More information

Outburst Fitness
123 East San Carlos #541
San Jose, CA 95112
United States
More information

Wellth House
517 Bryce Ct
Milpitas, CA 95035
United States
More information



23 and Me


23andMe
OUR SERVICES
HOW IT WORKS
REPORTS
STORIES
SHOP
SIGN IN
EDITORS' CHOICE
PCMAG.COM
Find out what your DNA says about your health, traits and ancestry.
add to cart
$199 $139
see all reports
A trademark of Ziff Davis, LLC Used under license.
Reprinted with permission. © 2018 Ziff Davis, LLC. All Rights Reserved.
MEETS FDA REQUIREMENTS
NOW WITH 150+ REGIONS
Ancestry
Discover where your DNA is from out of 150+ regions worldwide - and more.
Wellness
Learn how your genes play a role in your well-being and lifestyle choices.
MEETS FDA REQUIREMENTS
Carrier Status*
If you are starting a family, find out if you are a carrier for certain inherited conditions.
Traits
Learn how your DNA influences your facial features, taste, smell and other traits.

ANCESTRY

European	100%
British & Irish Ireland	39.1%
French & German Germany	32.8%
Scandinavian	2.1%
Iberian	1.9%
Italian	1.0%
Eastern European	1.0%
Sardinian	0.3%
Broadly Northwestern European	18.8%
Broadly Southern European	1.1%
Broadly European	2.1%

#AncestryDNA raw data download

#This file was generated by AncestryDNA at: 09/21/2018 17:09:47 MDT
#Data was collected using AncestryDNA array version: V1.0
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#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 base pair 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.

rsid	chromosome	position	allele1	allele2
rs4477212	1	82154 T	T	
rs3131972	1	752721	A	G
rs12562034	1	768448	G	G
rs11240777	1	798959	A	G

•Apolipoprotein E4 (APOE 4) The E4 allele (epsilon 4 allele or APOE ε4) is characterized by a “C” nucleotide at both the rs7412 and rs429358 SNPs . Though only present in about 14% of the population, nearly 40% of Alzheimer’s disease patients have a copy of this Apolipoprotein E allele.

rs7412

The ancestral allele is C. The **rs7412**(T) allele, also known as Arg176Cys, generally indicates the presence of an Apoε2 allele; see the ApoE page for a full discussion of the ApoE alleles and their association with Alzheimer's disease.

Another SNP related to ApoE is rs429358.

[PMID 20406466] Genetic variants associated with fasting blood lipids in the U.S. population: Third National Health and Nutrition Examination Survey

[PMID 20429872] Additive effects of LPL, APOA5 and APOE variant combinations on triglyceride levels and hypertriglyceridemia: results of the ICARIA genetic sub-study

[PMID 21263195] An APOE Haplotype Associated with Decreased ?4 Expression Increases the Risk of Late Onset Alzheimer's Disease

Orientation	plus
Stabilized	plus

Geno	Mag	Summary
(C;C)	1	part of APOE4 genoset evaluation
(C;T)	1	part of APOE4 genoset evaluation
(T;T)	1	part of APOE4 genoset evaluation

Reference	GRCh38 38.1/141
Chromosome	19
Position	44908822
Gene	APOE
is a	snp

… how carriers might ameliorate risk through lifestyle and nutrition. We use these data as a basis to speculate a precision nutrition approach for *ApoE4* carriers, including a low-glycemic index diet with a ketogenic option, specific Mediterranean-style food choices, and a panel of seven nutritional supplements.

Open Access | Perspective

Precision Nutrition for Alzheimer's Prevention in *ApoE4* Carriers

by Nicholas G. Norwitz [1,*], Nabeel Saif [2], Ingrid Estrada Ariza [2] and Richard S. Isaacson [2]

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[*] Author to whom correspondence should be addressed.

Academic Editor: Ligia J. Dominguez

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(This article belongs to the Special Issue **Precision Nutrition: Better Strategies for Research and Practice Aimed at Prevention and Management of Complex, Common, Chronic Diseases**)

More about bitter taste

Biology of taste

Taste buds are covered with tiny molecular sensors, called "taste receptors," that specialize in detecting the five basic tastes: sweet, salty, sour, bitter, and umami (a savory, meat-like taste). The types of taste receptors you have determine what tastes you can, or cannot, detect in foods. Some vegetables, like broccoli and brussels sprouts, contain naturally bitter chemicals. Scientists think some people may be unable to detect these bitter chemicals based on what taste receptors they have.

Genetics of bitter taste detection

The TAS2R38 gene contains instructions for a protein, or taste receptor, that can detect the bitter chemical called "PTC." PTC isn't usually found in the human diet, but it is similar to chemicals present in vegetables like broccoli and brussels sprouts. People with the G variant have a taste receptor that can detect these PTC-like chemicals. This means people with the G variant may taste bitterness in these foods and avoid them all together.

Genetic result	What it means
GG	Likely able to detect certain bitter tastes
GC	Likely able to detect certain bitter tastes
CC	Likely unable to detect certain bitter tastes

Bitter Taste

A bitter warning

Scientists believe the bitter taste sense developed to help animals detect toxins or poisons in food. But not everyone can taste the same things.

Your Traits Result

Of 23andMe research participants with genetics like yours:

51% are likely to taste.

49% are unlikely to taste.

LACTOSE INTOLERANCE

Evolution in action

Your DNA determines whether you can produce lactase after childhood, a trait known as "lactase persistence." Research suggests that ancient humans were lactose intolerant, and different genetic variants associated with lactase persistence evolved at different times in different parts of the world. This report is based on a genetic variant associated with lactase persistence that evolved in Europe within the last 20,000 years.

	Genetic result	What it means
	GG	Likely lactose intolerant
	AG	Likely not lactose intolerant
You	**AA**	**Likely not lactose intolerant**

See the percentage of customers with these results

Genetics and Lactose Intolerance

What does it mean to be lactose intolerant?

Dairy products like milk, yogurt, and cheese contain a type of sugar called lactose. Although dairy is a staple of many diets, at least 70% of adults worldwide have trouble digesting lactose.

The severity of lactose intolerance varies from person to person – some people can drink a full glass of milk without experiencing indigestion, while other people will feel uncomfortable after just a bite of cheese. Also, some people's personal experience does not match their genetic result. This is because other factors – including your diet, your digestive system, other genetic variants, and other health conditions – can impact whether you experience symptoms of lactose intolerance.

Approximate lactose content per serving

Clinical Nutrition Applications

- How does a Dietitian use this information?
- Tailored wellness and nutrition interventions
- e.g. MTHFR - If someone has an MTHFR defect, the mutation interferes with the body's ability to use the converted folate it needs. That's when MTHFR symptoms arise. People with MTHFR gene defects should decrease or stop supplements of synthetic folic acid and add a methyl folate supplement (L-5-MTHF supplement) under a doctor's care.

Have questions? Visit https://www.reddit.com/r/SNPedia

rs1801133

rs1801133 is a SNP that is relatively common and has been studied for (relatively) a long time. Also known as C677T, Ala222Val, and A222V, it encodes a variant in the MTHFR gene, which encodes an enzyme involved in folate metabolism.
Homozygous rs1801133(T;T) individuals have ~30% of the expected MTHFR enzyme activity, and **rs1801133**(C;T) heterozygotes have ~65% activity, compared to the most common genotype, **rs1801133**(C;C).

"Our Take on The MTHFR Gene," is a 23andMe blog posting (January 5, 2017), a meta-analysis finding that the past two decades of scientific evidence as it relates to specific MTHFR-influenced health conditions to be inconclusive or conflicting, with two exceptions, 1. women with two copies of C677T variant, 2. a very rare variant that may cause homocystinuria. Their takeaway, "Based on the existing data, scientists at 23andMe have concluded that people should not interpret their genotypes at the common MTHFR variants as having an effect on their health."

This reduced activity (i.e. this SNP) has been linked at least once to each of the following disorders (though not necessarily reproducibly):

- autism
- cancer, including
  - gastric cancer
  - lung cancer

Folic acid processing; homocysteine levels

Orientation minus
Stabilized minus

Geno	Mag	Summary
(C;C)	0	Common genotype: normal homocysteine levels
(C;T)	2.2	1 copy of C677T allele of MTHFR = 65% efficiency in processing folic acid
(T;T)	2.8	homozygous for C677T of MTHFR = 10-20% efficiency in processing folic acid = high homocysteine, low B12 and folate levels

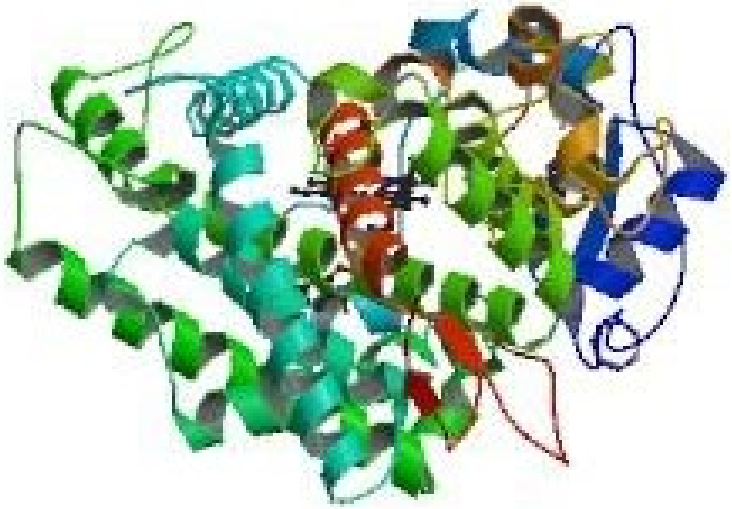
Reference GRCh38 38.1/141
Chromosome 1
Position 11796321

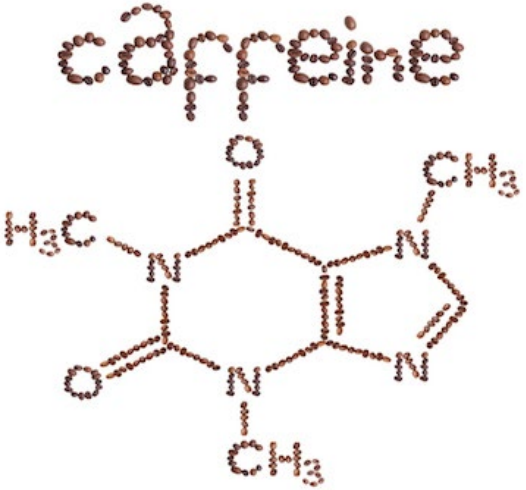
MTHFR Gene, Folic Acid, and Preventing Neural Tube Defects

Did results from a genetic test tell you that you have a methylenetetrahydrofolate reductase (*MTHFR*) gene variant? You may have questions about what this means for your health, especially when it comes to your body's ability to process folate.

What is the *MTHFR* gene?

RS762551 – Caffeine Metabolism





Genetics and Caffeine

Genetics

This report is based on genetic variants near two genes that play a role in how your body handles caffeine. The first gene, CYP1A2, contains instructions for an enzyme that breaks down 95% of the caffeine you consume. The second gene, AHR, contains instructions for a protein that ramps up production of the CYP1A2 enzyme. Variants in these genes may affect how quickly the body breaks down and clears away caffeine.

Promethease Report

file:///G:/May 2017/Genetics/Cary Results 10_4_2017/promethease.html

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Promethease

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Coffee (8)

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Magnitude: 0 4

Publications: 0 315

Frequency: 0 100

Require: Frequency

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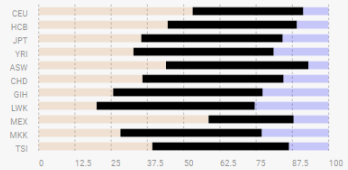
rs762551(A;C)

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...

more info

2.1	Magnitude
38.1%	Frequency



2013-12-14	Geno Modified
0.3522	GMAF
39	Publications
CYP1A2	Genes
15	Chromosome
74749576	Position
2.5	Max Magnitude
2017-09-03	Rs Modified

SNPedia Caffeine Metabolism

rs762551

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A study of healthy premenopausal non-hormone using women concluded that drinkers of 3 or more cups of coffee per day tended to have lower breast volume (smaller breasts), but only if they had at least one **rs762551**(C) allele (p(interaction)=0.02), which was said to be consistent with reports that coffee protects only C-allele carriers against breast cancer.[PMID 18813311]

Orientation	plus
Stabilized	plus

Geno	Mag	Summary
(A;A)	2	Fast Caffeine Metabolizer.
(A;C)	2.1	Carrier of one CYP1A2*1F allele; Slow Caffeine Metabolizer.
(C;C)	2.5	CYP1A2 slow caffeine metabolizer.

Reference	GRCh38 38.1/141
Chromosome	15
Position	74749576
Gene	CYP1A2
is a	snp
is	mentioned by
dbSNP	rs762551
dbSNP (old)	rs762551

Format: Abstract

Send to

Hum Mol Genet. 2016 Dec 15;25(24):5472-5482. doi: 10.1093/hmg/ddw334.

Genome-wide association study of caffeine metabolites provides new insights to caffeine metabolism and dietary caffeine-consumption behavior.

Cornelis MC[1], Kacprowski T[2,3], Menni C[4], Gustafsson S[5], Pivin E[6], Adamski J[7,8,9], Artati A[7], Eap CB[10,11], Ehret G[12,13], Friedrich N[3,14], Ganna A[15,16], Guessous I[6,17,18], Homuth G[2], Lind L[19], Magnusson PK[20], Mangino M[4], Pedersen NL[20], Pietzner M[3,14], Suhre K[21,22], Völzke H[23], Swiss Kidney Project on Genes in Hypertension (SKIPOGH) team, Bochud M[6], Spector TD[4], Grabe HJ[24], Ingelsson E[5,25].

Author information

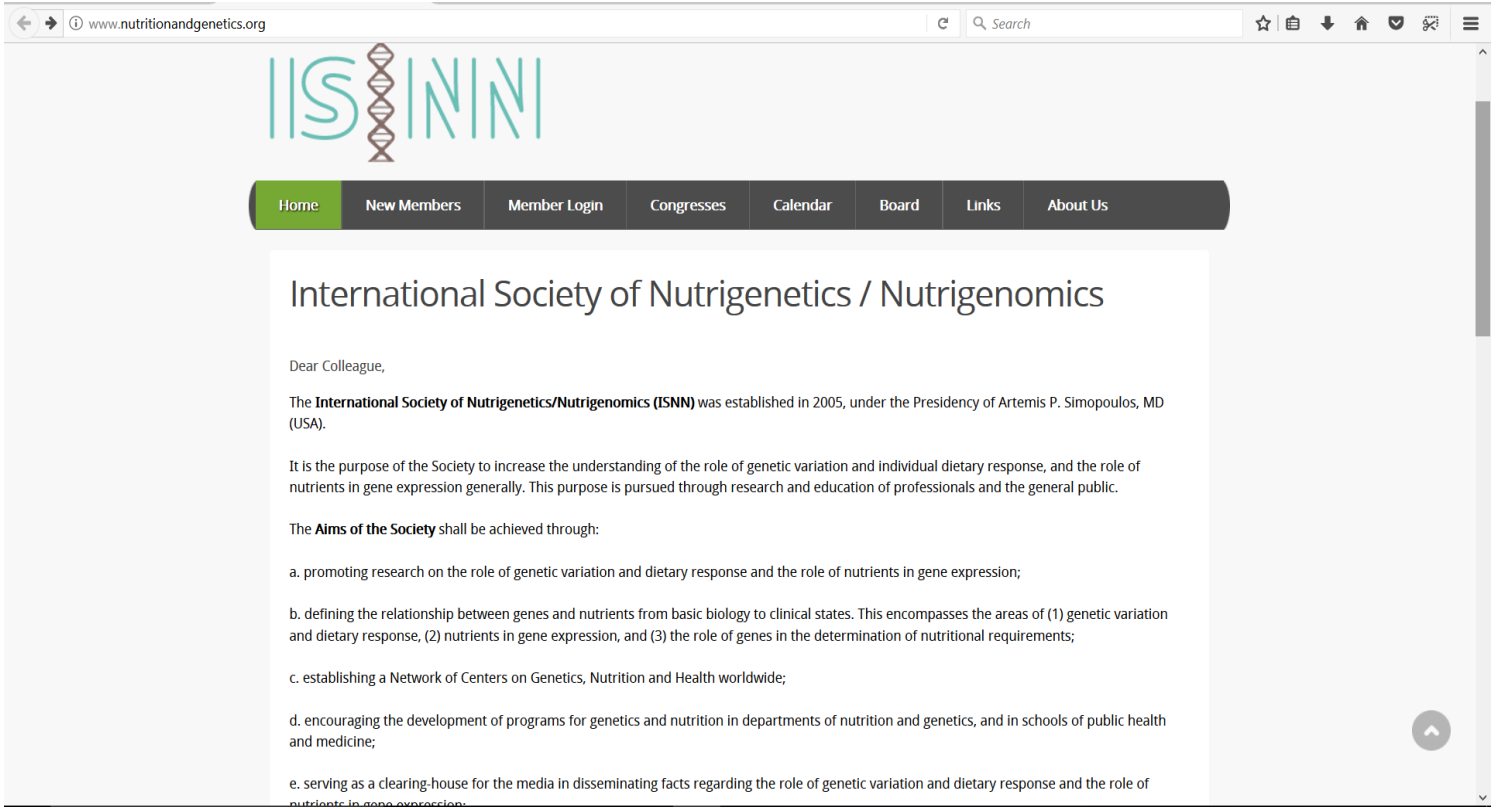
Abstract

Caffeine is the most widely consumed psychoactive substance in the world and presents with wide interindividual variation in metabolism. This variation may modify potential adverse or beneficial effects of caffeine on health. We conducted a genome-wide association study (GWAS) of plasma caffeine, paraxanthine, theophylline, theobromine and paraxanthine/caffeine ratio among up to 9,876 individuals of European ancestry from six population-based studies. A single SNP at 6p23 (near CD83) and several SNPs at 7p21 (near AHR), 15q24 (near CYP1A2) and 19q13.2 (near CYP2A6) met GW-significance ($P < 5 \times 10\text{-}8$) and were associated with one or more metabolites. Variants at 7p21 and 15q24 associated with higher plasma caffeine and lower plasma paraxanthine/caffeine (slow caffeine metabolism) were previously associated with lower coffee and caffeine consumption behavior in GWAS. Variants at 19q13.2 associated with higher plasma paraxanthine/caffeine (slow paraxanthine metabolism) were also associated with lower coffee consumption in the UK Biobank ($n = 94\,343$, $P < 1.0 \times 10\text{-}6$). Variants at 2p24 (in GCKR), 4q22 (in ABCG2) and 7q11.23 (near POR) that were previously associated with coffee consumption in GWAS were nominally associated with plasma caffeine or its metabolites. Taken together, we have identified genetic factors contributing to variation in caffeine metabolism and confirm an important modulating role of systemic caffeine levels in dietary caffeine consumption behavior. Moreover, candidate genes identified encode proteins with important clinical functions that extend beyond caffeine metabolism.

Example: 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

International Society of Nutrigenomics and Nutrigenetics (ISNN)



International Society of Nutrigenomics and Nutrigenetics (ISNN)

https://www.nutritionandgenetics.org/join/

RD Membership $125

Student $ 25

VISIT - Webinars - AND Dietetic Practice Group Dietitians in Integrative and Functional Medicine (DIFM)

Legal, Ethical, Confidentiality

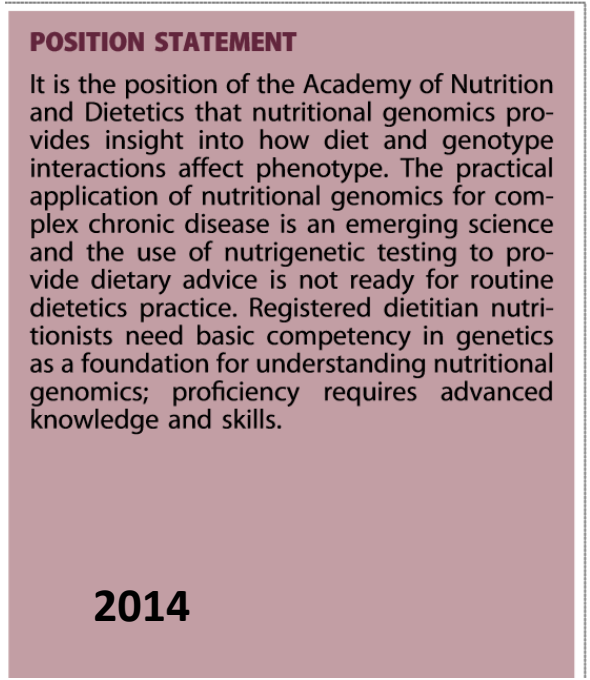
1. Not to be taken lightly, what if?
2. If data are not used now could they be used in future?
3. How can you protect your data?
4. What will you do with the information?

Genetic Information Nondiscrimination Act (GINA) 2008

- Ensures that Americans will not be discriminated against with respect to employment and health insurance.
- California Genetic Information Nondiscrimination Act (CalGINA)(2011)

Next Steps

- Spit, Explore, Learn
- Apply – in addition to existing assessment measures
- Exercise caution
- Cracking Your Genetic Code (2015) NOVA
- Ghost in Your Genes (2007) (ihavenotv.com) NOVA
- *AND Consensus Report* July 2020 “This systematic review ….. Weak quality evidence ….. Field is still maturing”.
- Read research articles



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

Recent SNPs Studied by Students at USC

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)