Personalized Nutrition and the Future of Dietary Supplements

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Science

Practice

Regulation
The Future of Dietary Supplements and Personalized Nutrition

Dilip Ghosh

352 pages
July 2017, Wiley-Blackwell
Who is he?
Who is he?
Who is he?
Internet DNA-ting: I’ll show you mine if you show me yours

Gene Gen: Prof. Barry Marshall's Lifetime Risk

1st Aussie Celebrity to post his full genetic code on the internet

<table>
<thead>
<tr>
<th>Disease or Condition</th>
<th>Marshall</th>
<th>Population Average</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alzheimer's Disease</td>
<td>11.7%</td>
<td>6%</td>
</tr>
<tr>
<td>Heart attack</td>
<td>33.3%</td>
<td>42%</td>
</tr>
<tr>
<td>Testicular cancer</td>
<td>1.1%</td>
<td>0.5%</td>
</tr>
<tr>
<td>Type 2 diabetes</td>
<td>32.2%</td>
<td>25%</td>
</tr>
<tr>
<td>Obesity</td>
<td>30%</td>
<td>39.5%</td>
</tr>
<tr>
<td>Alcohol-induced flush</td>
<td>No</td>
<td>Some</td>
</tr>
</tbody>
</table>

*Compared to male population

SMH June 2011

Letting it all hang out... Fairfax Media photographer Alex Ellinghausen projected a copy of Barry Marshall’s genetic code onto his face during Marshall’s appearance at the National Press Club in Canberra yesterday.
Prof. Barry Marshall:

1st Aussie to post his full genomic code

What are his lifetime RISKs?

Macular degeneration: 3 times

Alzheimer's Disease: 2 times

Heart attack: marginally

Type 2 diabetes: marginally
Two words changing the world: Customisation and Personalisation

Customisation of supplemented products is based on 4 tenets:

- Shift towards natural ingredients
- Cultural customization to suit specific regions and specific target groups
- Shift towards new delivery mechanisms
- Disease/Condition specific formulations
Criteria underlying consumer personalization

<table>
<thead>
<tr>
<th>Platform</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Taste &amp; flavour</td>
<td>• Most immediate &amp; easily accessed criteria.</td>
</tr>
<tr>
<td></td>
<td>• Genetic diversity of taste &amp; olfactory sensation are now well established.</td>
</tr>
<tr>
<td></td>
<td>• Olfactory preference is most driving force</td>
</tr>
<tr>
<td>Cultural mores</td>
<td>• Based on religious &amp; philosophical value system.</td>
</tr>
<tr>
<td></td>
<td>• Halal, Kosher, vegan, religious fasting etc.</td>
</tr>
<tr>
<td>Life stage</td>
<td>• Specific physiological needs of the stages of life stages.</td>
</tr>
<tr>
<td></td>
<td>• Pregnancy, lactation, weaning, infancy, aging, recovery from illness etc.</td>
</tr>
<tr>
<td></td>
<td>• Both short term and long term supplementation</td>
</tr>
<tr>
<td>Lifestyle</td>
<td>• Products for athletes at different stages of training.</td>
</tr>
<tr>
<td></td>
<td>• High altitude training</td>
</tr>
<tr>
<td></td>
<td>• Frequent traveler</td>
</tr>
<tr>
<td>Lifestyle diseases</td>
<td>• Diagnostics related to high risk disease condition as a direct result of chronic lifestyle choices.</td>
</tr>
<tr>
<td></td>
<td>• Excess body weight, intestinal discomfort, smoking, sedentary behavior, high-fat diet etc.</td>
</tr>
<tr>
<td>Inherited Diseases</td>
<td>• Relevance to family history of inherited diseases</td>
</tr>
<tr>
<td></td>
<td>• Food &amp; supplement intervention is recognized an integral part of this solution such as allergies &amp; intolerances.</td>
</tr>
<tr>
<td></td>
<td>• Inborn error of metabolism, phenylketonuria can well managed by metabolite-based diagnostics with low phenylalanine food &amp; supplements</td>
</tr>
<tr>
<td>Genetic Predispositions</td>
<td>• Personalisation based on genetic variations</td>
</tr>
<tr>
<td></td>
<td>• Target population-based product development</td>
</tr>
<tr>
<td></td>
<td>• Strong linkage with ethical-legal-social issues</td>
</tr>
</tbody>
</table>
Personalisation in different way

Coca-Cola puts people’s names on bottles in ‘Share a coke’ campaign
**MyMuesli:** Another example of personalisation

**Just three easy steps!**

1. Choose your Muesli Base
2. Add Dried Fruits, Nuts, Seeds & our delicious Naughty Bits
3. Name your Mix, and check-out

Create your own muesli in minutes and have it delivered straight to your door!

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**Science**  
**Practice**  
**Regulation**
Challenge 2: We’re not all the same!

And We do not want to be!!!!
Welcome To the World of 'Omics
Different allele frequencies of 4 variants in CYP (Cytochrome P450) genes among various ethnic groups

Diet: driving force for human evolution

The greatest divergence between the genome of humans and chimpanzee is found among genes that control metabolism and are closely associated with DIET

Somel et al. 2008
“Every individual is different from another and hence should be considered as a different entity”

Charaka 4000, Ayurvedic Medical system

Chinese medicine is a highly developed personalized or individualized medicine, are not designed to treat symptoms of a specific illness; rather, they are tailored specifically to the individual

Sasang typology, a Korean traditional medical system, explains the individual differences in behavioral patterns, physical characteristics, and susceptibility to a certain disease on the basis on their biophysiological traits
Potential areas for development of personalised medicines/functional foods

- Type 2 diabetes & Obesity
- Antidepressants
- Inflammatory Bowel Disease (IBD)
- Anti-coagulant/Thromboembolism
  - Few Cancers (breast/colorectal/lung/prostate)
  - Asthma
  - Nicotine dependence
Platforms

Niche Products

- Gluten-free foods for celiacs
- Familial hypercholesterolemia patients without saturated fats
- Dairy protein-free food for inherited galactosemia
- Mood Enhancement foods

Mass-Market Products (for Critical genetic variations & Biomarkers):

- Low glycaemic load products for Insulin resistance, Obesity & Diabetes.
- Optimised sports nutrition in all phases of the life cycle
- Anti-depressants
Story starts with-----

**BiDil**
Heart failure drug for African-American

**Vioxx**
Merck
Anti-inflammatory

**Hepceptin**
Roche
To treat certain breast cancers

**NitroMed**

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**Science**

**Practice**

**Regulation**
Nutrigenomics is the study of the response of humans to food and food components using genomics, proteomics and metabolomics approaches. In near future, nutrigenomics will most probably revolutionize the human comprehension of the entire field of nutrition based on individual human genotypes.
Diet & Genes Interaction

Food/Diet
Developing food concepts for individually tailored clients

Human Health & Performance
Understanding the genetic variation among individuals that effect health, performance & susceptibility to disease

Science Practice Regulation
Gene-Diet-Environment Interaction

Nutrition

Intrinsic Genetic Susceptibility

Behavior/Age/Stage of Development

Human Health/Disease

Science Practice Regulation
DNA to Genome

A brief journey

Intentionally skipping this section
Tiny differences

• Effects on health are different from one person to the next

• What determines these differences?

Although 99.9% of human DNA sequences are identical, the 0.1% difference between any two individuals has profound biological significance.
Some Scientific Disciplines of Nutrigenomics

- Genetics
- Nutrition
- Statistics
- Molecular biology
- Physiology
- Informatics

Biocomputation

Ethics

Science  Practice  Regulation
Nutrigenomics & Nutrigenetics: two sides of a coin

Mutch et al. 2005
Regulation of genes by nutrients

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Gene impact</th>
<th>Disease potential</th>
</tr>
</thead>
<tbody>
<tr>
<td>Folic acid</td>
<td>DNA methylation</td>
<td>Cancer</td>
</tr>
<tr>
<td>Fatty acid</td>
<td>Bind to transcription factors</td>
<td>Obesity</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>mRNA stability</td>
<td>Kidney disease</td>
</tr>
<tr>
<td>Flavones</td>
<td>Increase mRNA synthesis</td>
<td>Cancer</td>
</tr>
<tr>
<td>Theaflavins</td>
<td>Decrease mRNA synthesis</td>
<td>Arthritis</td>
</tr>
</tbody>
</table>

Source: Foodtechnology, 2005
Variation in Glucosinolate Among Cruciferous vegetables (µmol/g DryWeight)

Daidzein in Soy Converted to Equol in Some but not All Individuals!

Science

Practice

Regulation

F Rafii et al, Arch Microbiol 180: 13, 2003
Coffee: Recent media headline
Genes decide if coffee hurts or helps your heart

By Roxanne Khamsi

Coffee can raise or reduce your chances of suffering a heart attack – it all depends on your genes, researchers suggest.

People with a genetic makeup that causes them to metabolise caffeine more slowly have a 36% greater risk of heart attack if they drink two to three cups of coffee a day than people with the same gene who drink one cup or less a day, according to a new study. And if they drink more than four cups, this risk rises to 64%.

“Our data suggest that the longer caffeine is lingering in the system, the more harm it can do,” says Ahmed El-Sohemy at the University of Toronto, Canada, who led the study.

On the other hand, individuals who metabolised caffeine quickly and consumed two to three cups of coffee a day had a 22% reduction in the risk of heart attack compared with those with the same genetic makeup who consumed just one cup or less each day.

Genes determine coffee heart risk

Drinking large amounts of coffee each day could increase the risk of heart attack for people with a particular genetic profile, a study has suggested.

Four thousand people in Costa Rica were monitored in the Journal of the American Medical Association study.

Those who were slow at breaking down caffeine were 64% more likely to suffer a heart attack.
First Successes and What We Learned

Caffeine

*Fast metabolizers*
- Low risk for heart disease

*Slow metabolizers*
- Higher risk for heart disease

Courtesy: Dr A El-Sohemy, Canada
Why genetics/genomics affect us?

Nutrition ————→ Health Outcome

Genes

Genotype A ———→ Increase
Genotype B ———→ No Effect
Genotype C ———→ Decrease

One size doesn’t fit all.

Courtesy: Dr A El-Sohemy, Canada
Is Coffee associated with CVD?

Coffee → Genes → Genotype A → Increase or Genotype B → No Effect or Genotype C → Decrease → CVD

Courtesy: Dr A El-Sohemy, Canada
Bioactives in Coffee

- Magnesium
- Aliphatic acids
- Caffeine
- Potassium
- Diterpenoids
- Melanoidins
- Polyphenols

Courtesy: Dr A El-Sohemy, Canada
Caffeine (1,3,7-trimethylxanthine)

Courtesy: Dr A El-Sohemy, Canada
Coffee, CYP1A2 Genotype, and Risk of Myocardial Infarction

Marilyn C. Cornelis, BSc
Ahmed El-Soehmy, PhD
Edmond K. Kabagambe, PhD
Hannia Campos, PhD

Context The association between coffee intake and risk of myocardial infarction (MI) remains controversial. Coffee is a major source of caffeine, which is metabolized by the polymorphic cytochrome P450 1A2 (CYP1A2) enzyme. Individuals who are homozygous for the CYP1A2*1A allele are "rapid" caffeine metabolizers, whereas carriers of the variant CYP1A2*1F are "slow" caffeine metabolizers.

Cornelis et al. JAMA, 2006, 295: 1135-41

CYP1A2 genotype modifies the association between coffee intake and the risk of hypertension

Paolo Palatini\textsuperscript{a}, Giulio Ceolotto\textsuperscript{a}, Fabio Ragazzo\textsuperscript{a}, Francesca Dorigatti\textsuperscript{a}, Francesca Saladini\textsuperscript{a}, Italia Papparella\textsuperscript{a}, Lucio Mos\textsuperscript{b}, Giuseppe Zanata\textsuperscript{c} and Massimo Santonastaso\textsuperscript{d}

J Hypertension, 2009, 27: 1594-1601
Coffee Intake and Risk of Hypertension/Risk of Impaired Fasting Glucose

Palatini et al., J Hypertens 27: 1594-1601, 2009

Genetic Variation in CYP1A2-163 A>C
Other side of the coin
(Commercial use of great science)
A large Dutch Insurance company (VGZ) aspires to improve public health by refunding (up to €40 a year) customers who buy pharma food products from Unilever (e.g. Becel pro-activ products)
“Did you ever wonder about your most ancient ancestors? The Genographic Project will introduce you to them, and explain the genetic journeys that bond your personal lineage over tens of thousands of years.”

Genographic Project by National Geographic & IBM
“Personalised genomes go to mainstream”

Nature 30 Oct. 2007

2 Silicon Valley start-up will start giving customers a peek at their genomes for a few thousand dollars

- 23andMe (Google back-up)
- Navigenetics

Watson's gene sequenced less than a million $
Sciona provides personalized health and nutrition recommendations based on an individual’s diet, lifestyle and unique genetic profile. The company has created a powerful set of tools enabling consumers and consumer product companies to harness the scientific information derived from the Human Genome Project.

14/03/2007 - Australia's Genetic Technologies (GTG) has bestowed a license to its non-coding DNA patents to personalised nutrition company Sciona, which is expected to be the start of a long relationship in the lifestyle and life-extension arena.
Now Pandora Box Is Open

Not only Sciona

Other players are

- Genelex
- Market America
- Suracell
### List of Relevant Genes Tested

<table>
<thead>
<tr>
<th>Company</th>
<th>Tests offered</th>
</tr>
</thead>
<tbody>
<tr>
<td>23andMe (California)</td>
<td>Taste perception/breast &amp; prostate cancer/Crohn's disease/type 1 &amp; 2 diabetes &amp; more</td>
</tr>
<tr>
<td>Consumer Genetics (California)</td>
<td>Caffeine &amp; alcohol metabolism/fetal gender</td>
</tr>
<tr>
<td>Cygene Direct (Florida)</td>
<td>Osteoporosis/thrombosis/athletic performance</td>
</tr>
<tr>
<td>DeCODE</td>
<td>Asthma/cancers/MS/more</td>
</tr>
<tr>
<td>Genelex (seattle)</td>
<td>Diet &amp; weight management/celiac disease</td>
</tr>
<tr>
<td>Mygenome (Massachusetts)</td>
<td>Alzheimer's/CVD/thrombosis</td>
</tr>
<tr>
<td>Navigeneics (California)</td>
<td>No tests offered yet</td>
</tr>
</tbody>
</table>

*Genetics & Public Policy Center; Company websites*
Coffee, CYP1A2 Genotype, and Risk of Myocardial Infarction
Marilyn C. Cornelis, BSc, Ahmed El-Sohemy, PhD, Edmond K. Kabagambe, PhD, Hannia Campos, PhD
JAMA. 2006; 295: 1135-1141

Try the new CaffeineGEN™ test today
Standard $129.00 in 5 business days
Express $159.00 in 2 business days

Which Gene Do I Have?
CaffeineGEN™ Test is an easy-to-do genetic test that tells you whether you have the “fast” or “slow” variant of the gene for breaking down caffeine. Knowing which gene you have will help you make lifestyle choices that would be more healthy for your unique genetic makeup.
## TABLE 1: PREDICTIONS FOR DISEASE RELATIVE RISKS FOR FIVE INDIVIDUALS

<table>
<thead>
<tr>
<th>Disease</th>
<th>Female A</th>
<th>Female B</th>
<th>Female C</th>
<th>Male D</th>
<th>Male E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast cancer</td>
<td>↑↑↑</td>
<td>↑↑↑</td>
<td>↓↓↓</td>
<td>↓↓↓</td>
<td>↓↓↓</td>
</tr>
<tr>
<td>Coeliac disease</td>
<td>↓↓↓</td>
<td>↓↓↓</td>
<td>↓↓↓</td>
<td>↓↓↓</td>
<td>↓↓↓</td>
</tr>
<tr>
<td>Colon cancer</td>
<td>= =</td>
<td>= =</td>
<td>= ↓</td>
<td>↑↑</td>
<td>= ↓</td>
</tr>
<tr>
<td>Crohn’s disease</td>
<td>↓↑</td>
<td>↓↑</td>
<td>↓↓</td>
<td>↓↓</td>
<td>↓=</td>
</tr>
<tr>
<td>Heart attack</td>
<td>↓↓</td>
<td>= ↓</td>
<td>= ↓</td>
<td>= ↓</td>
<td>↑↑</td>
</tr>
<tr>
<td>Lupus</td>
<td>↑↓</td>
<td>↓↓</td>
<td>↓↓</td>
<td>↑=</td>
<td>↑=</td>
</tr>
<tr>
<td>Macular degeneration</td>
<td>↓↓</td>
<td>↓↓</td>
<td>↑=</td>
<td>↓↓</td>
<td>↓↓</td>
</tr>
<tr>
<td>Multiple sclerosis</td>
<td>↑↑</td>
<td>↓↓</td>
<td>↓↓</td>
<td>↓↓</td>
<td>↓↓</td>
</tr>
<tr>
<td>Prostate cancer</td>
<td>↑↑</td>
<td>↓↑</td>
<td>= =</td>
<td>↓↑</td>
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</tr>
<tr>
<td>Psoriasis</td>
<td>↓↑</td>
<td>↑↓</td>
<td>↑↓</td>
<td>↑↑</td>
<td>↓↓</td>
</tr>
<tr>
<td>Restless legs syndrome</td>
<td>= ↓</td>
<td>↑↑</td>
<td>= =</td>
<td>↓↑</td>
<td>↑↑</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>↑↑</td>
<td>↑↑</td>
<td>↓↓</td>
<td>↓↓</td>
<td>↑↑</td>
</tr>
<tr>
<td>Type 2 diabetes</td>
<td>↓↓</td>
<td>= ↓</td>
<td>↓↓</td>
<td>↑↓</td>
<td>= ↓</td>
</tr>
</tbody>
</table>

↑ increased risk (RR > 1.05), ↓ decreased risk (relative risk (RR) < 0.95), = average risk (0.95 ≤ RR ≤ 1.05). First prediction is from 23andMe; second prediction is from Navigenics. Different predictions are highlighted in beige.

### James Watson Decoded

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Time taken</td>
<td>13 yrs</td>
<td>4 yrs</td>
<td>4.5 mos</td>
</tr>
<tr>
<td>Number of scientists (as authors)</td>
<td>&gt;2,800</td>
<td>&gt;31</td>
<td>&gt;27</td>
</tr>
<tr>
<td>Cost of sequencing</td>
<td>$2.7 bn</td>
<td>$100 mn</td>
<td>&lt;$1.5 mn</td>
</tr>
<tr>
<td>Coverage</td>
<td>8-10 x</td>
<td>7.5 x</td>
<td>7.4 x</td>
</tr>
<tr>
<td>No of institutes involved</td>
<td>16</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>No of countries involved</td>
<td>6</td>
<td>3</td>
<td>1</td>
</tr>
</tbody>
</table>

**QUICKER, SMALLER, CHEAPER**

$5,000 genome next year, company promises

Complete Genomics, California

Innovation

6 October 2008 | Nature
What Consumer’s think?
US Consumers' Genomics Awareness

Source: Schmidt et al. 2010
Interest in Genetically Tailored Products

Source: Schmidt et al. 2010
Regulation

trundles along belatedly after New Technologies, like a RUBBISH VAN AFTER A PARADE
Types of Tests Available

• medical condition
  - with or without possibility of intervention

• lifestyle / educational
  - optimise health through lifestyle changes

• recreational
  - genealogy, love matches

Courtesy - Nola Ries
Science fiction or science fact? Could we soon be stopping off for a quick genetic test to let us know which foods and supplements to take to reduce our risks of certain diseases?
“With nutrigenomics, this is looking to the horizon. There are a lot of knowledge gaps, particularly in terms of what the research is saying and what is actually possible”

Dr. Andrew Shao, Ex-VP, US Council for Responsible Nutrition
Should nutrigenomics testing be delivered directly to consumers or through healthcare professionals?

Who should be tested?

Who should have access to test information?

How should individual privacy be protected?

How should genetic discrimination be prevented?
Future

Genetics has always been special—specially controversial. It began with polemics between Darwinism & religion, followed by the 19th century Eugenics debate to recent GM controversy.
MY GENOME MADE ME DO IT!
It would never work, Nicole! I’m in the experimental group and you’re in the control."

(HARDIN)
Thank you!

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