Epigenetics

Kenneth R. Pelletier, MD, PhD, clinical professor of medicine, University of California School of Medicine, US
Epigenetics Era

• Health Biomarkers vs Disease Prediction
• Genomics
  – Study of the *entire* genome
    (Sequencing, Mapping & Interactions)
• Epigenomics
  – Study of post-translational genetics modifications
• Metabolomics (Genetic Expression)
  – Study of the complete set of metabolites or small molecules
    (Metabolic Intermediates, Byproducts, Hormones, Signaling Compounds) present in a cell or organism
• Microbiome: Study of all the microbes in and on a person
GENETICS
This is how it works
Epigenetics: A Tripartite Assay
"Bad news, its curiosity"
SNPs act as a rheostat to express or suppress genetic predisposition

Genetic Variation: central to personalized medicine

SNPs influence by diet/nutrition, stress/meditation, radiation, physical and psychosocial environment, Rxs, and sense of purpose

>3 million SNPs identified

Estimated potential 10+ million SNPs in the human genome

SNPedia: 83,452 reference SNPs
“You don’t look anything like the long haired, skinny kid I married 25 years ago. I need a DNA sample to make sure it’s still you.”
A Tripartite Assay Pilot Study

Stool Microbiome, Pathogens, and Infectious Agents Among Olympic, Elite Athletes, and Extremely Healthy Adults

DESIGN and PURPOSE:

Olympic athletes, non-Olympic elite athletes, and other extremely healthy adults may have genetic and metabolic profiles that are unique. These profiles may contribute to the caliber of their performance, and they may provide keys to understanding select genetic and metabolic conditions.

For further details contact:

Dan McEvoy, President – Thorne/WellnessFX
dmcevoy@thorne.com
(917) 859-2505
What Do We Test?

Genetics

• Whole genome base mapping using next generation sequencing technology
• SNP based and whole gene based analytics

Blood

• More than 100 key blood biomarkers covering all key health and wellness problems

Microbiome

• Genome sequencing based microbiome and metabolomics analysis for up to 300 key biomarkers
Genetic biomarker selection criteria:

1. Gene biomarkers are stable from one time of testing to the next by the same laboratory. Genes are stable unless there is a specific intervention that alters them;

2. Changes can be made in the expression of these genes by actionable, modifiable, self care lifestyle interventions;

3. Changes can be detected in a maximum time frame of 10-12 weeks although many change in a matter of hours or days; and

4. Are commercially available.
<table>
<thead>
<tr>
<th>Pillar</th>
<th>Description</th>
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<tbody>
<tr>
<td><strong>Methylation</strong></td>
<td>Methyl (CH3) molecules with genes on and off to govern DNA expression</td>
</tr>
<tr>
<td><strong>Inflammation</strong></td>
<td>Acute vs. chronic and destructive</td>
</tr>
<tr>
<td><strong>Oxidative Stress</strong></td>
<td>Excessive oxidation (PON1 and SOD2)</td>
</tr>
<tr>
<td><strong>Detoxification</strong></td>
<td>Phase one and Phase two breakdown and excretion of toxins</td>
</tr>
<tr>
<td><strong>Immunity</strong></td>
<td>Differentiate self from not self with hypo- and hyper-immunity</td>
</tr>
<tr>
<td><strong>Lipid Metabolism</strong></td>
<td>Genetic expressions govern optimal lipid metabolism</td>
</tr>
<tr>
<td><strong>Mineral Metabolism</strong></td>
<td>Govern metabolism of nutrients and trace element from whole foods</td>
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</tbody>
</table>
“Eat less, exercise more and invent a time machine so you can go back and choose parents with better genetics.”
DATA ANALYTICS: GENETICS, BLOOD, AND MICROBIOME

Type 2 Diabetes

Enterobacteriaceae
Ruminococcaceae

PPAR-R
Gene GC, rs2282679 presence

Vitamin D
Fasting Blood Glucose
HbA1c

Microbiome

Blood

Genetics

There are certain known microbial signatures that are closely associated with a number of conditions. For example, inflammation is linked to conditions such as IBD. Lactose intolerance and gluten intolerance are also important considerations in certain health conditions. The microbiome, including the relative abundance and diversity of various bacterial phyla, can provide insights into the health status and potential underlying conditions.
Your cardiovascular system is made up of your heart and blood vessels, and is responsible for transporting oxygen, nutrients, hormones, and waste products throughout the body. A healthy cardiovascular system ensures a good balance of nutrients and optimal brain and body function.

**Basic Lipid Panel**

The basic lipid panel includes cholesterol levels (both the good HDL and the bad LDL and other non-HDL cholesterols), as well as triglycerides. Elevated levels of triglycerides or non-HDL cholesterol can increase your risk of cardiovascular disease, which can lead to heart attacks and strokes. Higher levels of artery-clearing HDL, however, can reduce this risk.

<table>
<thead>
<tr>
<th>Metric</th>
<th>Value</th>
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<tbody>
<tr>
<td><strong>Total Cholesterol</strong></td>
<td>184</td>
</tr>
<tr>
<td><strong>LDL</strong></td>
<td>92</td>
</tr>
<tr>
<td><strong>HDL</strong></td>
<td>68</td>
</tr>
<tr>
<td><strong>Triglycerides</strong></td>
<td>111</td>
</tr>
<tr>
<td><strong>Total to HDL Ratio</strong></td>
<td>2.7</td>
</tr>
<tr>
<td><strong>Triglycerides to HDL</strong></td>
<td>1.6</td>
</tr>
</tbody>
</table>

**LDL Particles**

Higher levels of LDL or “bad” cholesterol can result in increased amounts of plaque in your blood vessels, which can obstruct blood and oxygen flow to vital organs. While almost half of those with heart attacks have normal basic lipid panels, two-thirds of heart-attack victims have elevations in other types of LDL particles. By reducing those deeper LDL numbers, you can reduce your risk of a heart attack and stroke.

<table>
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<tr>
<td><strong>Apo B</strong></td>
<td>64</td>
</tr>
<tr>
<td><strong>Lp(a) Mass</strong></td>
<td>32</td>
</tr>
<tr>
<td><strong>vLDL-C</strong></td>
<td>29</td>
</tr>
</tbody>
</table>
I DEMAND A DNA TEST!
There are about one trillion bacteria living in the GI tract, ten times higher than the total amount of cells composing the human body.
Pharmacy

“Don’t take these if you are nursing, pregnant, or about to become pregnant.”
System Summary

**Foundation 1**
Ingestion Sensor

*What it identifies*
• That a specific pill, tablet or other ingested product (or combination) was ingested.
• Composed and powered entirely from materials found in the daily diet.

**Foundation 2**
Wearable Sensor

*What it senses*
• Precise time & identity of ingestions.
• Certain physiologic responses and consumer behaviors over time.
  – HR, HRV, activity, sleep, temperature.
• Acts as communications hub between ingested product and phone.

**Foundation 3**
Mobile Applications

*What it influences*
• Consumer reported wellness metrics.
• Correlations between ingestion adherence, patch physiologic measures, and data from other telemetric devices.
• Enable collaboration with clinicians and caregivers.
Tracking Adherence Enables Carers to Identify Patients Who Need Help

**Good Adherer**
A patient who takes pills at the same time everyday. No Intervention needed.

**Poor Adherer**
A patient who skips pills some days and has inconsistent dosing time. Reminders or other interventions may be beneficial.
ACCESSIBLE, SIMPLE BLOOD COLLECTION, ANYWHERE

Virtually painless
No big needles

Simple to use
Can be self-administered

No cold chain required
Ease of shipping

Anywhere, Anytime Sampling
O Master, is it proper for a monk to use email?

Sure... as long as there are no attachments!
Epigenetics – What is Known

• Tripartate Assay: Genetic, Blood (CBC), and Microbiome
• Genes predict probabilities not certainties
• Biomarkers of health not disease prediction
• Applications of single gene = single disease is very limited
• Genes work within complex genetic and environmental matrices
• Human base is @ 21,000 genes – DNA for protein coding is only 5% of this entire genome = “Dark Genome”
• Genes are turned on or off like a rheostat - Epigenetics
• Gene expression changes – What we do matters
• Majority of genes governed by beliefs and lifestyle choices
• Neanderthal genes are alive and well – Stress Responses
That's all for now folks!
FOUR DISTINCT CLASSES
Genes - CBC

1. Genes with No Direct Molecular Correlate in Blood
2. Genes with Direct Molecular Correlates in Blood
3. Genes with Direct Pathway/Network Correlates in Blood
4. Genes with Clinical & Molecular Phenotype Correlates
Personalized Nutrition

- Founded in 2015 by Neil Grimmer with over $32 Million in funding by Campbell’s Soup
- Based on DNA, fasting blood, a metabolic challenge, and a food behavioral assessment
- “Challenge Shake” is high fat, high protein, high dairy, and high sugar designed to “challenge” your body
- Finger stick blood draws at baseline, 30 mins after drinking a “Challenge Shake”, and at 120 minutes
- Test results are converted into 7 recommended diets based on the bell curves generated in the course of your metabolism & a genetic assessment
- Ongoing R&D with EXOS, Blue Cross/Blue Shield, and a leading healthcare provider