

A Decade of Nutrigenomics: What does it mean for dietetic practice?

September 11, 2014

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choices affecting wellness
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Today's Faculty

- ▶ Judith A. Gilbride, PhD, RD, CDN, FADA

Chair and Professor, Director of Dietetics Programs

Department of Nutrition, Food Studies, and Public Health

Steinhardt School of Culture, Education, and Human

Development New York University

- ▶ Moderator:

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NUTRI-BITES®

Webinar Series

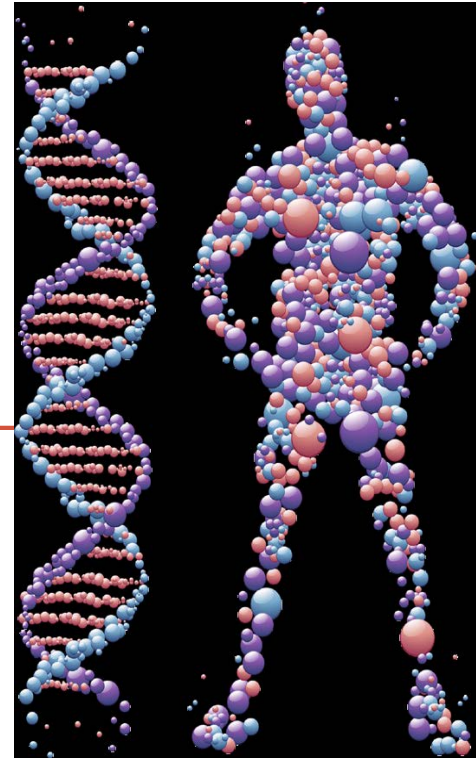
Learning Objectives

After the webinar the participant will be able to:

- ▶ Review the nutrigenomics research directions since the human Genome was mapped
- ▶ Recognize some of the challenges and opportunities for practicing dietitians and nutritionists
- ▶ Discuss how to use genetic information to guide current food and nutrition practice and its future potential

A DECADE OF NUTRIGENOMICS

Judith A. Gilbride , PhD, RDN, FAND
Professor, New York University



Objectives of Today's Discussion

- To review the Nutritional Genomics research directions since the human genome was mapped
- To recognize some of the challenges and opportunities for practicing dietitians and nutritionists
- To discuss how to use genetic information to guide food and nutrition information now and its future potential

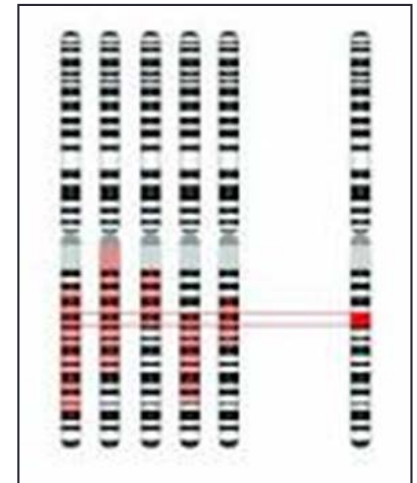


Nutrition and Dietetics Post-Genome

- ◆ Euphoria – Human Genome sequenced
- ◆ Awareness, Education and Preparation
- ◆ Reality of the Science
- ◆ Finding the Evidence to alter Practice

Mapping of Human Genome

- ◆ Completion in 2003, cost of \$300 Million
- ◆ ‘Decoding the Book of Life’
- ◆ International scientific effort
- ◆ New era for detecting, understanding and treating human disease (and Health)
- ◆ 3-5% of \$3 billion to study ethical, legal and social implications (ELSI)



Dawn of Genomic Medicine

- ◆ Improved diagnosis of disease
 - >1800 disease genes discovered
- ◆ Earlier detection of genetic predispositions to disease
 - >1000 genetic tests now available
- ◆ Gene therapy
- ◆ Pharmacogenomics "custom drugs"
 - ◆ Comparison to nutrigenomics



Public Interest

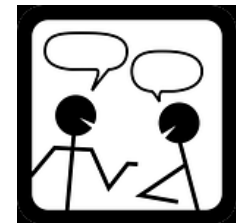
What does the public want? *IFIC Surveys*

Dietary intervention based on knowledge of nutritional requirements, nutritional status, and genotype to prevent, mitigate, or cure chronic disease.

Personalization and Privacy

Impact

- ◆ Nutrition research designs often specific to either environment or genes
- ◆ New technology permits both factors to be considered concurrently
 - High output technologies for investigating all genes, proteins, and metabolites allow study of these elements in relation to each other
- ◆ New terminology and action across medicine, basic science and the health professions



AWARENESS

EDUCATION

PREPARATION

Definitions

Nutritional Genomics broad encompassing term

Nutrigenetics – genetic variations that affect response to and metabolism of nutrients in health status and disease risk

Nutrigenomics – interactions and synergies between dietary components and the genome

Nutritional Epigenomics – diet influence on changes in gene expression without changing the DNA sequence

Nutritional Genomics

Functional interaction of diet and its components with the genome at the molecular, cellular, and systemic level

- How genetic polymorphisms affect nutrient requirements
- How nutrition influences genetic expression and impacts metabolic pathways
- How regulation is disturbed in diet-related diseases

Goal is to use diet to prevent or treat disease.


Technology for Nutrition Science

DNA arrays and high data analysis to examine all genes, proteins and metabolites together

Other - omics, “complete” or “all”

- Proteomics—study a complete collection of proteins in a cell at one time,
- Metabolomics—investigating metabolic pathways using non-invasive biomarkers
- Transcriptomics—profile gene expression patterns of thousands of genes or an entire genome in a single experiment





Human Genome Education Model Project

- ◆ Needs Assessment, *Emerging Issues Confronting Health Professionals*
- ◆ Education and Training
 - ◆ Core Course *“Incorporating Genetics into Teaching and Practice”*
 - ◆ Regional Workshops, *“The New Genetics: Implications for Dietetic Practitioners”*
- ◆ Evaluation of Education Effectiveness

Education in Genetics

	AND	Total
	362	1958
Genetics/Bio. degree	6%	7%
Formal course 1+	11%	14%
Genetics content	44%	44%
No Formal Education	37%	35%
Noncredit Seminar	13%	19%

Genetics Services to Clients

	AND	Total
Discuss genetic component	68%	70%
Refer for genetic counseling	6%	19%
Refer for genetic testing	6%	16%
Counsel on genetic concerns	24%	30%
Have genetic disorder	22%	18%
Gen. + Environmental	43%	35%

Major Findings of Health Professionals

Low confidence and low involvement in providing services to individuals and families with genetic conditions

Inadequate knowledge of HGP and genetics

HGP II Survey

Accreditation Manual, 2002

Knowledge and skills in Dietetics Education

“graduates will have knowledge of genetics”



Accreditation Council for Education of Nutrition and Dietetics

Genetics Education for RDNs

- Genetics is one of the most important components of nutrition and dietetics education.

1. Strongly agree
2. Agree
3. Neutral
4. Disagree
5. Strongly Disagree

Survey of use NCHPEG Competencies

- ◆ B.S. program directors 35% Response rate
- ◆ 38% not familiar with NCHPEG competencies
- ◆ 80% had some genetics in nutrition, physiology, microbiology and biochemistry
- ◆ Most likely content: genetic factors in maintaining health and preventing disease
- ◆ Least likely: genetic counseling process/referral to specialists
- ◆ “Evidence of no or little genetic content in dietetics”

Vickery CE Cotugna N Incorporating human genetics into dietetics curricula remains a challenge. *JADA*:2005:4:583-566.

Will Nutrigenomics help RDNs?

Most RDNs believe application would result in:

- ◆ greater individualization of diet prescriptions (84%)
- ◆ stronger foundation for nutrition recommendations (76%)
- ◆ dietary prescriptions that manage and/or prevent certain diseases (75%)

Rosen R, Earthman C, Marquart L, Reicks M. Continuing education needs of registered dietitians regarding nutrigenomics. J Amer Diet Assoc. 2006; 106 (8):1242-45.

Your Training in Genetics

- Have you had any academic courses or intense workshops in nutritional genomics/genetics?
 1. Genetics course/degree
 2. Genetics content
 3. Certificate workshop
 4. Seminars
 5. No formal education

National Coalition for Health Professional Education in Genetics (NCHPEG)

- ◆ Develop a comprehensive, web-based genetics information center
- ◆ Develop a core curriculum to serve as a template for modification for each health professional discipline
- ◆ Integrate genetics content into continuing education programs, licensure and certification exams



Academy Awarded NCHPEG Grant

February 1, 2007 - grant to build a web-based genetics curriculum,
joint participation

Four Case Scenarios

MTHFR

Role of genes in common disorders

MCADD

Interpretation of family history, newborn screening, inheritance patterns

Celiac Disease

Genes and environment, genetic testing, genetic variants and susceptibility

Cystic Fibrosis

Effect of genetic mutations on body systems and growth, impact of early nutrition therapy

www.nchpeg.org/nutrition

Prepare for Nutrition Practice

UNDERSTAND:

- ◆ The basics of genetics
- ◆ Genetic testing and counseling
- ◆ How nutrition combines with genes in multifactorial diseases
- ◆ Enhance services and work with genetics professionals
- ◆ Ethical, legal, social issues

Is this our Nutrigenomics future?

Use genetic differences among individuals to develop interventions that alter health outcomes and are more effective for preventing disease in selected individuals

Use genotyping to guide food and nutrient selection and functional food use

Providing Genetic Information

- For how many clients, have you discussed the genetic component of their problems?
 1. Most
 2. Some
 3. A few
 4. None
 5. Not applicable to my practice

MORE SCIENCE Potential Value of Nutritional Genomics

- ◆ Large potential to reduce health care costs IF it can show statistically significant and large effects
 - Information potentially of global value
 - Genetic testing a lifetime investment for each person
 - Nutrition is potentially a low cost prevention strategy
- ◆ Greatest for high-risk diseases and population subgroups
- ◆ Greatest if variance of population response is large and testing is cheap
- ◆ Optimal regulatory strategy is a critical issue for further research

Multifactorial Diseases

- ◆ Breast cancer, colorectal cancer, HIV infection, diabetes, hypertension, asthma, obesity
- ◆ 50% of disease risk is attributable to genes
- ◆ 50% to environmental factors
 - ◆ smoking,
 - ◆ **diet**
 - ◆ exercise

New York Times Sept. 16, 2007

“Cancer Free, but Weighing a Mastectomy”

The DNA Age
Changing the Odds

Ethical, Legal and Social (ELSI) Arising from the HGP

- ◆ **Fairness in the use of genetic information** by insurers, employers, courts, schools, adoption agencies, and the military, among others.
 - *Who should have access to personal genetic information, and how will it be used?*
- ◆ **Privacy and confidentiality** of genetic information.
 - *Who owns and controls genetic information?*
- ◆ Genetic Information Non-discrimination Act (GINA) passed in July 2008

Referral for Genetic Counseling

- For how many clients, have you made referrals for genetic counseling?
 1. Most
 2. Some
 3. A few
 4. None
 5. Not applicable to my practice

Interactions Between Genes and the Environment

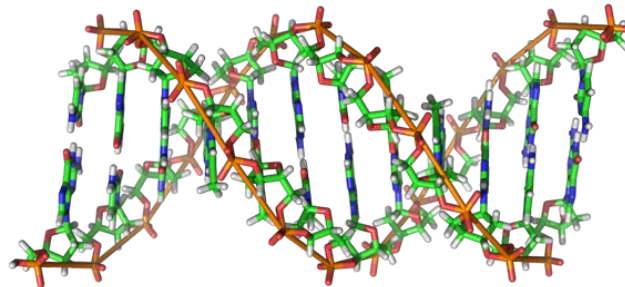
Tobacco, drugs, toxic exposures, education, socioeconomic status

Food is the environmental factor we are permanently exposed to from inception to death

Thus, dietary factors may be the most important environmental factor modulating gene expression throughout the lifespan

Impact of Epigenetics on practice?

- ◆ Study of inherited changes in gene expression which occur without a change in DNA sequence
- ◆ Cancer, genetic disorders, pediatric syndromes and contributing in aging, autoimmune diseases
- ◆ Critical for cell growth and development
- ◆ Mechanisms: DNA methylation, histone modification, chromatin remodeling and noncoding regulatory RNA



Nutritional Epigenomics

Identifying and understanding those reversible, heritable chemical modifications on chromosomes (DNA methylation and histone acetylation) that alter gene expression leading to phenotypic variation in health outcomes.

Rodriguez RL. Director, UC Davis Center of Excellence in Nutritional Genomics

Genetic Biomarkers

<u>Gene</u>	<u>Nutrient</u>	<u>Condition</u>
Phe enzyme	protein (Phe)	PKU
APOe	dietary fats	CVD Risk
MTHFR	folate	CHD
Brca 1/2	dietary fat	Breast Cancer
CMET	alcohol	HTN
FTO	kilocalories	Obesity

Choline Story and Methylation

Objective: To improve understanding of choline metabolism, function and diet requirements during pregnancy

Method: 12 week feeding study with low and high choline intakes

Findings: Folate not adequate with MTHFR 677 TT genotype, due to methylation, a nutrigenetic effect

Implication: To demonstrate show how genomic approach advances nutritional science

Source: West AA, Caudill MA. *Applied choline-omics: Lessons from human metabolic studies for the integration of genomics research into nutrition practice. J Acad Nutr Diet.*; 114 (8):1242-50.

Cancer and the Secrets of Your Genes

- New finding PALB2 gene predicts mutations in a gene to increase risk of breast cancer
 - Caution ‘cannot predict cancer risk correctly by just sequencing gene’
 - Genetic testing is a process not a 1-time event
 - Getting data on whole genome sequencing costs less than \$2000 but having the data interpreted can cost hundreds or thousands of dollars
 - “ ...need to have patience with pace of research”
-
- Ross, T. New York Times Opinion, August 17, 2014

Questions to explore genetic and treatment options in nutrition care

- ◆ How would you describe the condition and manifestations?
- ◆ What is the history and evolution of the disorder?
- ◆ What is the genetic involvement and specific gene mutations?
- ◆ How is the disease inherited? How detected?
- ◆ Can the carrier be detected? Is the carrier functionally impaired?
- ◆ Is the condition linked to other characteristics? Age, ethnicity, gender, age, phenotype?
- ◆ Are there ethical issues in diagnosis and treatment?
- ◆ What supports and resources are available?
- ◆ Are there special foods or medical foods required?

Internet Genetic Testing Direct to Consumer (DTC)

Fees range from <\$100 to \$1000+

- Collect DNA mostly from cheek swab, typically analyze between 4-19 genes, and include questions about sex, age, weight, and lifestyle
- Demand on the rise--one company reports 35,000 nutrigenetic tests since 2003
- Exceedingly complex area since we have 20-25,000 Genes, 5-8 Million SNPs

Confidence to Guide on Genetic Tests

- How confident are you in your ability to guide clients with genetic conditions about whether or not to have genetic testing?
 1. Very confident
 2. Moderately confident
 3. Somewhat confident
 4. Low confidence
 5. No confidence

Issues: Nutritional Genomics Tests

The Test

Is it analytically valid?

Does it identify the genetic marker(s) in question?

Are there multiple tests of different markers?

The genetic marker(s)

What are they? Are they patented?

Do they increase risk?

Does identifying them contribute to a changed patient outcome?

What other factors contribute?

Clinical Utility

Without an analytically valid test that accurately predicts disease or treatment outcomes, clinical utility (CU)is not likely to be established.

Differs depending on use of test

CU of BRCA testing is established for women with + family hx of breast, ovarian (b/o) cancer and a relative with a known BRCA 1,2 mutation

BRCA testing in general population not recommended due to low risk for developing b/o cancer associated with BRCA1,2 mutations in the absence of a family hx

Genetic Testing

- **Analytical Validity** accurate measurement of the specific genetic variation
- **Clinical Validity** accurate prediction of presence or absence of phenotype or disease
- **Clinical Utility** Improve patient outcomes?

Gaps in oversight of DTC Testing

- ◆ Absence of review of DTC genetic testing promotional materials by FDA lacking
- ◆ Lack of evidence of clinical validity and utility for most health-related DTC tests
- ◆ Privacy and research protections for consumers
 - Federal regulations may not apply to DTC tests
 - State protections inadequate
- ◆ Insufficient knowledge about genetics among consumers and health providers

Future Considerations

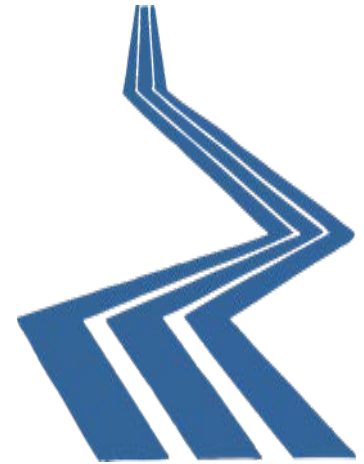
- ◆ Personalized dietary recommendations to prevent chronic diseases based on an individual's genetic makeup may need to begin early in life
- ◆ Newborn screening and treatment of monogenetic disorders is a simplified version of this concept
 - Simple solution of dietary manipulation spares lethal consequences of the genetic defect
 - Passed in 2008, what will impact be?
 - Is it more realistic to test infants at birth for their nutrigenetic profiles?
 - Is whole genome screening for infants ethical?

Change and Challenge

- Coursework on diet and gene interactions
- Human genetics on CDR exam
- DPG on diet and genetics
- Internet web page on diet and gene (ISONG)
- Sessions at annual meetings
- Practice specialty in diet and genetic counseling
- Value and reimbursement for counseling on diet-gene interactions

Patterson et al. The genetic revolution: Change and challenge for the dietetics profession. *J Am Diet Assoc.* 1999; 11; 1412-1420.

How Best to Prepare?



- ◆ Adopt a lifelong learning orientation
- ◆ Think genetically and ethically
- ◆ Set your own roadmap in nutrigenomics
- ◆ Develop solid foundation with genetic team
- ◆ Consider the evidence from public health and clinical practice
- ◆ Monitor patient outcomes based on nutrition interventions and gene-based mechanisms

Understanding Nutritional Genomics will allow us to:

- ◆ Study individual genetic differences in response to dietary components
- ◆ Develop safe and effective diet therapies based on genomic data
- ◆ Develop gene-environmental models to provide new screening/diagnostic tools and research
- ◆ Create a database to identify genes that interact with diet to influence disease
- ◆ Expand jobs and services

Top 10 What to know/do in Nutrition

- ◆ Integrate genetics role with other disciplines
- ◆ Communicate genetic complexity to clients
- ◆ Know consequences of genetic variants on function
- ◆ Understand the impact of nutrient-gene interactions on chronic disease progression
- ◆ Interpretation of family pedigrees, family histories
- ◆ Using food/diet to alter gene expression
- ◆ Genetics and functional foods
- ◆ Use of genetic tests for diet decisions
- ◆ Ethical and social issues affecting one's practice
- ◆ Most valuable resources for nutritional genomics

Many Questions to Answer

- Will public health be improved with individualized tailored recommendations?
- How costly will individualized genetic assessment and counseling be?
- Will people be motivated to adhere to a tailored diet?
- Will this approach be a luxury for those with money, education, and intense involvement in their own health maintenance?

Position of the Academy of Nutrition and Dietetics: Nutritional Genomics

“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 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.”

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

The image shows the cover of a position paper titled "Position of the Academy of Nutrition and Dietetics: Nutritional Genomics". The cover features the "eat right." logo on the left and the "FROM THE ACADEMY Position Paper" header on the right. The main title is centered. Below the title, there is a "MESSAGE" section and a "PURPOSE OF THE PAPER" section. The "MESSAGE" section discusses the position of the Academy of Nutrition and Dietetics regarding nutritional genomics, stating that it provides insight into how diet and genotype interactions affect phenotype, but that its practical application for complex disease is an emerging science and not ready for routine dietetics practice. The "PURPOSE OF THE PAPER" section states that the paper's purpose is to provide a foundation for understanding nutritional genomics and to outline the advanced knowledge and skills required for proficiency. The cover also includes a "SEQUENCING THE HUMAN GENOME" section and a "NEW ACADEMY POSITION STATEMENT ON GENETICS" section. The bottom of the cover features the "eat right." logo and the "JOURNAL OF THE ACADEMY OF NUTRITION AND DIETETICS 319" text.

Points in Nutritional Genomics Paper

1. Need a foundation in genetics to understand the research and its potential for application
2. Proficiency requires advanced knowledge and skills
3. Genotyping alone not sufficient to personalize diet and improve health profile
4. Genetic mutations only part of predicting disease risk; Tools are family history, biochemical markers, risk factors, tests
5. Use caution with genetic tests: risk interpretation, regulations vary, access to geneticists and counseling

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

Exciting opportunities for the Future

‘Although the discipline of nutritional genomics holds promise for tailoring diet to a person’s genotype and influencing chronic disease development, the science is still emerging...’

Position on Nutritional Genomics. J Acad Nutr Diet. 2014;114: p. 310

We must monitor our approach to Nutrigenomics and patient outcomes, keep up with the latest research, weigh the evidence to alter practice, and follow ethical guidelines related to research, genetic testing and clinical practice.



Selected Genetic Resources

Camp KM, Trujillo E. Position of the Academy of Nutrition and Dietetics: Nutritional Genomics. *J Acad Nutr Diet.* 2014;114(2): 299-312.

Selected websites: www.ncbi.nlm.nih.gov/

www.geneclinics.org

www.acmg.net/resources

www.genome.gov

www.nchpeg.org

www.cdc.gov/genomics/gtesting

Questions?



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Based on this webinar, learners should:

- ▶ Be familiar with the nutrigenomics research directions since the human Genome was mapped
- ▶ Recognize some of the challenges and opportunities for practicing dietitians and nutritionists
- ▶ Understand how to use genetic information to guide current food and nutrition practice and its future potential



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 - ▶ Nutrition and Oral Health: What Dietitians Should Know
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Creighton University

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Thank you!

