Recent Advances on Nutrigenomics Research

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What are the lecture outcomes?

Core concept in molecular biology
What is nutrigenomics?
Why do we study nutrigenomics?
Progress on nutrigenomics research
Challenges in nutritional research
Core concept on molecular biology
Core concept on molecular biology
Where is nutrigenomics among science?
What is nutrigenomics and nutrigenetics?

**Nutrigenomics**

“**Nutrigenomics** refers to the application of genomics in nutrition research, enabling associations to be made between specific nutrients and genetic factors, *e.g.* the way in which food or food ingredients influence gene expression… Nutrigenomics should facilitate greater understanding of how nutrition affects metabolic pathways and how this process goes awry in diet-related diseases.”


**Nutrigenetics**

“**Nutrigenetics** is the study of individual differences at the genetic level influencing response to diet. These individual differences may be at the level of single nucleotide polymorphisms rather than at the gene level…It is envisaged that nutrigenetics may lead to individualized dietary advice.”
What is nutrigenomics and nutrigenetics?

**Nutrigenomics**

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


**Nutrigenetics**

“Nutrigenetics examines the effect of genetic variation on the interaction between diet and disease or on nutrient requirements. Genetics has a pivotal role in determining an individual’s risk of developing a certain disease.”
What is nutrigenomics and nutrigenetics?

**Nutrigenomics**

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


“**Nutrigenomics** focuses on the effect of nutrients on the genome, proteome, and metabolome.”


**Nutrigenetics**

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

“**Nutrigenetics** examines the effect of genetic variation on the interaction between diet and exercise. This includes…gene variants associated with, or responsible for, differential responses to nutrients.”
Why study nutrigenomics?

Development personalized nutrition recommendation

Promotion of health and prevention and management of chronic disease

The biological effects of nutrients and food bioactive are elicited by interdependent physiological processes, including:

- Absorption
- Transport
- Biotransformation
- Uptake
- Binding
- Storage
- Excretion

Cellular mechanism of action (energy metabolism, binding to nuclear receptors or regulating transcription factor)

May be affected by genetic variants exerting functional effects or affecting gene expression level

Why study nutrigenomics?
Nutrigenomics Platform

Nutrigenomics study - case 1

Zanzer YC, Dieguez C, Nogueiras R. 2013. University of Santiago de Compostela
Liver fatty acid-binding protein (L-FABP) is a highly conserved key factor in lipid metabolism. Amino acid replacements in L-FABP might alter its function and thereby affect glucose metabolism in lipid-exposed subjects, as indicated by studies in L-FABP knockout mice.
A277-to-G polymorphism substituting Thr$^{94}$ by Ala amino acid replacement or Ala/Ala$^{94}$-mutation contributed significantly to reduced glycogenolysis and less severe hyperglycemia in lipid-exposed humans and was further associated with reduced body weight in a large cohort.

Weickert et al. 2007. Am J Physiol Endocrinol Metab. 293:E1078-E1084
Nutrigenomic study - case 3

EVIDENCE FOR GENE-DIET INTERACTION IN THE RESPONSE OF BLOOD PRESSURE TO DIETARY FIBRE

Robert A. Hegele MD, Martin Jugenberg, Philip W. Connelly PhD and David J.A. Jenkins MD
DNA Research Laboratory (RAH, MJ), and
Clinical Nutrition and Risk Factor Modification Centre (DJAJ),
Division of Endocrinology and Metabolism (PWC, RAH, DJAJ),
St. Michael's Hospital, Toronto, Canada;
and Departments of Medicine (RAH, PWC, DJAJ),
Nutritional Sciences (DJAJ) and Biochemistry (PWC)
Faculty of Medicine, University of Toronto.

- Variation of AGT codon 235 strongly associated with severe hypertension.
- In caucasian common allelic variant AGT M235 (methionine), less common variant AGT T235 (threonine).
- AGT T235 allele has been linked with hypertension in North American, French, Japanese BUT NOT in Australian and British.

Variation in **blood pressure response** to high fibre diets is **associated** with a specific **DNA marker** of AGT, whose product is the **substrate** for the **production** of angiotensin II, one of the most potent human vasoconstrictors.

Discrepancies in the **response of blood pressure** to dietary fibre may have been **related to inter-individual genetic differences** in response to different types of fibre.

Nutrigenomic study - case 4

Polyunsaturated fatty acids modulate the effects of the APOA1 G-A polymorphism on HDL-cholesterol concentrations in a sex-specific manner: the Framingham Study\textsuperscript{1-3}

Jose M Ordovas, Dolores Corella, L Adrienne Cupples, Serkalem Demissie, Alison Kelleher, Oscar Coltell, Peter WF Wilson, Ernst J Schaefer, and Katherine Tucker

- The gene encoding for apolipoprotein A-1 (APOA1) is highly polymorphic and specific SNPs in its promoter S75G->A has been extensively studied in association with HDL cholesterol concentration.
- Women carrying A allele, HDL concentration significantly increased with increased PUFA intake.
- Women carrying G allele, HDL concentration significantly decreased with increased PUFA intake.


Lund University
**FIGURE 1.** Mean (±SE) HDL-cholesterol and apolipoprotein (apo) A-I concentrations by APOA1 genotype and polyunsaturated fatty acid (PUFA) intake categories (□, <4%; □, 4%–8%; ■, >8% of energy) in women. Means were adjusted for age, body mass index, alcohol consumption, tobacco smoking, and intakes of energy, saturated fatty acids, monounsaturated fatty acids, and PUFAs. The $P$ values shown were obtained for the interaction between APOA1 genotype and PUFA intake in the multivariate linear regression models.

Epigenetic changes can be defined as changes induced in a cell that alter the expression of the information of the genome at the transcriptional, translational, or posttranslational level without change in DNA sequence.
Epigenetics mechanisms

DNA Methylation: Essential for Normal Functioning of an Organism

1. Ingestion of nutrients
2. Nutrients metabolized
3. Nutrients absorbed by small intestine and transported via the blood stream to cells in the body
4. Dietary methionine, folate and choline enter the cells
5. Methyl group attach to specific sites on the DNA strand
6. DNA methylation in promoter region down-regulates and silences gene expression. Cell division is suppressed
Epigenetics mechanisms

**EPIGENETICS**

A mechanism for regulating gene activity independent of DNA sequence that determines which genes are turned on or off:
- in a particular cell type
- in different disease states
- in response to a physiological stimulus

**WRITERS**
- Enzymes that add histone modifications.

**ERASERS**
- Enzymes that remove histone modifications.

**READERS**
- Proteins that bind to histone modifications and alter gene activity and protein production.

**HISTONE TAIL**

**DNA**
Epigenetics Studies

Epigenome marks
H3K9Ac
H4PanAc
H3K79me2
H3K4me2
H3K9me3
H3K4me1

Early Predictive LONGEVITY

Correlation with C. elegans different lifespan

Epigenetics Studies

Roseboom et al. 2006. Early Hum Dev 82:485-491
Chronic high-fat diet in fathers programs β-cell dysfunction in female rat offspring

Sheau-Fang Ng, Ruby C. Y. Lin, D. Ross Laybutt, Romain Barres, Julie A. Owens & Margaret J. Morris

The global prevalence of obesity is increasing across all ages in both sexes. This is contributing to the early emergence of type 2 diabetes and its related epidemic. Having either parent obese is an independent risk factor for childhood obesity. Although the detrimental impacts of diet-induced maternal obesity on adiposity and metabolism in offspring are well established, the extent of any contribution of obese fathers is unclear, particularly the role of non-genetic factors in the causal pathway. Here we show that paternal high-fat-diet (HFD) exposure programs β-cell 'dysfunction' in rat F1 female offspring. Chronic HFD consumption in Sprague–Dawley fathers induced increased body weight, adiposity, impaired glucose tolerance and insulin sensitivity. Relative to controls, their female offspring had an early onset of impaired insulin secretion and glucose tolerance that worsened with time, and normal adiposity.

Table 1 | Hormonal and metabolic parameters and pancreas morphology

<table>
<thead>
<tr>
<th>Group and parameter</th>
<th>Control</th>
<th>HFD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fathers</td>
<td>n = 8</td>
<td>n = 9</td>
<td></td>
</tr>
<tr>
<td>Body weight (g)</td>
<td>550 ± 13</td>
<td>705 ± 17</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>Length (cm)</td>
<td>26.8 ± 0.3</td>
<td>27.8 ± 0.3</td>
<td>0.017</td>
</tr>
<tr>
<td>Liver (g)</td>
<td>15.16 ± 0.43</td>
<td>19.51 ± 1.23</td>
<td>0.006</td>
</tr>
<tr>
<td>BAT (mg)</td>
<td>0.462 ± 0.026</td>
<td>0.779 ± 0.100</td>
<td>0.013</td>
</tr>
<tr>
<td>Mesenteric WAT (g)</td>
<td>4.76 ± 0.35</td>
<td>12.43 ± 1.23</td>
<td>&lt;0.0005</td>
</tr>
</tbody>
</table>

Ng SF et al. 2010. Nature 467:963-967
Epigenetics study

Ng SF et al. 2010. Nature 467:963-967
Summary

• The facts of human genes, 3% functional DNA and 97% considered as ’junk’ DNA; 99.8% genetically similar among humans; more than 1.4 million SNPs found
• The biological effects of foods elicited by interdependent physiological processes, including absorption, transport, biotransformation, storage, binding, excretion
• There are growing evidence of nutrigenomics study in human clinical research-based
• Other potential factor outside genetics (epigenetics) that may involve towards gene regulation are evidently grows and such mechanisms is a challenge being revealed
Finished project
Finished project

ClinicalTrials.gov
A service of the U.S. National Institutes of Health

New Available for Public Comment: Notice of Proposed Rulemaking (NPRM) for FDAAA 801 and NIH Draft Reporting Policy for NIH-Funded Trials

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Effect of Brazilian Fruits Peel on Metabolic Regulation and Appetite in Healthy Subjects (BRASIL-MET)

This study is currently recruiting participants. (see Contacts and Locations)
Verified September 2014 by Lund University

Sponsor:
Lund University

Collaborator:
University of Campinas, Brazil

Sponsors and Collaborators
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University of Campinas, Brazil

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History of Changes

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