We assume people are average.

But we should assume that there are groups that differ in requirements.

People have different microbes in their gut (microbiome).

These microbes see food often before we do and metabolize it.

Epigenetics

Marks on genes that “retune” metabolism.

GENETIC VARIATION

Many of us have variations in our genetic code.

SNPs are mistakes that occur in at least 1% of the population.

It is estimated that each of us has 50,000 such gene mistakes.
MICROBIOME, EPIGENETICS OR SNPS CAN RESULT IN INEFFICIENT METABOLISM

Nutrient → Metabolism → Metabolite

MUST ALSO HAVE DIET INFO TO ID NUTRITIONALLY RELEVANT MODULATORS

Nutrient → Metabolism → Metabolite

MICROBIOME, EPIGENETICS OR SNP

Precision Nutrition
The catalog of SNPs, epigenetic marks and microbiomes that change nutrient requirements will be the basis for practicing precision nutrition.

Precision Medicine
Genetic test now required before treating a patient with the blood thinner Warfarin.

Personalized dosing based on a gene test is needed so that you aren’t over- or under-dosed.

Precision Nutrition
Also important for diminishing variability in nutrition research – Responders vs. nonresponders

HOW WILL PRECISION NUTRITION WORK?

From: www.sidra.org/
Predicting roadblocks in metabolism using genetic testing and then providing individualized nutrition advice.

Gene variants can predict whether you drink > 4 cups of coffee and get a “buzz” when you drink coffee.

<table>
<thead>
<tr>
<th>Gene/SNP</th>
<th>Allele “spelling”</th>
<th>Africans</th>
<th>Asians</th>
<th>Caucasians</th>
</tr>
</thead>
<tbody>
<tr>
<td>CYP1A2</td>
<td>T &gt;4 cups</td>
<td>2%</td>
<td>0%</td>
<td>23%</td>
</tr>
<tr>
<td></td>
<td>C</td>
<td>98%</td>
<td>100%</td>
<td>77%</td>
</tr>
<tr>
<td>AHR</td>
<td>T &gt;4 cups</td>
<td>53%</td>
<td>63%</td>
<td>37%</td>
</tr>
<tr>
<td></td>
<td>C</td>
<td>44%</td>
<td>37%</td>
<td>63%</td>
</tr>
<tr>
<td>ADORA2A</td>
<td>T sensitive</td>
<td>66%</td>
<td>44%</td>
<td>39%</td>
</tr>
<tr>
<td></td>
<td>C</td>
<td>34%</td>
<td>51%</td>
<td>61%</td>
</tr>
</tbody>
</table>

Heart attack and hypertension more likely if you are a slow metabolizer of caffeine and drink >4 cups/day. Fast metabolizers are not at risk.

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<th>Asians</th>
<th>Caucasians</th>
</tr>
</thead>
<tbody>
<tr>
<td>CYP1A2</td>
<td>A fast</td>
<td>56%</td>
<td>44%</td>
<td>67%</td>
</tr>
<tr>
<td></td>
<td>C slow</td>
<td>44%</td>
<td>56%</td>
<td>33%</td>
</tr>
<tr>
<td>GSTM1</td>
<td>null</td>
<td>56%</td>
<td>44%</td>
<td>67%</td>
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</table>

People with MTHFR SNPs need 10% more folate

<table>
<thead>
<tr>
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<th>Asians</th>
<th>Caucasians</th>
</tr>
</thead>
<tbody>
<tr>
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<td>44%</td>
<td>41%</td>
<td>15%</td>
</tr>
<tr>
<td></td>
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<td>56%</td>
<td>59%</td>
<td>85%</td>
</tr>
<tr>
<td>n1801131</td>
<td>T</td>
<td>40%</td>
<td>41%</td>
<td>13%</td>
</tr>
<tr>
<td></td>
<td>C</td>
<td>60%</td>
<td>59%</td>
<td>87%</td>
</tr>
</tbody>
</table>

Genotype and vitamin C

GSTs are a family of phase 2 enzymes that detoxify both naturally occurring and xenobiotic compounds by catalyzing the transfer and conjugation of glutathione to the molecule.

GSTM1 gene is deleted in ~50% of the human population.

The concentration of serum vitamin C is higher in GSTM1-0 genotype.
The fat mass and obesity-associated gene (FTO) identified in GWAS as increasing risk for obesity.

FTO polymorphisms effect on BMI risk is dependent on SFA

GOLDN study Rs9939609 17% AA
BPRHS study Rs1121980 16% TT

ID people with metabolic bottlenecks due to SNPs and develop Rx to bypass problems

Nutrient → Metabolite
Nutrient → SNP signature → Medical food

Precision Nutrition
Medical Food formulated based on genetic roadblocks identified – provides specific nutrients (metabolites) needed to bypass metabolic roadblocks

People with health problem (e.g., fatty liver) → Test → No genetic roadblock → Medical Food Rx → Resolved health problem (e.g., fatty liver) → No genetic roadblock

Fatty liver occurs in many people when they become overweight or obese (75-100 million people in US).
Fatty Liver

Calories → Export fat to tissues → Store fat in liver

Characteristic gene signature in pathways that mediate export of fat.

NAFLD PREDICTED BY SNP SIGNATURE

20 genes in 1-carbon, FA transport, FA synthesis pathways

SNPs and SPERM DYSFUNCTION

Deletion of Chdh results in poorly motile sperm

Deletion of Chdh results in dysmorphic mitochondria

Deletion of Chdh results in low ATP
Betaine restores ATP

Betaine restores ATP from FASEB Journal 24: 2752–2761, 2010

Men with CHDH rs12676 G233T

CHDH rs12676 G233T have dysmorphic mitochondria

CHDH rs12676 G233T have low ATP

NUTRITION CLINICAL STUDIES NEED TO BE ENHANCED BY NUTRIGENETICS

- Young women half need to eat choline, half don’t. Mixed together – large variation in data.
- Fatty liver versus muscle damage response to low choline. Mixed together – confusing.
- Sperm dysfunction in men.

CHDH rs12676 G233T

CHDH G>T

rs12676

Need more choline

Mexico

Asia

Africa

Europe

GG

GT

TT

Choline

Betaine

Young women

Half need to eat choline, half don’t.

Mixed together – large variation in data.

Fatty liver versus muscle damage response to low choline.

Mixed together – confusing.

Sperm dysfunction in men.
NGx studies can identify people with different requirements for a nutrient.

Precision Nutrition
Also important for diminishing variability in nutrition research – Responders vs. nonresponders.

NUTRITION RESEARCH CAN BE ENHANCED BY NUTRIGENETICS
When a nutrition intervention seems to identify a subset of responders:
• Identify genetic variants in responders and nonresponders.
• Helps reduce noise in study.
• Foundation of precision nutrition.

NUTRITION CLINICAL STUDIES NEED TO BE ENHANCED BY NUTRIGENETICS
• Young women half need to eat choline, half don’t. Mixed together – large variation in data.
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• Sperm dysfunction in men.

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