Nutrigenomics: Do our genes determine what we should eat for health and performance?
Disclosures

A.E-S. is the Founder and holds shares in Nutrigenomix Inc.

N.G. is a consultant and serves on SAB of Nutrigenomix Inc.
Genetic Testing

Disease Risk Genes

vs

Modifier Genes
The Science of **NUTRIGENOMICS**

using genetic testing to determine why individuals respond differently to the same foods, beverages and supplements they consume.
Genetic variant in the glucose transporter type 2 is associated with higher intakes of sugars in two distinct populations

Karen M. Eny,1 Thomas M. S. Wolever,1,2 Bénédicte Fontaine-Bisson,1 and Ahmed El-Sohemy1

1Department of Nutritional Sciences, University of Toronto; and 2St. Michael’s Hospital, Toronto, Canada

Submitted 10 July 2007; accepted in final form 14 March 2008
Craving something sweet? Blame it on your DNA

JOSEPH HALL
HEALTH REPORTER

If you have a sweet tooth, it won’t be found amongst your molars or canines. It’s inserted in your DNA instead.

Cake and cola and cookie lovers may well be able to blame their cravings on a common variant of a gene that controls the brain’s ability to sense sugars in the body, a new University of Toronto study suggests. About one in five people has the variant.

The gene may also have implications for a person’s risk of getting diabetes.

“In humans this gene functions as a glucose sensor in the brain to regulate appetite or food intake,” says U of T nutrition expert

SLIGAR continued on A17
Why are genetic differences important for nutrition?

One size does not fit all

Nutrition

Genes

Genotype A
Genotype B
Genotype C

Health Outcome

Increase
No Effect
Decrease
One man's food is another man's poison

- Lucretius (99-55 BC)
GENETICS CAN AFFECT

- smell
- taste
- metabolism
- appetite
- absorption
- digestion
- excretion
Cardiometabolic disease is the #1 cause of death and disability among US adults.

~50% of cardiometabolic deaths are attributable to poor diet.
Is coffee associated with CVD?

Genes

- Genotype A: Increase
- Genotype B: No Effect
- Genotype C: Decrease
Bioactives in Coffee

- aliphatic acids
- potassium
- magnesium
- melanoidins
- diterpenoids
- polyphenols
- caffeine
Caffeine

\[
\begin{align*}
\text{CYP1A2} & \quad \rightarrow \\
\text{Paraxanthine} & \\
1,7\text{-dimethyluric acid} & \quad 1\text{-methylxanthine} \quad 5\text{-acetylamino-6-formylamino-3-methyluracil} \\
\quad & \quad \text{1-methyluric acid}
\end{align*}
\]
Genetic Variation in CYP1A2

-163 A→C

- Bar graph showing the % Inducibility for different CYP1A2 genotypes:
  - AA: Fast genotype with high % Inducibility
  - AC: Intermediate genotype
  - CC: Slow genotype with low % Inducibility

- The graph illustrates the genetic variation and its impact on the inducibility of CYP1A2.
Coffee Intake and Risk of Myocardial Infarction

Odds Ratio

- <1 cup/d
- 1 cup/d
- 2-3 cups/d
- ≥4 cups/d

Total Population

*
Coffee Intake and Risk of Myocardial Infarction

<table>
<thead>
<tr>
<th>CYP1A2 Genotype</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>AA</td>
<td>0</td>
</tr>
<tr>
<td>AC + CC</td>
<td>1</td>
</tr>
<tr>
<td>&lt;1 cup/d</td>
<td>2</td>
</tr>
<tr>
<td>1 cup/d</td>
<td>3</td>
</tr>
<tr>
<td>2-3 cups/d</td>
<td>4</td>
</tr>
<tr>
<td>≥4 cups/d</td>
<td>*</td>
</tr>
</tbody>
</table>

*Significant difference

Coffee Intake and Risk of Myocardial Infarction
Coffee, CYP1A2 Genotype, and Risk of Myocardial Infarction

Marilyn C. Cornelis, BSc; Ahmed El-Sohemy, PhD; Edmond K. Kabagambe, PhD; et al

Article Information

Gene that could make your next coffee your last

New research suggests that some people cannot process caffeine as quickly as others and may therefore be more vulnerable to a heart attack, Sam Lister reports.
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}

Palatini et al., J Hypertens 27: 1594-1601, 2009
Coffee Intake and Risk of Hypertension

Hazard Ratio

- Abstainers
- 1-3 cups/day
- ≥4 cups/day

CYP1A2 Genotype

Coffee Intake and Risk of Hypertension
DOI 10.1007/s10654-015-9990-z

CARDIOVASCULAR DISEASE

Association of coffee consumption and CYP1A2 polymorphism with risk of impaired fasting glucose in hypertensive patients

Paolo Palatini · Elisabetta Benetti · Lucio Mos · Guido Garavelli · Adriano Mazzer · Susanna Cozzio · Claudio Fania · Edoardo Casiglia
Weight Management

DO THESE GENES MAKE ME LOOK FAT?
Loss of fat mass after 2 years of low or high protein diet.
Effects of a High-Protein/Low-Carbohydrate Diet versus a Standard Hypocaloric Diet on Weight and Cardiovascular Risk Factors: Role of a Genetic Variation in the rs9939609 FTO Gene Variant

Daniel Antonio de Luis  Rocío Aller  Olatz Izaola  David Primo
Silvia Urdiales  Enrique Romero

FTO genotype, dietary protein intake, and body weight in a multiethnic population of young adults: a cross-sectional study

David C. Merritt*, Joseph Jamnik† and Ahmed El-Sohemy*
DNA-based dietary advice resulted in:
- greater understanding of recommendations
- greater interest in learning more
- greater motivation to change eating habits

Does genetic information influence behavior?

A randomized trial of genetic information for personalized nutrition

Daiva E. Nielsen · Ahmed El-Sohemy
Does genetic information influence behavior?

DNA-based dietary advice resulted in:
- greater compliance after 1 year

Disclosure of Genetic Information and Change in Dietary Intake: A Randomized Controlled Trial

Daiva E. Nielsen, Ahmed El-Sohemy

Published: November 14, 2014 • https://doi.org/10.1371/journal.pone.0112665
Provision of actionable advice more likely to result in health behavior change
Is DNA-based Dietary Advice Ready for Prime Time? Yes

- Scientific evidence is robust (for some markers)
- Independent of ethnic background
- Improved compliance (evidence from RCT)
- Information is actionable and “personalized”
- Increasing consumer awareness and demand
- More effective through HCPs, rather than DTC
personalized dietary advice vs public health recommendations
Nudge

Improving Decisions About Health, Wealth, and Happiness

“One of the few books . . . that fundamentally changes the way I think about the world.” —Steven D. Levitt, coauthor of FREAKONOMICS
The efficacy of nudge theory strategies in influencing adult dietary behaviour: a systematic review and meta-analysis

Anneliese Arno and Steve Thomas
Genetics may define diets of the future

Scientists look at how personalized nutrition could change how and what we eat

By Carrie Peyton Dahlberg
BEE STAFF WRITER

Deep in each person’s genetic code may lie the answers to which medicines can help them, which environmental toxins can kill them, and even which foods they should eat to live well.

The tantalizing prospect of personally tailored diets, dictated by our genetic makeup, drew hundreds of scientists and dietitians from around the world to UC Davis over the weekend for a conference on nutritional genomics.

The fast-growing field “will be huge,” said Jim Kaput, who next month will take over as head of the U.S. Food and Drug Administration’s division of personalized nutrition and medicine. “We are definitely not ready for it.”

In interviews, Kaput and other con...
HEALTH | YOUR HEALTH

Test Your Genes to Find Your Best Diet

Genetic testing can reveal what nutrients you’re missing and if you’re drinking too much coffee
“Positive health requires a knowledge of man’s primary constitution and of the powers of various foods, both those natural to them and those resulting from human skill.”

Hippocrates

480BC
Performance

Department of Nutritional Sciences
Faculty of Medicine
University of Toronto

NANCI Guest, PhD, RD, CSCS
The Assembly Line…
Going for Gold?
#Personalize
Nutrition plans need to be personalized to the individual athlete to take into account the specificity and uniqueness of the event, performance goals, practical challenges, food preferences, and responses to various strategies.
Sport Nutrigenomics: Personalized Nutrition for Athletic Performance

Nanci S. Guest, Justine Horne, Shelley M. Vanderhout, and Ahmed El-Sohemy

1 Department of Nutritional Sciences, University of Toronto, Toronto, ON, Canada; 2 Nutrigenomix Inc., Toronto, ON, Canada; 3 Department of Health and Rehabilitation Sciences, University of Western Ontario, London, ON, Canada

Exposure

Nutrient → SNP

Genotype 1

Genotype 2

Genotype 3

Health or Performance Response

Improve

No Effect

Impair

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Genes Encode All *Endogenous Proteins*

If...

Variation = change in nutritional biochemistry

= changes in nutritional *requirements*
Genetic Modifiers of Caffeine and Endurance Performance in Athletes
Research Gap

- Inconsistent study results
- Differences in response
- Genetic variation?
Hypothesis

Genetic variation in caffeine metabolism modifies the ergogenic effects of caffeine in athletes
Adenosine accumulates while you’re awake… zzzz

Caffeine **BLOCKS** Adenosine & **STIMULATES** you

**ADRENALINE**

**SEROTONIN & DOPAMINE**

Technically, the only two things you enjoy
Caffeine and the CNS - Ergogenic Activity

- During exercise
  - ↑ energy, ↑ HR, ↑ arousal
  - ↑ pain threshold (brain → muscle)
  - ↓ RPE (brain → muscle)
“Some individuals had a significantly... It’s probably due to genetics”

- HIIT
- High/Low Volume Training
- LCHF / performance
- High Protein / MPS
- Beetroot
- Creatine
- Caffeine
No effect of caffeine on exercise performance in high ambient temperature

Bart Roelands · Luk Buyse · Frank Pauwels · Frans Delbeke · Koen Deventer · Romain Meeusen

8 subjects:
4 improved with CAF ✓
4 no improvement ✗

the ergogenic effects of caffeine. However, other factors such as interindividual differences in response to caffeine and changes in neurotransmitter concentrations might also be responsible for the lack of performance improvement of caffeine in high ambient temperature.
10 km Cycling Time Trial: Placebo vs Caffeine

© 2019 Nanci Guest
10 km Cycling Time Trial: Placebo vs 4 mg Caffeine

- Improved
- No change (<12 sec; <1%)

Caffeine Dose / kg

© 2019 Nanci Guest
10 km Cycling Time Trial: Placebo vs 4 mg Caffeine

© 2019 Nanci Guest
Caffeine, CYP1A2 Genotype, and Endurance Performance in Athletes

NANCY GUEST, PAUL COREY, JASON VESCOVI, and AHMED EL-SOHEMY

1Department of Nutritional Sciences, Faculty of Medicine, University of Toronto, Toronto, Ontario, CANADA; 2Department of Statistical Sciences, Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario, CANADA; and 3Faculty of Kinesiology and Physical Education, University of Toronto, Toronto, Ontario, CANADA
PHYS ED
Can Coffee Rev Up Your Workout? It May Depend on Your Genes

Why Caffeine Might Not Make You Faster

Alex Hutchinson
Mar 16, 2018
Do our genes modify the response to caffeine associated with athletic performance?

Caffeine → Athletic Performance

CYP1A2

Genotype 1 → Faster?
Genotype 2 → No Effect
Genotype 3 → Slower?
Study Population

- 113 Male Athletes
- Pro, national, varsity, club
- All sports, as long as competing
  Hockey, Basketball, Snow board / Ski, Volleyball, Swimming, Field Hockey, Track & Field, Boxing, Soccer, Rugby, Marathon/Triathlon, CrossFit, Ultimate, Dragonboat
Objectives

1. Determine if 2 or 4 mg/kg caffeine affects
   a) power
   b) strength
   c) anaerobic capacity
   d) aerobic capacity

2. To determine whether genes that affect caffeine metabolism or response modify the performance-enhancing effects of caffeine
Objective 1:

Determine the effects of 2 and 4 mg/kg caffeine on aerobic endurance performance
Difference in Cycling Time: 4 vs 0 mg/kg

N=101
Objective 2:

To determine whether variation in $\text{CYP1A2} (\text{rs762551})$ modifies endurance performance
Average 10-km cycling time by caffeine dose and CYP1A2 genotype

At 4- vs 0 mg = AAs: **1.2 min FASTER** & CCs: **2.5 min SLOWER**

*2 mg and **4 mg/kg CAF trials sig diff from placebo (p = 0.0004; p = 0.001)

\( p \)-values generated from an adjusted model.

Guest et al., Med Sci Sport Exerc 50: 1570-78, 2018
Difference in Cycling Time: 0 vs 4 mg/kg

N=101

CYP1A2 genotype
- AA
- AC
- CC

Guest et al., Med Sci Sport Exerc 50: 1570-78, 2018

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Objective 3:

To determine whether variation in XXX modifies endurance performance
Average 10-km cycling time by CAF dose & XXX genotype

*2 mg/kg and **4 mg/kg CAF trials significantly different from placebo (p¹ = 0.0004; p = 0.001)

¹p-values were generated from an adjusted model.
**A)** CYP1A2 AA genotype (fast metabolizers)

*2 mg/kg and **4 mg/kg caffeine trials sig diff than placebo (*p = 0.0002; **p = <0.0001, respectively)*

**B)** CYP1A2 AC/CC genotype (slow metabolizers)

No differences in cycling time within or between genotypes

*p-values generated from an adjusted model*
Difference in Cycling Time 0 vs 4 mg/kg in XXX genotype

n = 101
Difference in Cycling Time: 4 vs 0 mg/kg XXX genotypes in CYP1A2 fast metabolizers

$n = 49$

CCs: 0 vs 4 mg; $p = <0.0001$
Summary

- Caffeine at 4 mg/kg vs 0 mg improves 10-km cycling performance by ~3%.

- Caffeine-gene interactions.
Caffeine → CYP1A2

- **FAST**
- **SLOW**

Endurance Performance

- **Faster**
- **No Effect**
- **or Slower**

Summary Continued
Implications

- Personalized nutrition / supplementation
- Improve dietary compliance with genetic testing
- This approach can be applied to other ergogenic aids in the field of sports nutrition
What else is affected by your genes?

- Vitamin A, C, D
- Calcium
- Iron
- Folate
- Sodium
- Choline
- Magnesium
- Caffeine
- Choline
- Saturated fats
- Omega-3 fats
- Protein
- Starch Digestion
- Gluten
- Lactose
- Salt craving, Sweet craving
- Excessive Snacking
- Metabolism
- Bone health

Learn how your genes can affect:

- Recovery
- Injury risk
- Motivation
- Metabolism
- Mental focus
- Eating habits
- Pain tolerance
- Aerobic capacity
- Food intolerances
- Body composition
- Nutrient requirements
- Exercise performance

Unleash Your Genetic Potential

- Body Composition
- Cardio-Metabolic Health
- Eating Habits
- Injury Risk
- Nutrient Requirements
- Food Intolerances

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