Mining Dense Dynamic Personal Data Clouds for Scientific Wellness

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Institute for Systems Biology
Seattle, WA

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Personalized Nutrition and Technology
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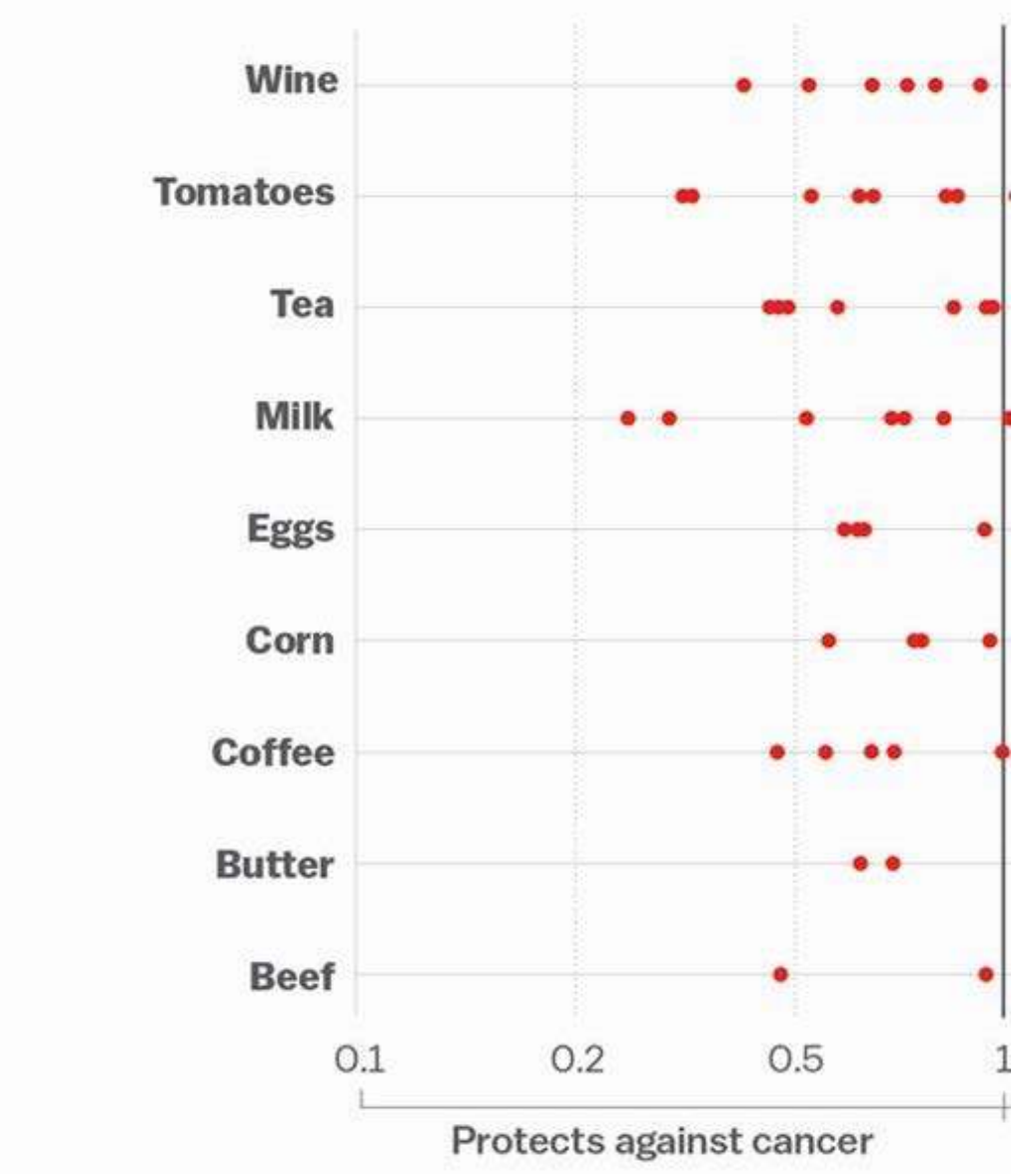
Disclosures

- Dr. Price is a Co-Founder of **Arivale**, a scientific wellness company that partially funded and may license discoveries resulting from the Hundred Person Wellness Project (to be described).

- Dr. Price is a Scientific Advisor to **Habit**, a new personalized nutrition company

Nutrition health effects…



Multiple studies demonstrate nutritional effects on disease risk

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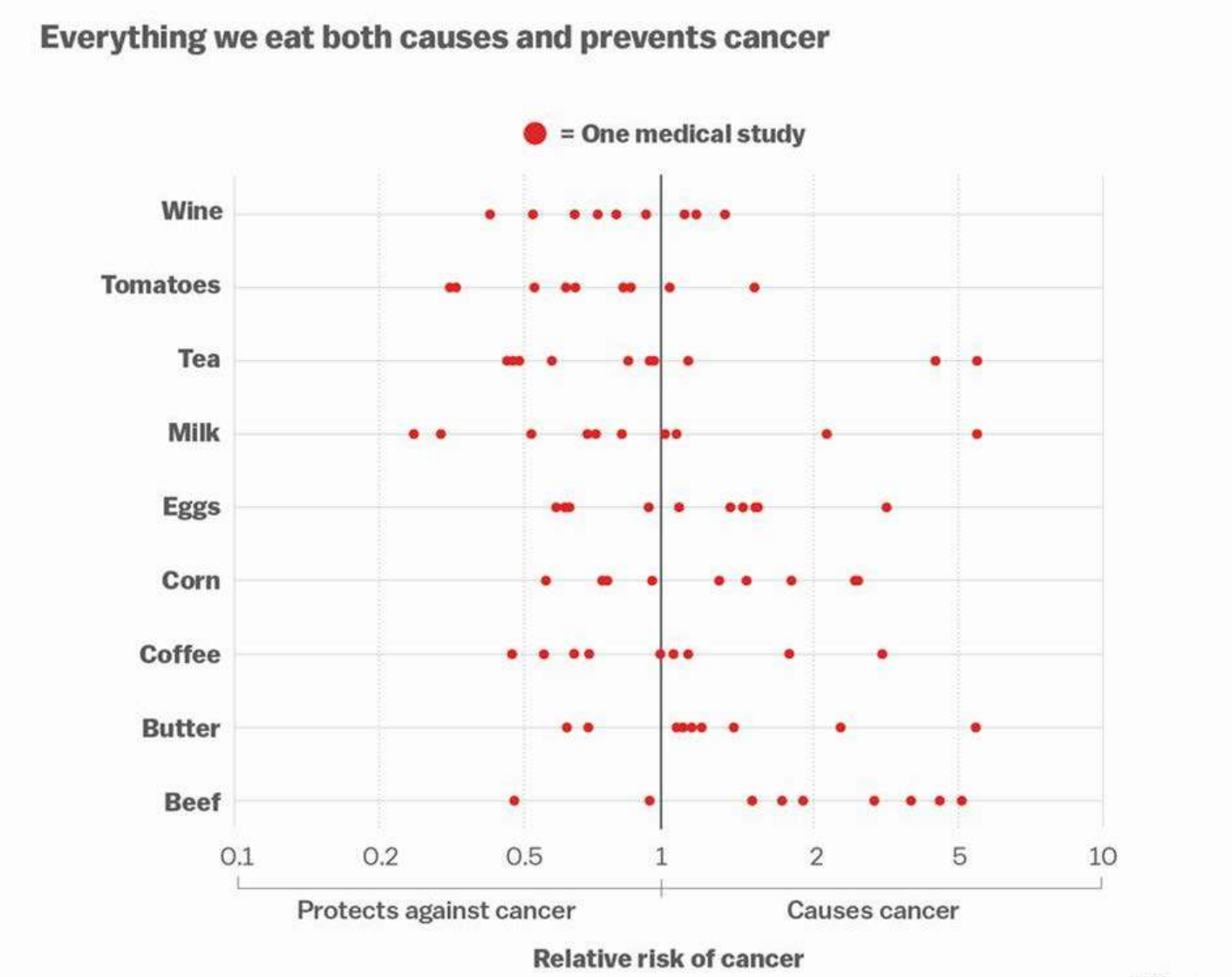
Nutrition health effects… are complex: Need context and personalization



Vox

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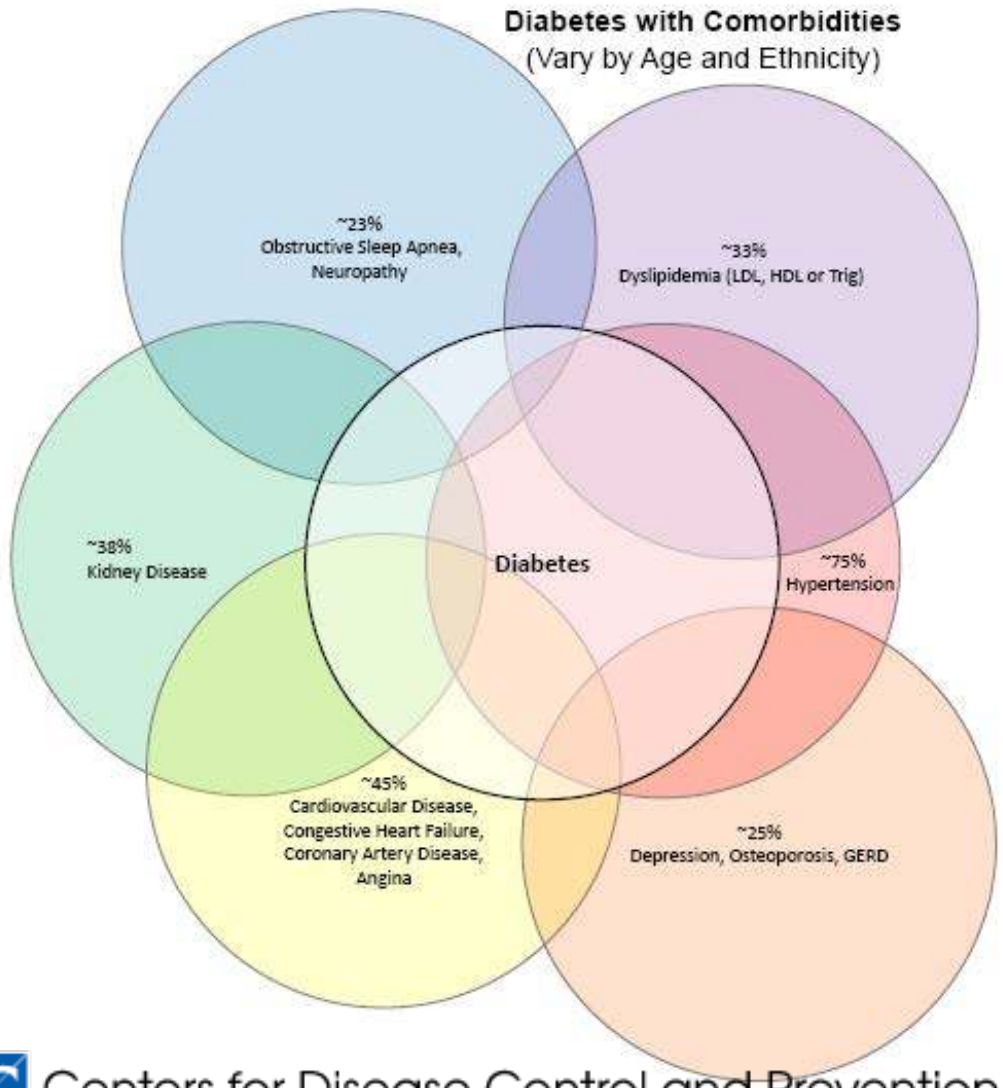
86% of Healthcare Costs Treat Chronic Disease

Chronic Diseases		Disease severity	Episodic or Steady state	Opportunities for DX Monitor	Cost Impact
Prevalence (Millions)	Direct Cost ($ Billions)				
Angina		High	Episodic	High	High
Anxiety disorders (social, etc.)		Medium	Episodic	High	High
Arthritis, Rheumatoid		High	Episodic	High	High
1.3 M	$12.4 B				
Asthma		Medium	Episodic	High	High
22.2 M	$14.7 B				
Atrial Fibrillation		Medium	Episodic	High	High
Chronic Kidney Disease		High	Steady Progression	High	High
26.0 M	$42.0 B				
Congestive Heart Failure		High	Steady Progression	High	High
5.3 M	$32.0 B				
COPD/Emphysema		High	Steady Progression	High	High
12.1 M	$26.7 B				
Coronary Artery Disease		High	Steady Progression	High	High
16.0 M	$87.6 B				
Depression		High	Episodic	High	High
18.1 M	$80.0 B				
Diabetes		High	Steady Progression	High	High
23.6 M	$116.0 B				
Gastroesophageal Reflux Disease (GERD)		Medium	Episodic	Medium	High
40.0 M	$9.6 B				
Hypertension		High	Steady Progression	Medium	High
73.0 M	$51.0 B				
Inflammatory Bowel Disease		High	Episodic	High	Medium
1.4 M	$18.8 B				
Lupus (SLE)		High	Episodic	High	High
1.5 M	$8.0 B				
Migraines		Medium	Episodic	High	High
Multiple Sclerosis		High	Episodic	High	Medium
Osteoarthritis		Medium	Episodic	High	High
Osteoporosis		High	Steady Progression	High	High
10.0 M	$14.0 B				
Stroke		High	Episodic	High	High
5.8 M	$43.7 B				

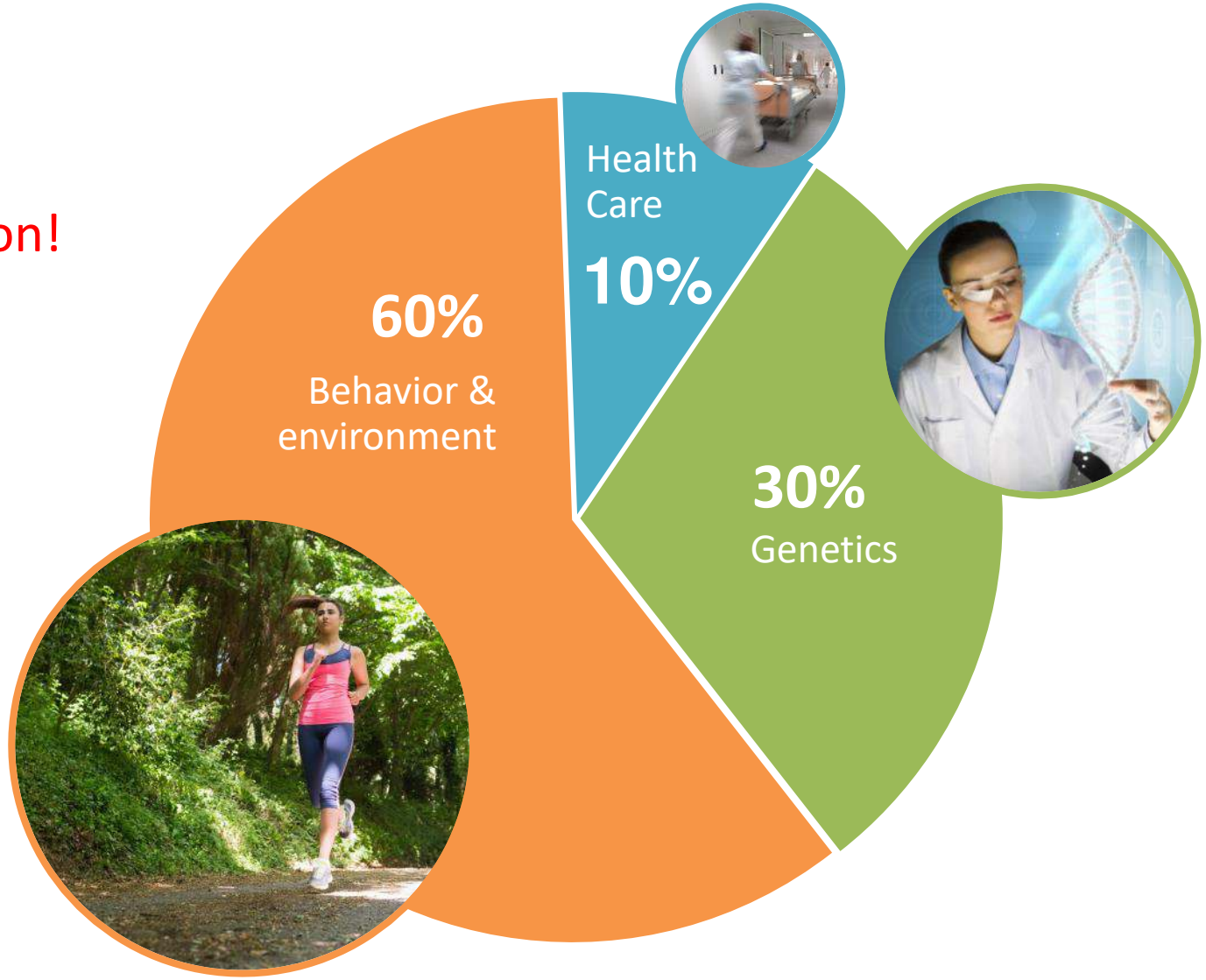
Top 20 examples of chronic diseases out of 91 studied by EAC.
Noted are 9 Chronic Diseases often seen as comorbidities of diabetes.



Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

Determinants of Health in U.S.

Nutrition!



Scientific Wellness → A New Industry

Wellness Industry

→

Scientific Wellness

↔

U.S. Healthcare Spending $3.8 Trillion (2014)

Proposing the 100K Wellness Project

Clinical OMICs INNOVATOR

Promoting Wellness & Demystifying Disease:
The 100K Project

Leroy Hood, M.D., Ph.D., and Nathan D. Price, Ph.D.

Hood and Price, *Clinical Omics*, (2014)

EDITORIAL

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L. Hood, N. D. Price, Demystifying disease, democratizing health care, *Sci. Transl. Med.* **6**, 225ed5 (2014).

SYSTEMS BIOLOGY

Demystifying Disease, Democratizing Health Care

UNSUSTAINABLE COST INCREASES THREATEN THE GLOBAL HEALTH CARE SYSTEM, and further progress is stymied more by societal than technological factors. Only by engaging health care consumers (that is, patients) as pioneers who provide both health-related data and insights into pathophysiology can we meet these societal challenges and thus accelerate the pace of biomedical innovation.

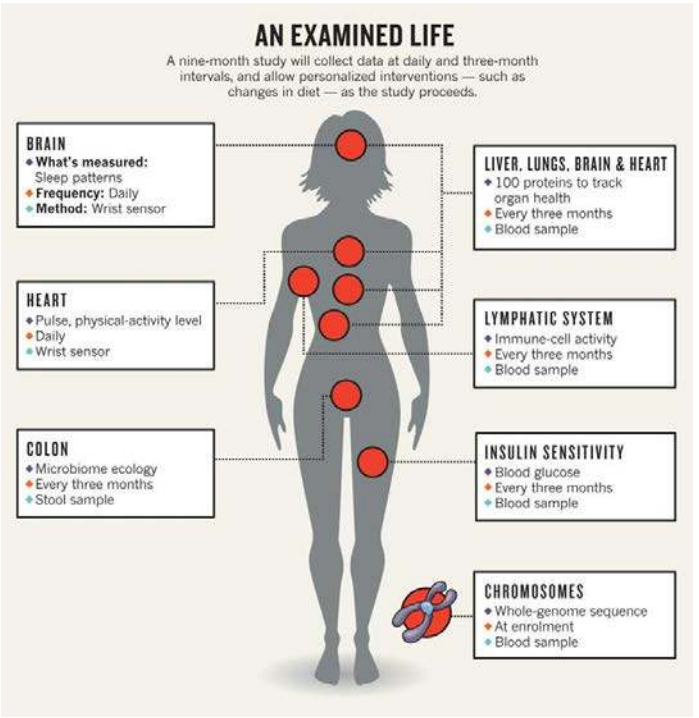
In March 2014, the Institute for Systems Biology will launch a longitudinal, Framingham-like study (www.framinghamheartstudy.org) of 100,000 (100K) healthy individuals that we believe will be instrumental in bringing predictive, preventive, personalized, and participatory (P4) medicine to patients. Participatory medicine means that patients, researchers, physicians, and the entire health care community join forces to transform the practice of medicine to make it more proactive than reactive—and, in turn, less expensive and more effective (*1*).

PEOPLE POWER

A systems approach is necessary for the effective management of complex diseases (*1*). This fundamental component of P4 medicine is built on two central features. The first is a conviction that, in 5 to 10 years, each patient will have a dynamic data cloud consisting of billions of diverse types of data points and that medicine will be informed by computational analyses that reduce high-dimensional data to actionable hypotheses designed with the intent of optimizing wellness and minimizing disease in individual patients. The second feature is that integration of patient data will reveal biological networks that specify health and are altered in disease, and that through an understanding of these differences, one can gain fundamental insights into disease mechanisms. Such insights are essential for developing more effective diagnostic and therapeutic approaches. Indeed, such an approach has already provided powerful new technologies and strategies (*2*) that have brought us to the brink of P4 medicine (*3*).

At its foundation, P4 medicine is about quantifying wellness and demystifying disease. Individual data clouds will let us predict future wellness and disease. The preventive element focuses on how well we can improve individual wellness and take actions to stop or de-

Nature, News piece, (2014)



Hood and Price, *Science Translational Medicine* (2014)

Scientific Wellness: Two Integrated Directions

Arivale

- A consumer facing scientific wellness company
- 5,000 individuals in the first 18 months
- Transform how biotech industry operates

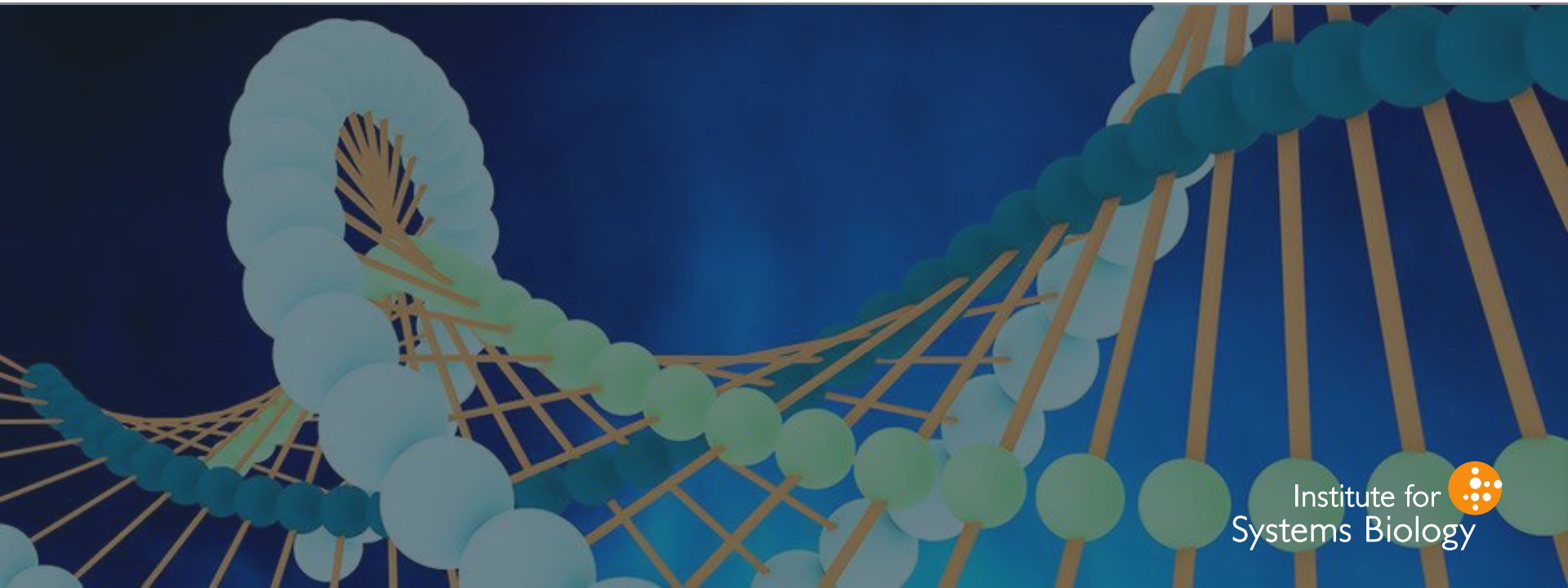
ISB-Providence

- Dense, dynamic, personal data clouds
- Research to validate wellness metrics
- Research for better assays
- Optimize wellness
- Study wellness to disease transitions
- Study disease [progression, response to therapy and transition to wellness

PIONEER 100 PROJECT

Principal Investigators: Lee Hood and Nathan Price

The 100K Wellness Project was initiated in 2014 with the generation of dynamic data clouds for 108 individuals. These data provided spectacular insights into what it is to be well and the nature of wellness to disease transitions (and vice versa).



Assays / Measurements—108 Pioneers

Creating dense and dynamic personal data clouds

GENOME

Whole Genome Sequencing.
SNPs Millions

LABS

Detailed lab tests 3x (blood, urine, saliva)
Clinical chem. 150
Metabolites 700
Proteins 400

Database of actionable possibilities that will grow over time

SELF-TRACKING

Continual self-tracking & lifestyle monitoring

MICROBIOME

Gut Microbiome 3x

Wellness coaching for participants

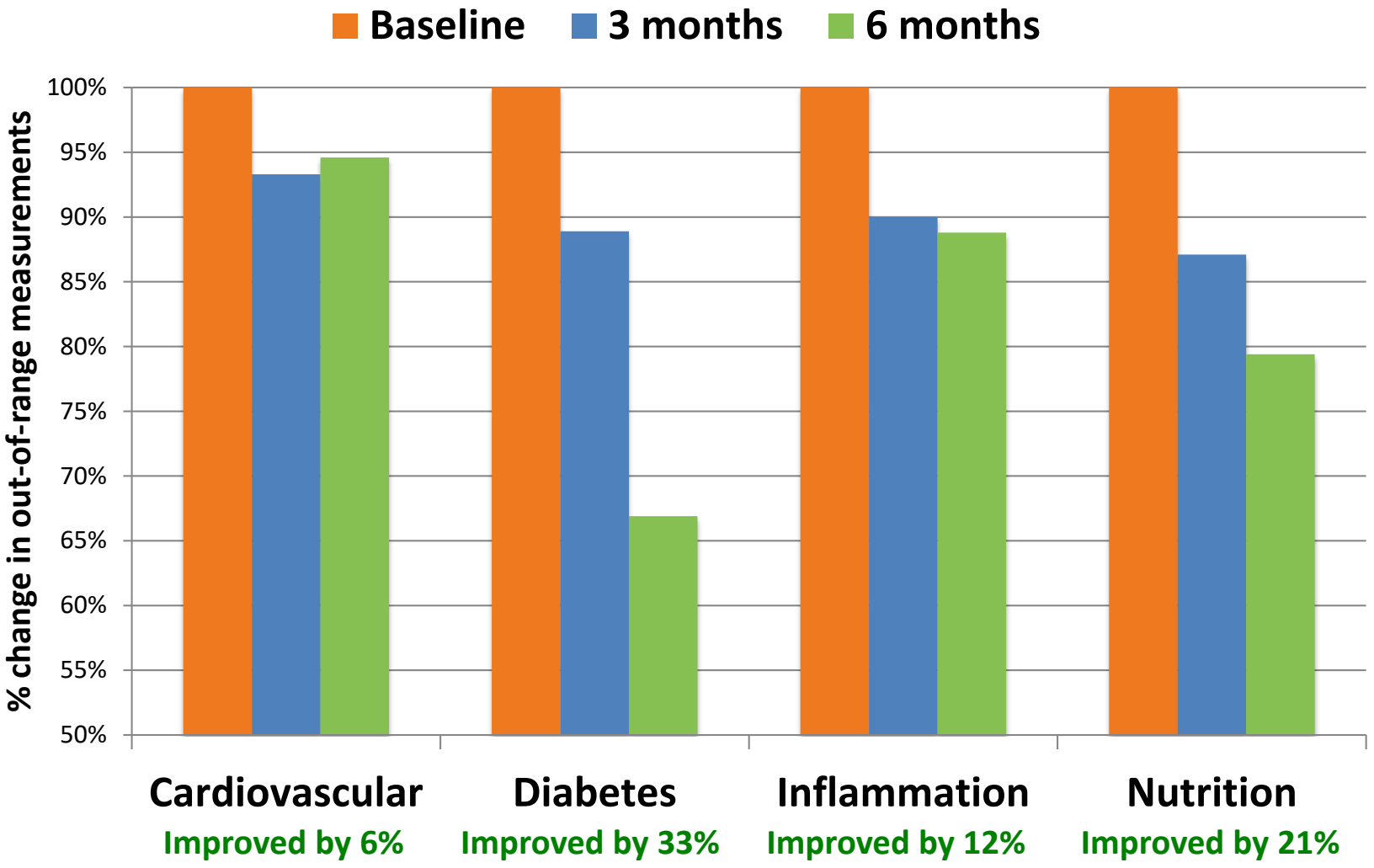
Wellness Coach

Sandi Kaplan, MS, RD

Study Physician

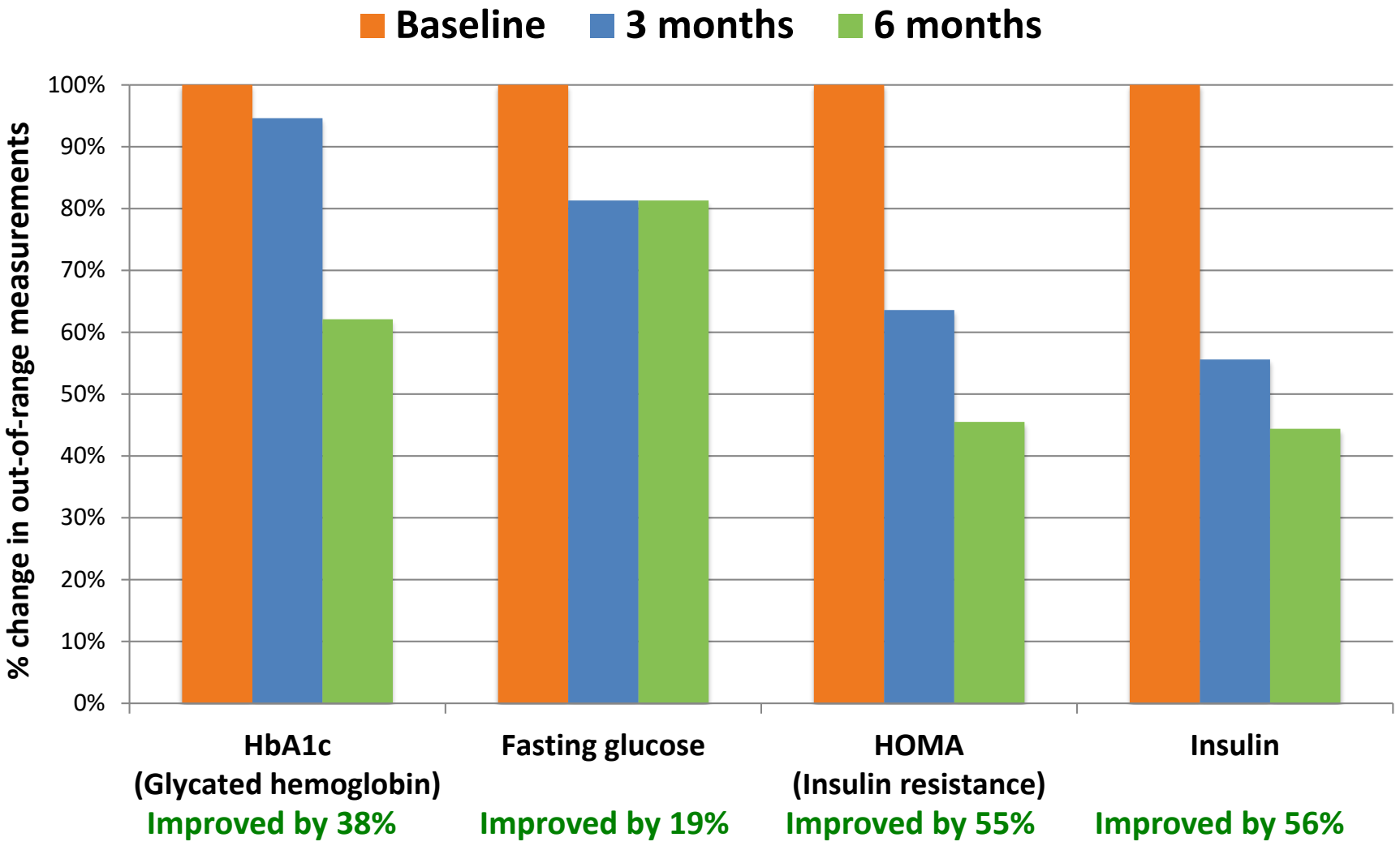
Craig Keebler, MD

Clinical Labs Discovery:
Improvements in blood health with behavioral coaching



Clinical Labs Discovery:
Significant pre-diabetes improvements

Seven participants with pre-diabetes were completely normalized in six months



Diet modification to reduce heavy metal toxicity

Toxic Elements

Element	Reference Range	Reference Range
Lead	0.027	<= 0.048 mcg/g
Mercury	0.0180	<= 0.0039 mcg/g
Antimony	0.002	<= 0.002 mcg/g
Arsenic	0.019	<= 0.071 mcg/g
Cadmium	0.000	<= 0.001 mcg/g
Tin	<dl	<= 0.0009 mcg/g

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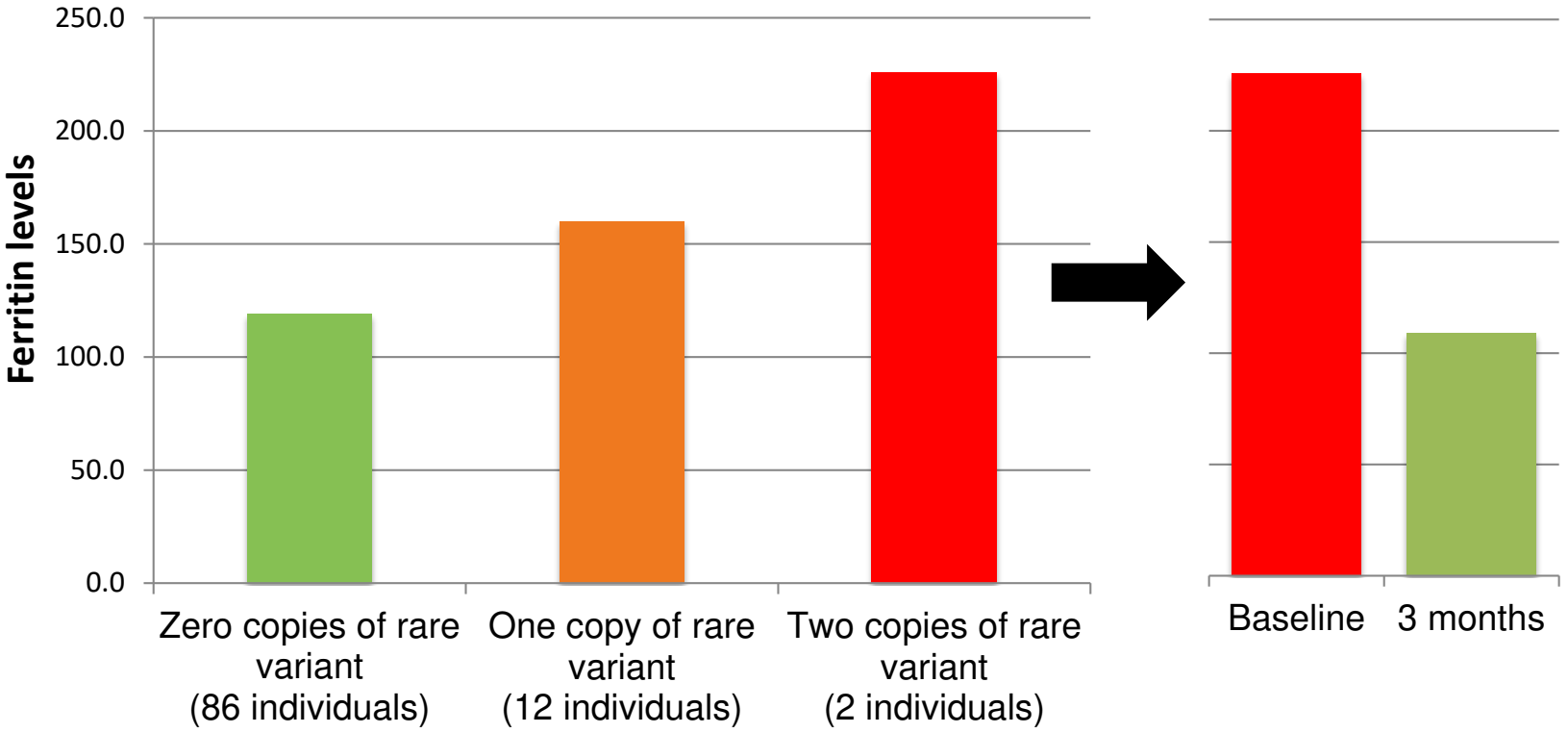
Tin	<dl	<= 0.0009 mcg/g

1. Baseline: High mercury levels in blood
2. Coached to modify diet
   - eight weeks of eating salmon sushi vs. tuna sushi (3x a week)
3. Reduced mercury levels in three months

A wellness to disease transition—genetics plus environment—an actionable possibility

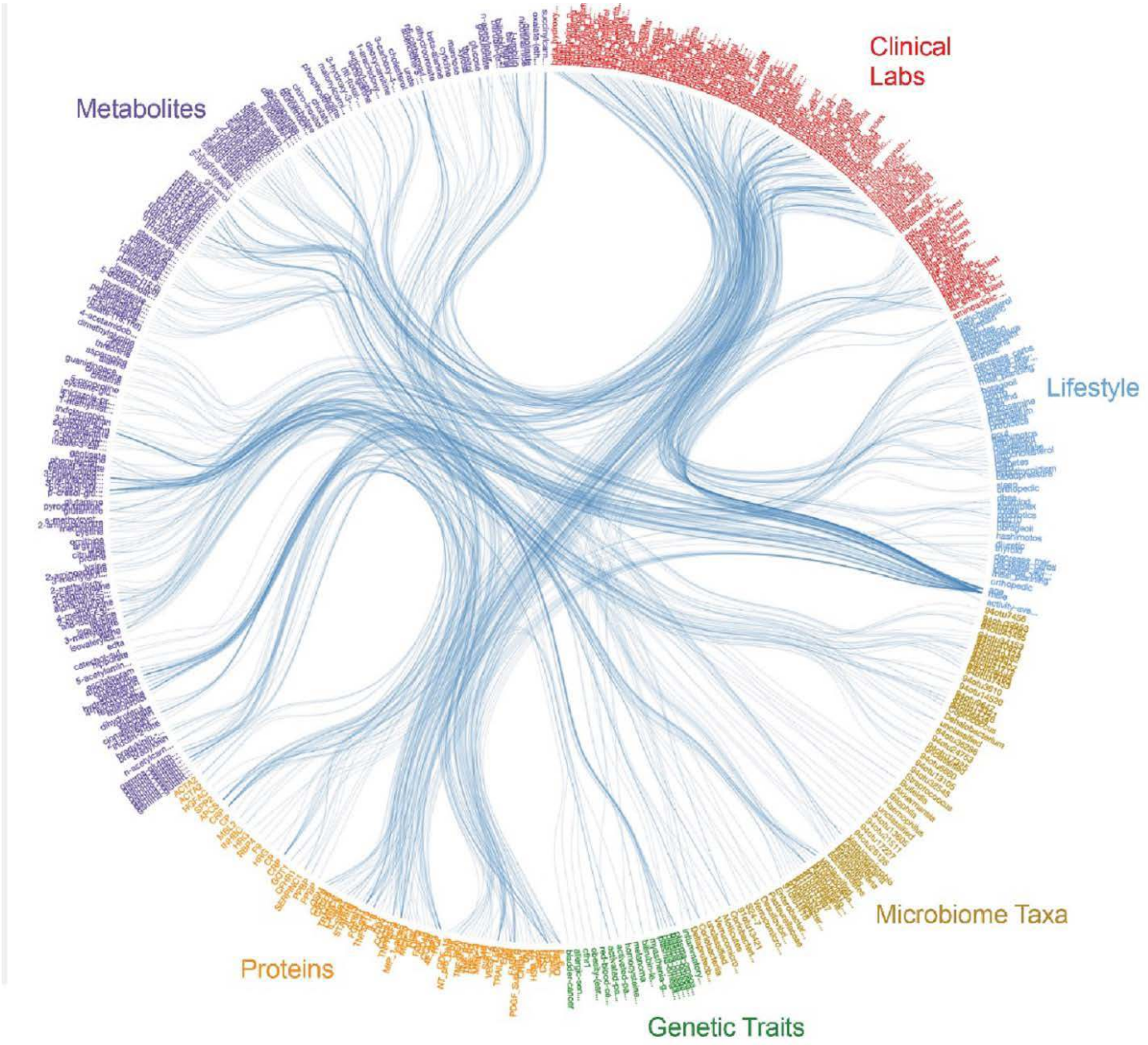
Genetics and Clinical Labs: Hemochromatosis

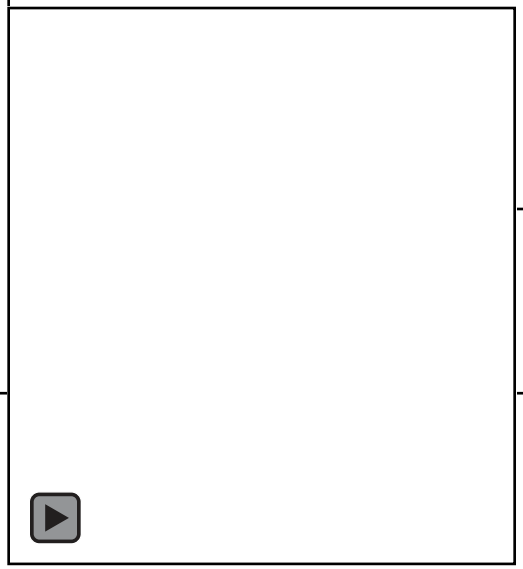
Detected risk of a deadly disease in two participants

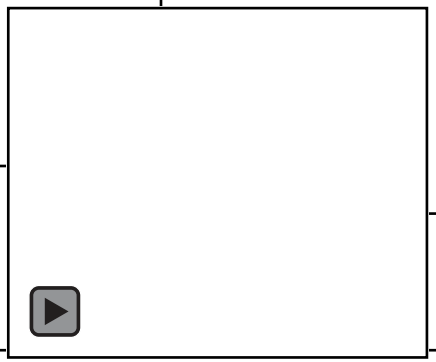


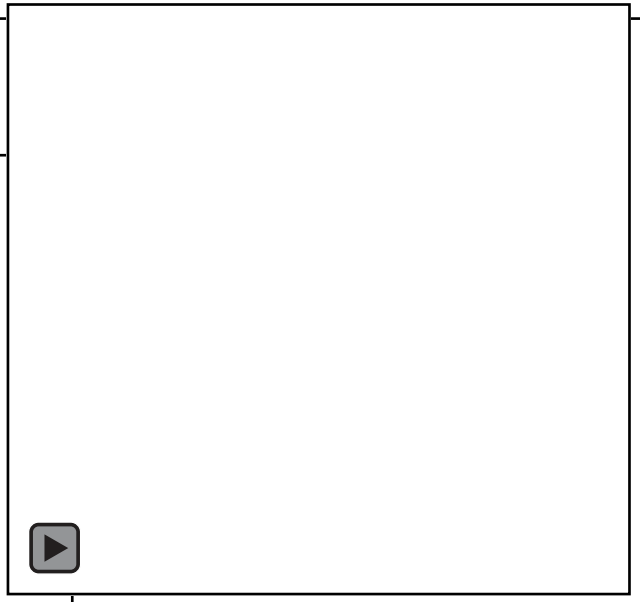
- Blood + Genetics illuminated the effects of increasing copies of the Hemochromatosis variant
- Left untreated, this disorder could lead to cartilage damage, liver cancer, diabetes, and heart disease: Easily treated by regular blood donations to reduce the iron stores
- One participant ALREADY had cartilage damage from his undiagnosed disease
- Subsequent family genetic testing detected other family members at risk

Deriving Insights from Data: New Frontiers

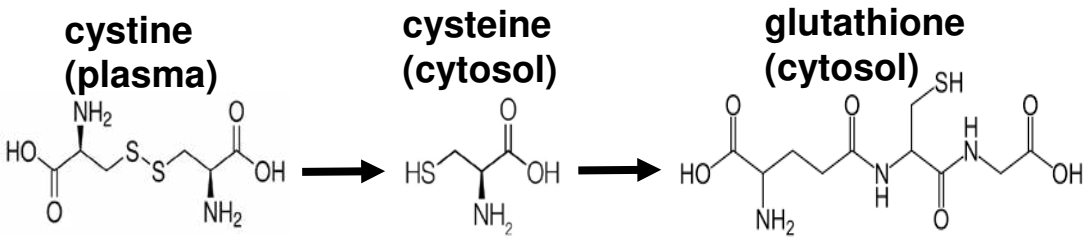




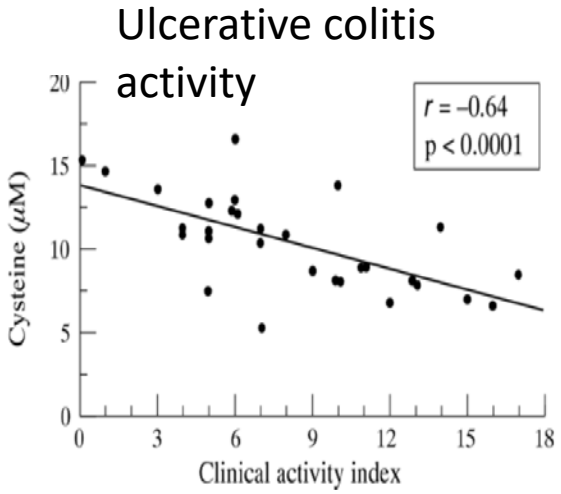


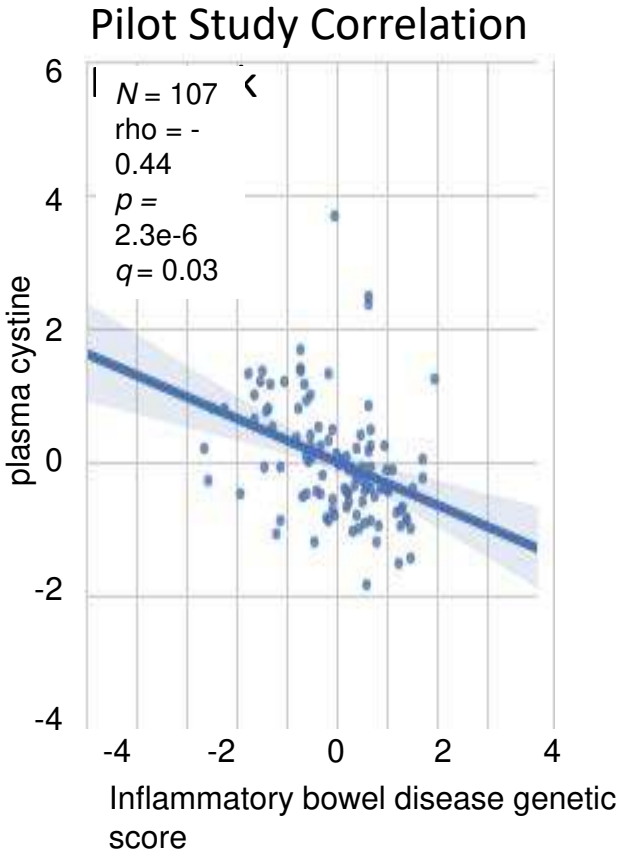


Nutrient measurements correlate with genetic predisposition for IBD



	Cystine
Control (n=65)	61.3 (1.7)
Crohn's disease (n=33)	
Before surgery	42.8 (2.4)***
10 days after surgery	56.0 (3.0)
3 months after surgery	52.7 (2.8)1-160
Ulcerative colitis (n=33)	
Before surgery	47.3 (1.8)***
10 days after surgery	64.3 (2.4)
3 months after surgery	64.5 (3.6)





Sido, B., Hack, V., Hochlehnert, A., Lipps, H., Herfarth, C., and Dröge, W. (1998). Impairment of intestinal glutathione synthesis in patients with inflammatory bowel disease. Gut *42*, 485–492.

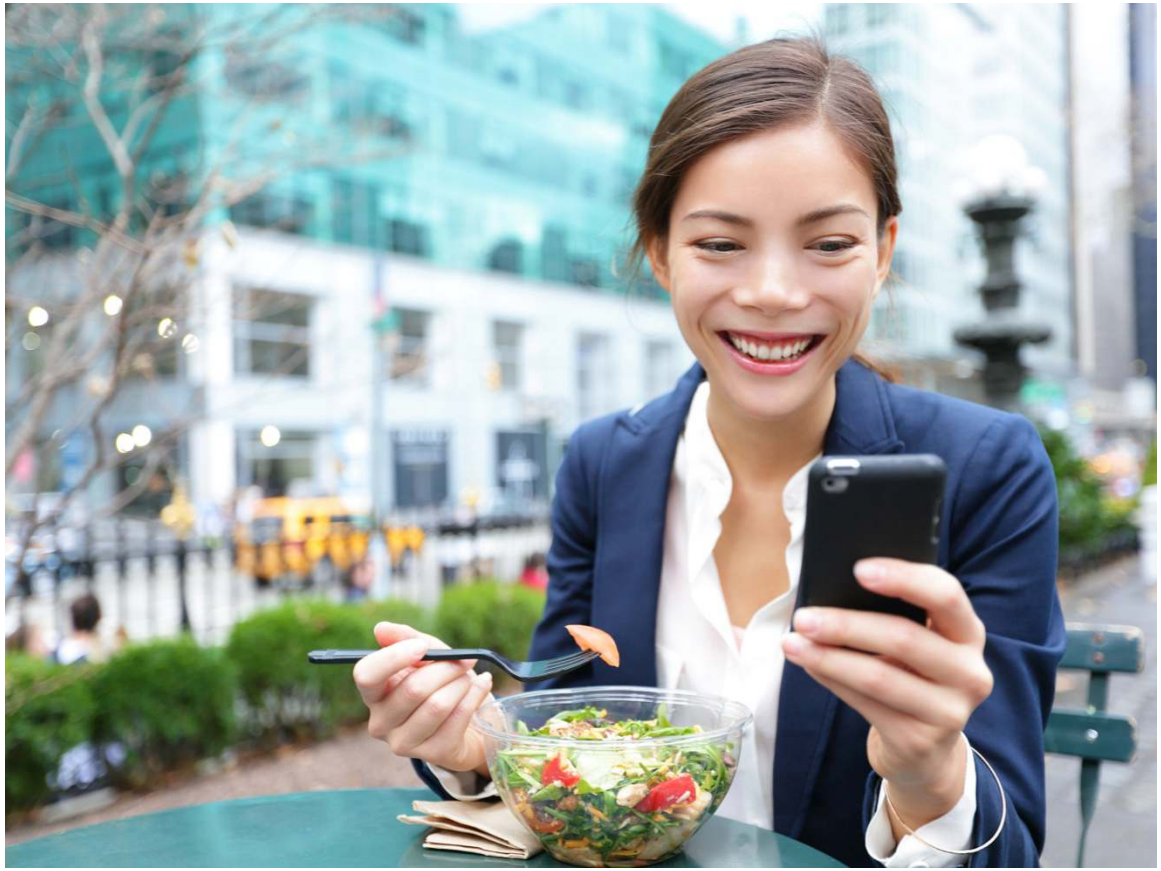
We can determine your genetic risk for at least 60 diseases.

Institute for Systems Biology

GWAS variants have been determined for about 60 diseases and traits

ADHD	COPD	Myopia
Alzheimer's disease	Crohn's disease	Obesity
Anorexia	Esophageal cancer	Osteoarthritis
Asthma	Gout	Osteoporosis
Atrial fibrillation	Grave's disease	Ovarian cancer
Breast cancer	Hematocrit	Pancreatic cancer
Bipolar disorder	Hypertension	Parkinson's disease
Blood pressure	Hypothyroidism	Primary biliary cirrhosis
Bone mineral density	Inflammatory bowel disease	Prostate cancer
Inflammation	Iron levels	Psoriasis
Calcium	Lung Cancer	Rheumatoid arthritis
Cardiovascular disease	Lupus	Schizophrenia
Celiac disease	Macular degeneration	Stroke
Cholesterol levels	Magnesium levels	Type 1 Diabetes
Chronic kidney disease	Metabolic syndrome	Type 2 Diabetes
Colorectal cancer	Migraine	Ulcerative colitis
Coronary heart disease	Multiple sclerosis	Urate levels

Enabling Individuals to take Responsibility for their Own Wellness (and Disease)



Individuals taking responsibility for their own health – with informed personalized nutrition – will dramatically reduce the cost of healthcare

ISB Hundred Person Wellness Project: Team

Special thanks to our funders: Robert Wood Johnson Foundation and M.J. Murdock Charitable Trust

Project Leadership

- Leroy Hood, MD, PhD
- Nathan Price, PhD
- Sean Bell, Business Director

Project Management

- Kristin Brogaard, PhD Project Manager
- Sara Mecca, Project Assistant
- Mary Brunkow, PhD, Project Coordinator

Participant Engagement

- Jennifer Lovejoy, PhD, VP Clinical Affairs
- Sandi Kaplan, Wellness Coach
- Craig Keebler, MD, Study Physician

Communications

- Gretchen Sorenson, Consultant
- Hsiao-Ching Chou, Commun. Director

Data Analytics

- Nathan Price, PhD – Analytics Lead
  Gustavo Glusman, PhD, Genomics
- Andrew Magis, PhD, Multi-omics
- John Earls, Data integration

Medical Advisory Board

- Robert Green, MD
- Jane Guiltinan, ND
- Michael Raff, MD
- Sarah Speck, MD

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