Personal Data: Using Omics Profiling and Big Data to Manage Health and Disease

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Conflicts: Personalis, Genapsys, SensOmics
Precision Medicine is of High Interest

January 2015
Health Is a Product of Genome & Exposome

Genome

Exercise

Health

Disease

Pathogens

Food

Stress

- Food
- Genome
- Exercise
- Pathogens
- Stress
Drivers of Big Data

DNA Sequencing

Human Genome Cost <$2K

Mass Spectrometry

http://www.genome.gov/
Personal “Omics” Profiling (POP)

- Genome
- Epigenome
- Transcriptome
- Proteome
- Cytokines
- Metabolome
- Lipidomics
- Autoantibody-ome
- Microbiome (Gut, Urine, Nasal, Tongue, Skin)

Initially 40K Molecules/Measurements
Now Billions!
General Goals

1) Understand how individuals change over time and during periods of health and disease at high resolution

1) Understand how different “omes” (microbiome, metabolome, proteome, genome) relate to one another dynamically

1) Understand how individual responses are similar and differ from one another when faced with specific perturbations

2) Identify factors that can affect and help manage the health of an individual

Year 1

Viral infection

Year 2 …
Personal Omics Profile
~79 months; >200 Timepoints; 10 Viral Infections

Chen et al., Cell 2012, unpublished
Genome Sequence (Illumina, Complete Genomics)

Predict Type 2 Diabetes

Glucose levels

Rong Chen and Atul Butte

Glucose (mg/dL)

Day Number (Relative to 1st Infection)

HbA1c (%) (Day Number)

0% 100%

RSV

HRV

LIFESTYLE CHANGE

Previously known

* Previously known
Molecules and Biochemical Pathways that Change During Acquisition of Diabetes

Example pathway: Insulin Biosynthetic Pathway

Glucose Regulation of Insulin Secretion

Platelet Plug Formation

RSV 18 days
gorge mias
Epigenetics: DNA Methylation

- Affected by nutrition, lifestyle factors, aging, and environment
- Causes gene silencing

Map all the methylated sites using whole genome bisulfite sequencing
Gene Inactivation by Mutation and Methylation: PDE4 involved in eosinophilia

Father

Mother

Methylated CpGs

Inactivated by mutation

Inactivated by DNA Methylation

Few RNAs

Lots of RNA

PDE4 DIP Gene

T → C

Kim Kukurba
Your Microbiome is Important for Your Health

- We have 10 Trillion human cells, but 10X more bacteria
- Helps digest food you eat
- Makes essential vitamins, eg, B12
- Implicated in Inflammatory Bowel Disease (Crohn’s and ulcerative colitis), Diabetes, Obesity, MI
Personal Omics Profile
79 months; >200 Timepoints; 10 Viral Infections

Chen et al., Cell 2012, unpublished
Identifying the Microbe Causing Illness

Nasal microbes
---Top 25 most abundant microbial species

Fever Recovery

Streptococcus pneumoniae

Wenyu Zhou
George Weinstock
Gut microbiome temporal profiles

-- At the family level analyzed by RTG

43 Healthy

57 Fever

58 Recovery

58b Healthy

Wenyu Zhou, George Weinstock
Longitudinal Profiling of 100 individuals (Prediabetics & Healthy) over periods of health, stress and disease

Year 1
- Viral infection
- Stress
- Diet change

Year 2 ...

Cell Host & Microbiome 2014
>1300 collections thus far

Most Datasets are Open Access!
Genome Sequencing – First 48 People

• Eight have important mutations to know about
  • SHBD (2X): high freq. of paraganglioma
  • PROC: Affects coagulation
  • RBM20: cardiomyopathy
  • HNF1A: MODY mutation
  • SLC7A9: Cystinuria
  • ABCC8: Hyperinsulinemic hypoglycemia
  • MUTYH: Colon cancer

• All have carrier mutations and pharmacogenetic variants

Shannon Rego et al.

Personalis, Inc
A subset of individuals undergo a dietary perturbation.

24 participants:

- 13 Insulin resistant
- 11 healthy controls (BMI matched)

Brian Piening, Wenyu Zhou, Gucci Gu, Kevin Contrepois
Baseline gene expression differences between IR and IS in blood PBMCs

**Insulin Sensitive**

- Maturity Onset Diabetes of the Young (e.g. HHEX) $q<0.0001$
- Oxidative Phoshorylation (e.g. COX5A, COX5B) $q<0.0001$
- Ribosome (e.g. RPL9, RPS7) $q<0.0001$
- Defensins (e.g. CCR2, CCR6) $q<0.0001$
- Platelet-Specific Genes (e.g. CXCL5, PF4V1) $q<0.001$
- Olfactory Signaling (e.g. OR10AD1, OR1K1) $q<0.0001$
- FGFR Binding and Activation (e.g. FGFR1, KLB) $q<0.015$
- EGF Signaling (e.g. EGR2, EGR3, FOSL1, JUN) $q<0.017$

**Insulin Resistant**

- Oxidative Phosphorylation
- Ribosome
- Defensins
- Platelet-Specific Genes
- Olfactory Signaling
- FGFR Binding and Activation
- EGF Signaling

**test statistic**

-3 -2 -1 0 1 2 3
Metabolic differences between IR and IS

Univariate analysis: Wilcoxon t-test p-value < 0.05 and fold change > 1.5

**PLASMA**
(56 metabolites)

- **Metabolites**
- **Participants at T1**

**Indolelactic acid**

**PLASMA**

- Insulin sensitive (IS)
- Insulin resistant (IR)

R² = 0.509
p-value = 9.1E-5
Example data: Short-term weight gain

Weight gain
30 days
T1 baseline

Maintain peak weight
7 days
T2 peak

Weight loss
60 days
T3 post

Analytes with similar longitudinal expression changes

Cluster A

Cluster B

Cluster C

Functional enrichment
Positive Regulation of Innate Immune Response
FDR q-val=0.0003

mRNA
protein
Integrative c-means clustering: pattern recognition across RNA-seq, proteome, metabolome, microbiome, cytokines

Pattern 1: Up at peak weight then down

KEGG: Hypertrophic Cardiomyopathy (q<0.001)
Blood cytokine profiles: 20 subjects at baseline
Participants’ fecal 16s microbial profiles stratified by Gender

-- For all quarterly visits that had 16s profiling completed
Microbial abundance pattern group by individual, not by dietary supplement

-- Distance matrix by Manhattan methods and Hierarchical clustering by Ward method
Understanding effects at an individual level

Perturbation

Outcome
Sensors: Measure Many Things

- Qardio Blood Pressure Cuff
- Apple Watch
- Basis Peak
- Radtarge Radiation
- Dexcom Constant Glucose Monitor
- Withthings Smart Scale
- Scanadu Scout
- Autographer – Life Logger
- iHealth Pulse Ox
- Athos – Smart Shorts
Early Detection of Lyme Disease

Heart Rate

Skin Temp.

Skin Temp.
The Future?

Genomic Sequencing

1. Predict risk
2. Early Diagnose
3. Monitor
4. Treat

Omes & Sensors: Personal Device

Amanda Mills
Overall Summary

1) Personal genome sequencing is here. It can be used to predict disease risk and manage health

2) Multi-omics analyses are valuable for determining pathways and biochemical activities involved in human disease.

3) Longitudinal profiles are very valuable for understanding personal disease states

4) Everyone’s profile is different

5) Individuals will be responsible for their own health
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Genomics and Personalized Medicine

What Everyone Needs to Know®

Michael Snyder

Available from Amazon
Device to Measure Glucose Levels — Useful for Diabetics
Different Foods Cause Different Glucose Spikes