Personal, Dense, Dynamic Data Clouds and the Future of Personalized Nutrition

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Seattle, WA

Nutrigenomics and the Future of Nutrition

National Academies Food Forum Meeting,

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Disclosures

- Co-Founder and Board of Directors of **Arivale**, which partially funded and may license discoveries from the Pioneer 100 Wellness Project (to be described).

- Scientific Advisory Boards for **Habit**, **Trelys**, **Novo Nordisk Foundation Center for Biosustainability, Roche** (personalized medicine division)

- Consultant, advisor, or received honoraria and/or grant funding from **Genentech**, **J&J/Janssen Pharmaceuticals**, **Sera Prognostics, Nature's Bounty**, **Just Therapeutics, Amgen**
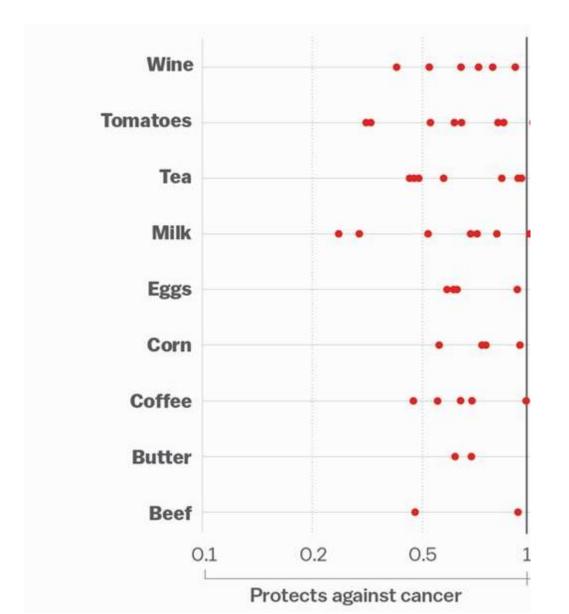
Founders

Clayton Lewis, CEO and Co-founder
Maveron, MarketLeader, Harborview Medical Center, Capitol

Lee Hood, MD, PhD, Co-founder, SAB Chair
ISB, Amgen, National Academies, Presidential Medal

Nathan Price, PhD, Co-founder, Board of Directors
ISB, University of Washington, University of Illinois, UCSD

Nutrition health effects...

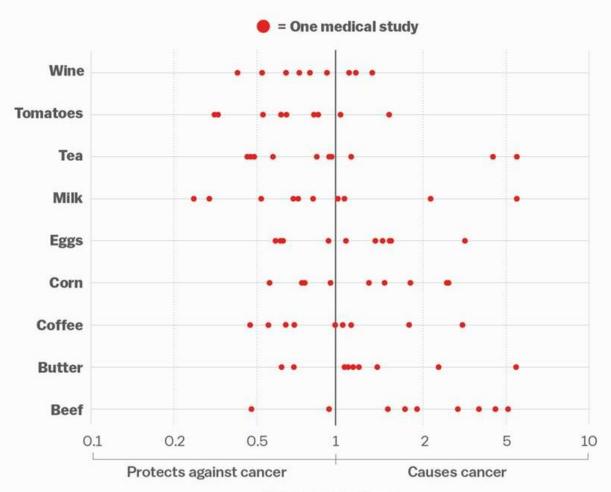**Multiple studies demonstrate nutritional effects on disease**

Nutrition health effects… are complex: Need context and personalization

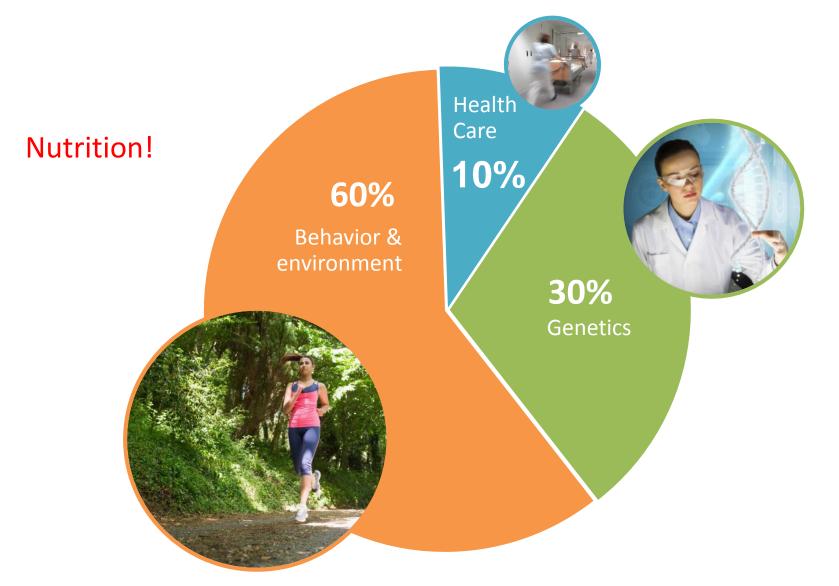**Everything we eat both causes and prevents cancer**

SOURCE: Schoenfeld and Ioannidis, *American Journal of Clinical Nutrition*

THE SCIENCE OF
You

Systems Biology Inputs

HEIGHT

AGE

🧬 DNA

FTO RS9939609

💧 BLOOD

CYP1A2 rs762551

GENDER

MTHFR rs1801133

METABOLIC FUNCTION

BMI

BODY METRICS

MCM6 rs4988235

CORE MEASUREMENT
MCM6 rs182549

ADAMTS9 rs4607103
WEIGHT
FTO rs1121980
LIVER FUNCTION

ACTIVITY

KIDNEY FUNCTION
GCKR rs780094

ADAMTS9 rs4607103
TCF7L2 rs7903146

HDL CHOLESTEROL
FASTING TRI'S

DISPOSITION INDEX
GLUCOSE 120 MIN
STRENGHT LEVEL
TOTAL CHOLESTEROL
LDL CHOLESTEROL
BLOOD PRESSURE

FASTING GLUCOSE

CARDIO LEVEL

30 MIN TRI'S

OMEGA 3 INDEX

CAROTENOIDS

VITAMIN A

120 MIN TRI'S

DAILY CALORIC BURN

VITAMIN D

FASTING GLUCOSE

ARA:EPA RATIO

Determinants of Health in U.S.

Nutrition!

60%
Behavior & environment

Health Care
10%

30%
Genetics

Scientific Wellness → A New Industry

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

SYSTEMS BIOLOGY

Demystifying Disease, Democratizing Health Care

Leroy Hood is President of the Institute for Systems Biology, Seattle, WA 98109, USA. E-mail: lhood@systemsbiology.org
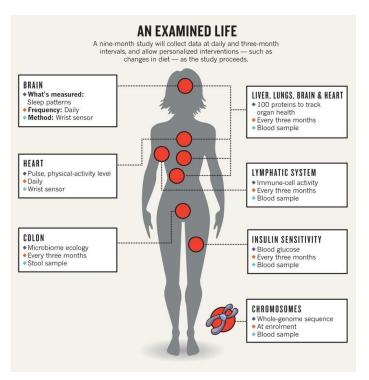
UNSUSTAINABLE COST INCREASES THREATEN THE GLOBAL HEALTH CARE SYSTEM, and further progress is stymied more by societal than technological factors. Only by engaging health care consumers (that is, patients) as pioneers who provide both health-related data and insights into pathophysiology can we meet these 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*).

Nathan D. Price is Associate Director of the Institute for Systems Biology, Seattle, WA 98109, USA. E-mail: nprice@systemsbiology.org

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-

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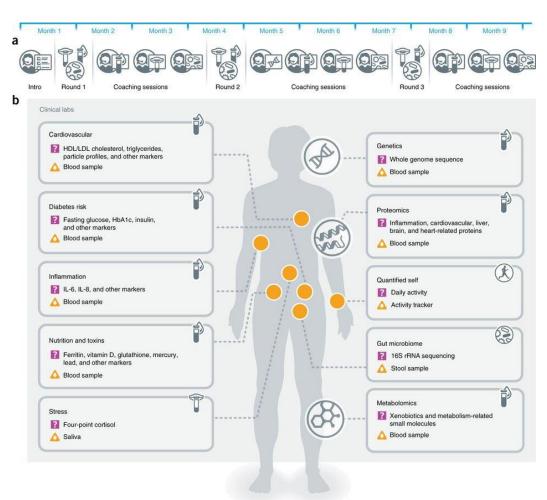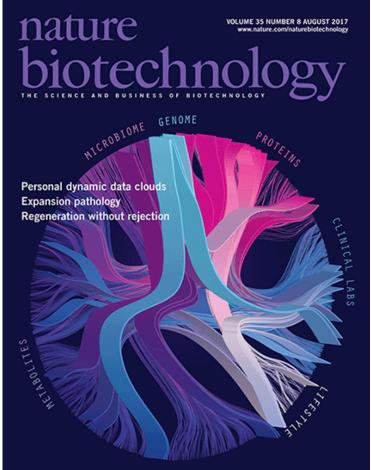L. Hood, N. D. Price, Demystifying disease, democratizing health care. *Sci. Transl. Med.* **6**, 225ed5 (2014).

Nature, News piece, (2014)

AN EXAMINED LIFE

A nine-month study will collect data at daily and three-month intervals, and allow personalized interventions — such as changes in diet — as the study proceeds.

BRAIN
- **What's measured:** Sleep patterns
- **Frequency:** Daily
- **Method:** Wrist sensor

LIVER, LUNGS, BRAIN & HEART
- 100 proteins to track organ health
- Every three months
- Blood sample

HEART
- Pulse, physical-activity level
- Daily
- Wrist sensor

LYMPHATIC SYSTEM
- Immune-cell activity
- Every three months
- Blood sample

COLON
- Microbiome ecology
- Every three months
- Stool sample

INSULIN SENSITIVITY
- Blood glucose
- Every three months
- Blood sample

CHROMOSOMES
- Whole-genome sequence
- At enrolment
- Blood sample

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

Pioneer 100 Wellness Project
PIs: Lee Hood and Nathan Price

Price, Magis, Earls et al, *Nature Biotechnology*, **2017**

Assays / Measurements—108 Pioneers

Creating personal, dense, dynamic data (PD3) clouds

GENOME

Whole Genome Sequencing.
SNPs Millions

LABS

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

SELF-TRACKING

Continual self-tracking & lifestyle monitoring

Database of actionable possibilities that will grow over time

MICROBIOME

Gut Microbiome 3x

April	May	June	July	August	September	October	November	December

Intro | Round 1 | Coaching Sessions | Round 2 | Coaching Sessions | Round 3 | Coaching Sessions

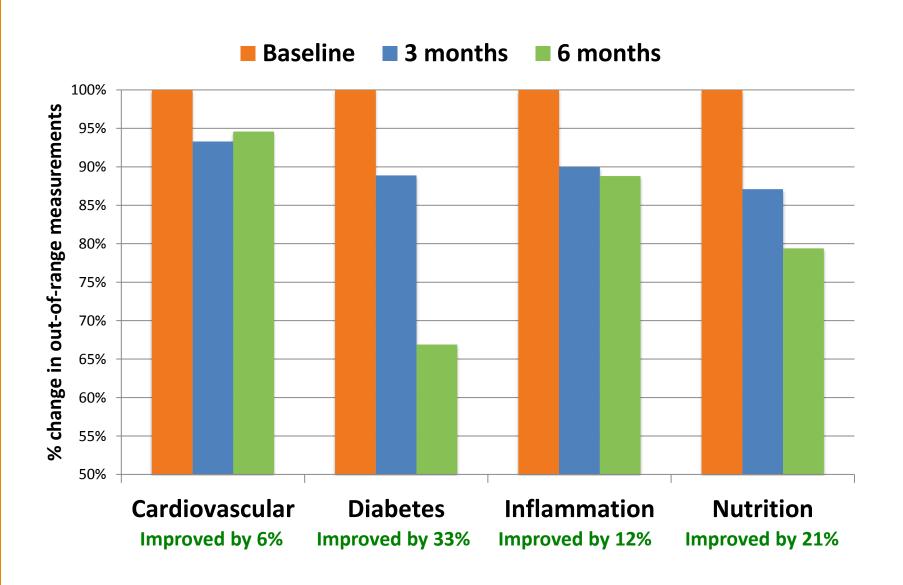# Wellness coaching for participants

Wellness Coach

Sandi Kaplan, MS, RD

Study Physician
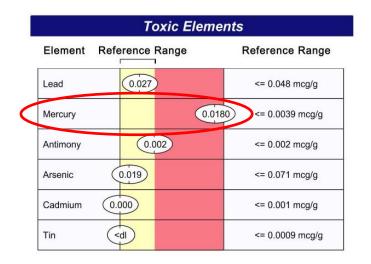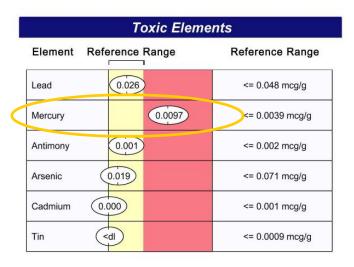
Craig Keebler, MD

Clinical Labs Discovery:
Improvements in blood health with behavioral coaching

Legend: ■ Baseline ■ 3 months ■ 6 months

Y-axis: % change in out-of-range measurements (50% to 100%)

Cardiovascular — Improved by 6%
Diabetes — Improved by 33%
Inflammation — Improved by 12%
Nutrition — Improved by 21%

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

Toxic Elements

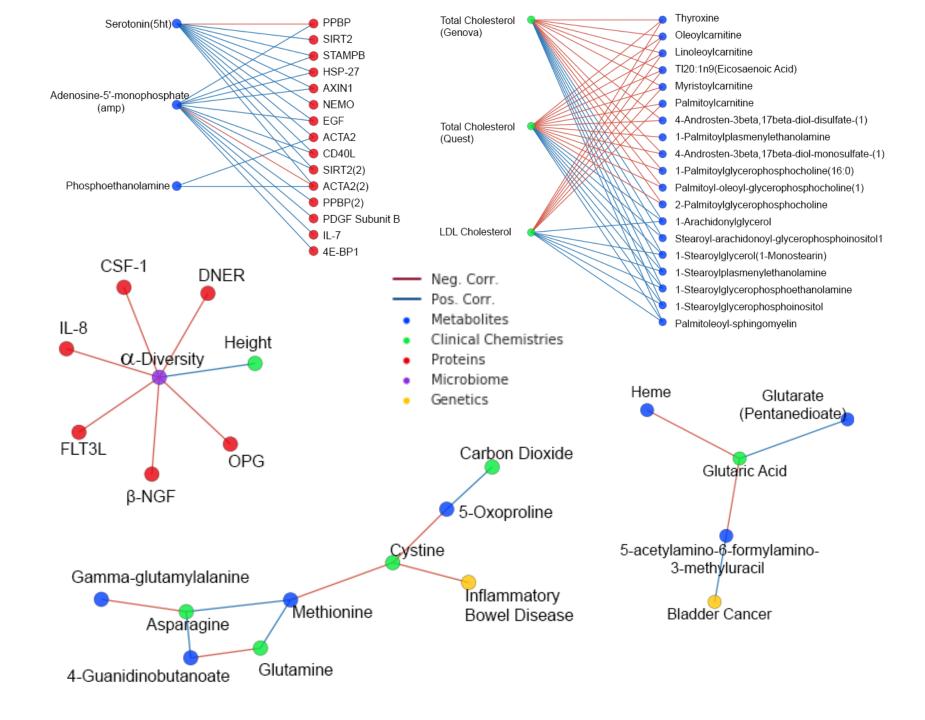| Element	Reference Range	Reference Range
Lead	0.026	<= 0.048 mcg/g
Mercury	0.0097	<= 0.0039 mcg/g
Antimony	0.001	<= 0.002 mcg/g
Arsenic	0.019	<= 0.071 mcg/g
Cadmium	0.000	<= 0.001 mcg/g
Tin	<dl	<= 0.0009 mcg/g

1. Baseline: High mercury levels in blood

2. Coached to modify diet - eight weeks of eating salmon sushi vs. tuna sushi (3x a week)
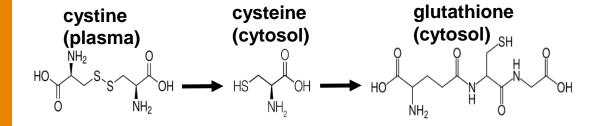
3. Reduced mercury levels in three months
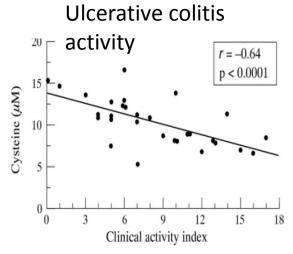
Nutrient measurements correlate with genetic predisposition for IBD

cystine (plasma)

cysteine (cytosol)

glutathione (cytosol)

	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)

Ulcerative colitis activity

$r = -0.64$
$p < 0.0001$

Pilot Study Correlation

$N = 107$
rho = -0.44
$p = 2.3e-6$
$q = 0.03$

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.
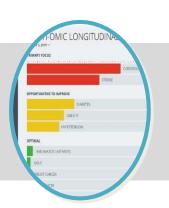
Personalized Nutrition in the Real World

Creation of a Consumer-Based Scientific Wellness Company

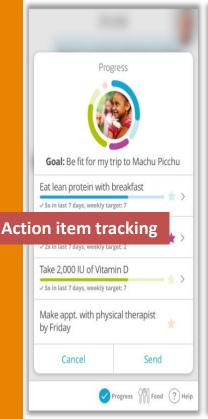**2015 LAUNCH**

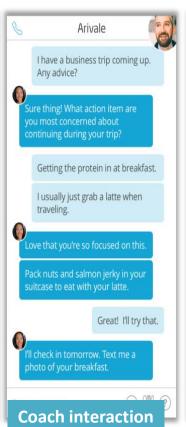# Members Value

Data + Coaching + Action = Results

Technology Amplifies Coach Relationship

Mobile App Amplifies Coach Engagement

Dashboard: Brings Data to Life

Food tracking

Action item tracking

Coach interaction

Personalized Nutrition

Key inputs for your personalized nutrition blueprint

Your DNA

Your diet influences gene expression and your genes program the systems that process your food–analyzing your genetic variations helps us give you evidence-based nutrition recommendations.

Your Phenotype

Biomarkers and body basics, like waist measurement, show us your phenotype–the unique interaction between your genes, food, and environment.

Your Phenotypic Flexibility

We help you understand how your body reacts to fats, carbs, and proteins by giving you a meal replacement drink and analyzing how your metabolism responds.

Your Habits and Goals

Your goals and habits contribute to revealing which foods are best for you right now. We even provide a coach to support you in achieving your goals and creating healthy habits.

Our Nutrition Intelligence Engine™

Our Nutrition Intelligence Engine™ uses decision trees based on your lab tests, activity level, goals, food preferences, and body basics to create a nutrition blueprint personalized just for you.

Personalized Nutrition From Test to Table™

Bio testing   **Results**   **Coaching**   **Personalized Meals**

Personal, Dense, Dynamic Data (PD3) Clouds

iPS CELLS
0100101011010101101
0110101010101011010
1010101101010101010

GENOME
GCGTAGTC
ATGCGTAG
GGCATGCT
ATGCCATG
ATAGCTGC

TRANSCRIPTOME
CUUAGUGC
UAUGCGUA
GCUAGGCG
CAUGCUUC
GAGUGAUA

TRANSACTIONAL
0100101011010101101
0110101010101011010
1010101101010101010

SINGLE CELL
0100101011010101101
0110101010101011010
1010101101010101010

PROTEOME
arg-his-pro-val-
gly-leu-ser-thr-
ala-trp-tyr-val-
met-phe-arg-

PHENOME
Na 143 K 3.7
BP 110/70
HCT 32
BUN 12.9
Pulse 110
PLT 150
WBC 92

METABOLOME
0100101011010101101
0110101010101011010
1010101101010101010

EPIGENOME
0100101011010101101
0110101010101011010
1010101101010101010

SOCIAL MEDIA
11010100010
10101011010
10101001000
10110100111
10110101010

Insights from PD3 clouds provide a data-rich foundation for the future of personalized nutrition

Institute for Systems Biology

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

Participant Engagement

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

Data Analytics

- Nathan Price, PhD – Analytics Lead

  Gustavo Glusman, PhD, Genomics
- Andrew Magis, PhD, Multi-omics
- John Earls, Data integration

Project Management

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

Communications

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

Medical Advisory Board

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

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Institute for Systems Biology
Revolutionizing Science. Enhancing Life.

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Noah McClean (U Chicago)

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Paul Shannon

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Shannon Fallen

Kelsey Scherler

Li Tang

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Simon Evans, PhD

Program Manager

Mary Brunkow, PhD

Executive Assistant

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Special Assistant to the President

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Jennifer Lovejoy, PhD, Arivale

Gilbert Omenn, M.D., U Michigan

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