Systems Medicine and Proactive P4 Medicine: Catalyzing a Revolution in Healthcare

Predictive, Preventive, Personalized and Participatory

Lee Hood
Institute for Systems Biology, Seattle
National Conference of Pharmaceutical Organizations
1-10-15
Take home lessons

- Systems medicine is key to dealing with the complexities of disease leading to new strategies and technologies for diagnostics and therapeutics
- Systems medicine has reach a tipping point and is enabling a medicine that is predictive, preventive, personalized and participatory (P4 medicine)—that is very different from contemporary medicine
- P4 medicine can transforming healthcare through the initiation of a Framingham-like, longitudinal, digital-age study of 100,000 well people for which we are seeking Congressional support
The grand challenge for biology and medicine is deciphering biological complexity
6 Blind Men and an Elephant
Paradigm Changes Drive Radical Changes in Science
I Participated in Five Paradigm Changes in Biology over 45 Years Leading to Systems Medicine and P4 Medicine

• **Brought engineering to biology**
  – Developed 6 instruments that led to high-throughput biology: big data in biology (1970 - present)

• **The Human Genome Project**
  – Invented enabling technology, advocate, participant, applying genomics to P4 medicine (1990-2003)—complete parts list human genes

• **Cross-disciplinary biology**
  – Created 1st cross-disciplinary department: enabled technology development to be driven by biology (1992-2000)

• **Systems biology**
  – Created 1st systems biology institute: deciphering the complexities of biology and disease (2000 – present)

• **Systems medicine / emergence of proactive P4 medicine**
  – Early advocate and pioneer of a P4 medicine that will transforming healthcare (2001 – present)
  – Pioneered systems driven technologies and strategies for P4
  – 100,000 person wellness project (2013—present)
Big data is one essence of systems medicine: Soon each individual will be surrounded by a virtual cloud of billions of multi-scale data points—big data.
Systems Medicine
Systems biology and disease-perturbed network of networks

- Integration of patient data will reveal **biological networks** that specify health and are altered in disease.
- Understanding differences in normal and disease-perturbed networks will provide fundamental insights into **disease mechanisms**.
- These insights are essential for developing **more effective diagnostic and therapeutic approaches**.
Why is the Institute for Systems Biology (ISB) uniquely positioned to transform systems medicine and catalyze a revolution in healthcare?
Evolution of the Vision for Systems Medicine (and P4 Medicine) 2001 - Present

• By 2005, the vision of Systems Medicine/P4 medicine had been clearly articulated by ISB
  – Key question: How to bring P4 to the healthcare system?

• In 2008, ISB formed a 5 year $100M strategic partnership with Luxembourg
  – Developed about 10 new systems-driven technologies and strategies
  – Placed P4 medicine at a tipping point for transforming the practice of healthcare

• In 2013, ISB first proposed the P4 pilot project to study 100,000 well people
  – Bringing the power of P4 medicine to the contemporary healthcare system
Three systems-driven strategies supported by Luxembourg
Dynamic network approaches to prion-induced neurodegeneration in mice
Global and Subtractive Brain Transcriptome Analysis—Differentially Expressed Genes (DEGs)

**Prion strains:**
- RML
- 301V

**Mouse strains:**
- C57BL/6J
- FVB/NCr
- BL6.I
- FVB/B4053

**Time-course array analysis:**
- Subtractive analyses to DEGs

**Inoculate w/ Prions**

- Prion infected brain
- Uninfected brain

**RNA from brain homogenate**

**Mouse Genome array:**
- 45,000 probe sets
- ~22,000 mouse genes.

300 DEGs encode the prion neurodegenerative response
Neuropathology Identifies 4 Major Disease-Perturbed Networks for Prion Disease

- PrP replication/accumulation
- Microglia/astrocyte activation
- Synaptic degeneration
- Nerve cell death
Sequential Disease-Perturbation of the Four Major Networks of Prion Disease

Clinical Signs

0 wk  7 wk  18~20 wk  22 wk

Prion accumulation  Glial Activation  Synaptic Degeneration  Neuronal Cell Death

Cholesterol transport
Sphingolipid synthesis
Lysosome proteolysis

Reactive Astrocytes
Leukocyte extravasation
*Arachidonate metab./Ca\(^+\) sig.

Na\(^+\) channels
Cargo transport
Caspases

Institute for Systems Biology
10 Disease-Perturbed Dynamical Networks in Prion Disease Explain Virtually all of the Pathophysiology of the Disease in Mice
A systems-driven network approach to glioblastoma in humans and mouse models—developing a network approach to the identification of new drug targets
A computational approach to cancer drug target identification through network analysis

Halobacterium

Yeast peroxisome biogenesis

Host-pathogen interactions

Cancer

BALIGA, Aitchison, Hood LABs
Strategy--Glioblastoma

• Mine omics and clinical data to generate disease-perturbed network signatures to:
  – Stratify disease into different subtypes

• Discover how networks are disease-perturbed within each patient to predict (identify) unique sets of druggable targets

• Use network architecture of druggable targets to prioritize drug combinations that are most likely to work on a given patient

• Use patient tumor-derived differentiated stem cells to perform high throughput screening to:
  – generate dose response-curves for individual drugs
  – perform combinatorial drug screens on network-predicted phenotypes
Possible outcomes for computational approaches to cancer

Methodology to reverse engineer disease-perturbed network dynamics directly from patient cohort data

– Biomarkers:
  • Stratify Disease
  • Analyze Individual Patients for Unique Features
  • Predict Clinical Outcomes
  • Predict Drug Responsiveness

– Rational Drug Discovery:
  • Identification of New Drug Targets
  • Drug Repurposing for New Indications
  • Combinatorial Drug Formulations
Making blood a window into health and disease
Dynamics of prion-induced neurodegeneration in mice as seen through the blood with brain-specific blood proteins
200 Brain-Specific Blood Proteins Reflect Key Networks

- Nerve growth factor signaling
  - RGS4, PEA15, CAMKII, RASGRF1, NR1
  - TAU, MAP2, CAMKII, EPHA5, UCHL1, NCA, M1
- Synaptic vesicle transport
  - APLP1, SNAP25, LG1, NAC M1, CLSTN2
  - KINESIN, MAP1B, SYT3, CTNNB1
- Calcium mediated signaling
  - CAMKII, PCL0, GRIA4, GLUR3, NSF, ANK2, ENO2, DOCK3, SCG3
  - RGS4, PEA15, CAMKII, RASGRF1, NR1, NEUROMODULIN, HUC, CA MKIIA, RIN, SYNAPSIN1, RG S4, PEA15, RA
- Synaptic Transmission
- Neurogenesis
- Cell surface receptor signaling
- GPCR signaling
- Anatomical structure development
- Cellular differentiation

200 Brain-Specific Blood Proteins Reflect Key Networks

- Calcium mediated signaling
  - CAMKII, PCL0, GRIA4, GLUR3, NSF, ANK2, ENO2, DOCK3, SCG3
  - RGS4, PEA15, CAMKII, RASGRF1, NR1, NEUROMODULIN, HUC, CA MKIIA, RIN, SYNAPSIN1, RG S4, PEA15, RA

Institute for Systems Biology
Revolutionizing Science. Enhancing Life.
Targeted MS Proteomics: Human Selective Reaction Monitoring (SRM)Atlas

ISB has developed SRM/MRM assays for most of the known 20,333 human proteins

Analyze 100-200 proteins quantitatively in 1 hour
Heavy isotope peptides for Q3 analyses allow precise quantification
15 Brain-Specific Blood Proteins Reflect the Early Detection and Progression of Prion Disease-Perturbed Networks

* indicates brain-specific blood proteins

Prion accumulation
- Cholesterol transport
- Sphingolipid synthesis
- Lysosome proteolysis

Glial Activation
- Apod*
- Scg3
- Cntn2*
- Ttc3*
- Reactive Astrocytes
- Leukocyte extravasation

Synaptic Degeneration
- Gria3*
- Gfap*
- L1cam
- Na⁺ channels
- Cargo transport

Neuronal Cell Death
- Mapt*
- Snap25*
- Myo5a*
- Kif5a
- Caspases
- Gria1*
- Bcas1

Clinical Signs
- 0 wk
- 18~20 wk
- 22 wk
Organ-specific blood proteins allow one to study the dynamics of human biological processes

- Development
- Physiology
- Aging
- Wellness
- Disease dynamics (diagnostics)
- Drug toxicity (liver)
- Multi-organ responses to disease (Alzheimer’s)
A second blood diagnostics approach: a systems approach to blood diagnostic for identifying benign lung nodules in human lung cancer

Integrated Diagnostics—Paul Kearney, Xiao-jun Li, etc.

Indeterminate Pulmonary Nodules

Is this cancer?

~3 million cases annually in the USA

Patrick Nana-Sinkham, MD  Ohio State University
Lung Nodules Found by CT Scan in USA

3 million cases/yr

Watchful waiting for 2 years

Repeat CT studies

PET Scan

Look for cancer

Needle Aspiration

Bronchoscopic Biopsy

600,000 in “dilemma zone”

Surgery for nodule removal

“watchful waiting” threshold

intermediate

~0.8 – 2.0 cm

higher

Cancer Risk

~0.8 – 2.0 cm

“watchful waiting” threshold

surgery threshold

Systems Approach to Distinguishing Benign from Malignant Lung Cancer Nodules (with Integrated Diagnostics)

- 371 SRM assays for lung cancer tissue/190 detectable in the blood
  - Differentially secreted (normal vs. neoplastic)
  - Differentially shed from cell surface (normal vs. neoplastic)
  - Candidates captured from the literature
- Discovery samples—analyze all 190 detectable proteins
  - 72 cancer vs. 72 benign/from four sites
- Discovery algorithm for “cooperative” proteins
  - Select the 32 (out of 190) best proteins for distinguishing nodules
  - A million random panels of 10 of 32 best proteins were scored
  - Identified 13 proteins that were highly “cooperative”—generally in most effective panels
- Validation study—13-protein panel
  - 52 cancer vs. 52 benign/from 4 old sites plus 1 new site
- InDi commercialize the panel of 13 blood proteins in Q4 2013
- Published in X. Li et.al. Science Translation Medicine: 5, 207, 2013

Red indicates systems approaches
Lung cancer blood biomarker panel

- Rule out for surgery about 40% of the benign nodules with 90% specificity—prevent 1/3rd of unnecessary surgeries
- Save the healthcare system in US about $3.5 billion per year
- Bring “peace of mind” to many patients
- Panel is independent of 3 classical criteria for lung cancer—age, smoking history and size of lung nodule
Three Lung Cancer Networks Monitored: 12/13 biomarkers map to these networks
Posttraumatic stress disorder—quantitative blood biomarkers for a neuropsychiatric disease—discovery phase

Performance of biomarker panels on 66 PTSD samples (36 negatives and 30 positives) #

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Panel of 8 (train)</th>
<th>Panel of 8 (Cross-validation)</th>
<th>Panel of 2 plasma only (train)</th>
<th>Panel of 2 plasma only (Cross-validation)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>0.97</td>
<td>0.90</td>
<td>0.83</td>
<td>0.79</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.92</td>
<td>0.81</td>
<td>0.91</td>
<td>0.86</td>
</tr>
<tr>
<td>Accuracy</td>
<td>0.94</td>
<td>0.85</td>
<td>0.87</td>
<td>0.82</td>
</tr>
</tbody>
</table>

Panel of 8: one blood protein, five circulating miRNAs and two PBMC miRNAs

#66 out of 140 samples have results for all the measurements

1. Panel was build based on the results from 46 measurements (1 protein +45 miRNAs) over 140 samples, 66 samples have results from all the measurements
2. Cross-validation was performed by leave-one-out approach.
3. Adding different measurements on the panel improves the performance of the diagnostic model
How Blood Biomarker Panels for Detecting Disease-Perturbed Networks Are Effective

• Distinguish normal individuals from diseased individuals
• Early diagnosis
• Follow progression
• Follow response to therapy
• Follow the reoccurrence of disease
• Reveal disease-perturbed networks which suggest mechanisms of disease and candidate drug targets
• Stratification of disease into different subgroups for impedance match against effective drugs—and proper prognosis
Systems Medicine Is at a Tipping Point and Is Transforming Healthcare through Systems-Driven Strategies and Technologies

- Providing fundamental insights into the early dynamics of disease and disease-perturbed networks—using orthologous animal models
- Family genome sequencing -- identifying disease genes
- Transforming blood into a window to distinguish health from disease with a systems approach to blood diagnostics
- Stratifying diseases into their distinct subtypes for an impedance match against proper drugs
- Using disease-perturbed networks to identify new drug target candidates and repurpose old drugs.
- Pioneering peptide protein-capture agents that will replace monoclonal antibodies over the next 10 years.
- Large-scale, longitudinal studies for the digital age—a dynamical understanding of wellness and disease
  - Longitudinal clinical trials for preterm birth, wellness, and Lyme Disease
The Emergence of P4 Medicine
Predictive, Preventive, Personalize, Participatory

Converging Megatrends
Driving the transformation of healthcare for patients
P4 Medicine vs. Contemporary Medicine

- **Proactive**
- **Focus on Individual**
- **Focus on Wellness**
- Generate, mine and integrate individual patient dynamical data clouds
  - Produce predictive and actionable models of wellness / disease
- **Clinical trials** -- large patient populations analyzed at single individual level (not population averages!)
  - Generate quantized stratification of patient populations and create the predictive medicine of the future. **N=1 experiments**

**Patient-driven social networks** are a key to driving the acceptance of P4 medicine
Conceptual Themes of P4 Medicine

P4 Medicine
- Predictive
- Preventive
- Personalized
- Participatory

Wellness Industry
- Wellness Quantified

Disease Industry
- Disease Demystified
Understanding Wellness is Key
Developed World

If the trend of the last 10 years of increases in life expectancy continue, more than half of all children born today in developed countries can expect to celebrate their 100th birthday.

A Framingham-like digital-age study of wellness in 100,000 (100K Project) patients longitudinally -- 20-30 years

2014 P4 Pilot Project
Hundred Person Wellness Project
(March 2014)
Assays / Measurements

- Whole Genome Sequencing
- Detailed lab tests 3x (blood, urine, saliva)
- Continual self-tracking & lifestyle monitoring
- Gut Microbiome 3x

Database of actionable possibilities that will grow exponentially over time
Health: What do we really want to understand from 100,000 well patients?

Wellness

Disease transition

Time

Wellness
The Wellness Well

- Information will bring individuals from minimal to maximum wellness

- The dimensions of the wellness well are unique for each individual: presumably determined genetically
Health: What do we really want to understand from 100,000 well patients?

Wellness

Disease transition

Time
Actionable Traits, Coaches and Positive Reinforcement

• Actionable possibilities from individual data types

• Actionable possibilities from integrated data types

• Coaches with MD advisors
  – Bringing actionable opportunities to each individual
  – Nourish relationship based accountability for participants

• Positive reinforcement / immediate gratification
  – Individuals can see improvement within a three-month period (from one blood draw or other sample to the next)
Scaling Up Rapidly

ISB 100K
WELLNESS PROJECT

10K

1K

PIONEER 100
Hundred Person Wellness Project
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

107 Individuals
Hundred Person Wellness Project Tests
Blood, Urine, Saliva, Stool

1. **Blood**
   - Whole genome sequence – 50x coverage
   - Comprehensive clinical chemistries focusing on nutrition, inflammation and metabolic function
   - Metabolomics targeting 600 metabolites—15% from gut microbiome
   - Organ-specific proteins for heart, brain and liver
   - 96 well ELIZA panels for inflammation and cardiovascular disease

2. **Urine**
   - Amino acid profile
   - Oxidative stress – lipid peroxidases

3. **Saliva**
   - Adrenal stress markers – cortisol and DHEA

4. **Stool**
   - 16S bacterial variable region 4 ribosomal RNA
Hundred Person Wellness Project Tests

Personal Health and Self-Tracking

1. **Personal Health Status**
   - Personal health history
   - Familial health history
   - Personality assessments

2. **Self-Tracking**
   - Activity (Fitbit)
   - Sleep (Fitbit)
   - Weight
   - Blood Pressure (Omron)
   - Heart Rate (Omron)
Knowledgebase—graph database

- There are currently 227,979 nodes in the graph database, and 2,375,362 edges—connecting genes, environment and actionable possibilities

- What information being incorporated into our analytics pipeline?
  - Database of human **phenotypes** (OMIM)
  - Database of human **clinical variants** (ClinVar, ACMG)
  - Database of **GWAS studies / traits** (GWAS Catalog)
  - Database of **actionable genetic variants** (ISB resource)
  - Database of human **metabolites** (HMDB)
  - Database of **pharmacogenomics** (PharmGKB)
  - Literature for actionable variants
Preliminary stories about actionable possibilities for the 107 Pioneers
Actionable possibilities from single data types
Baseline Health (Blood Draw #1)

Prevalence of Actionable Results in Pioneer 100 Labs

High rate of actionable lab results impacting various physiological systems, even in this supposedly healthy cohort.
Actionable possibilities: toxic metals

- High mercury from tuna
- High lead
Participant Action: Reducing Toxicity

Only change between blood draw #1 and blood draw #2:

- 8 weeks of having salmon sushi vs. tuna sushi (3x a week)
Searching for novel correlations: lead vs. age

\[
\text{rho} = 0.58, \ p = 7.45 \times 10^{-11}
\]
Actionable possibilities from two or more integrated data types
Vitamin D deficiency

• Vitamin D—90/108 Pioneers are low
  – Six genetic variants from 3 genes block Vitamin D absorption
  – Risks associated with low Vitamin D
    • Ricketts—improper bone mineralization
    • Increased risk of death from cardiovascular disease
    • Cognitive impairment in older adults
    • Severe asthma in children
    • Cancer
Presence of risk alleles in vitamin D binding proteins is negatively correlated with vitamin D levels

Vitamin D vs. risk alleles in GC, DHCR7, CYP2R1

Vitamin D is significantly increased across our participants.

Vitamin D was the most significantly changed metabolite out of 189 for which data are available.

\[ \mu_{R1} = 33.6 \text{ ng/mL} \]
\[ \mu_{R2} = 44.0 \text{ ng/mL} \]
\[ p_{\text{signedrank}} = 1.45E-9 \]
Common genetic variants—very small disease effects
Discovery and refinement of frequent genetic variants associated with lipid levels

- Study examined **188,577** individuals using genome-wide and custom genotyping arrays.
  - **94,595** in initial discovery set
  - **93,982** in validation set
- The study associates **72 loci** with total cholesterol levels.
Individuals contain different subsets of variants that affect cholesterol levels

Each individual harbors a subset of the universe of possible variants that affect a trait. Although each variant alone has only a small effect, the cumulative effect of an individual’s variant set can add up to significant differences between individuals.
Correlating cholesterol levels with 72 single nucleotide variants

The cumulative effect of the individual genetic profile of an individual for cholesterol-related variants strongly correlates with HDL concentrations, for all participants for which we have genetic data. Reference ranges are shown as red (inappropriately hi), orange, and green (healthy) shadings.
The multi-genome analysis paradigm

2000 genomes → Multi-genome reference models → Preliminary analysis → High-quality analysis

Individual genome
Cumulative sum for an individual can give an estimate of risk relative to a population of 2000 normal individual genomes.

Calculate the effects of all common variants within an individual.

Estimate the risk for high cholesterol relative to a population.
Major diseases and related GWAS-identified variants

<table>
<thead>
<tr>
<th>GWAS Trait</th>
<th># of variants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung Cancer</td>
<td>31</td>
</tr>
<tr>
<td>Obesity</td>
<td>139</td>
</tr>
<tr>
<td>COPD</td>
<td>55</td>
</tr>
<tr>
<td>Alzheimer’s Disease</td>
<td>230</td>
</tr>
<tr>
<td>Asthma</td>
<td>93</td>
</tr>
<tr>
<td>Breast Cancer</td>
<td>171</td>
</tr>
<tr>
<td>Stroke</td>
<td>21</td>
</tr>
<tr>
<td>Hypertension</td>
<td>35</td>
</tr>
<tr>
<td>Bipolar Disorder</td>
<td>126</td>
</tr>
<tr>
<td>Prostate Cancer</td>
<td>141</td>
</tr>
<tr>
<td>Multiple Sclerosis</td>
<td>182</td>
</tr>
<tr>
<td>Crohn’s Disease</td>
<td>220</td>
</tr>
<tr>
<td>Cholesterol (lipid) Levels</td>
<td>72</td>
</tr>
</tbody>
</table>

We have the capability to associate genetic variation with quantitative traits also being measured in the study. The NHGRI GWAS catalog provides a rich resource that can be mined for genetic-phenotype associations.
Wellness to disease transitions—an example—hemachromatosis
Hereditary hemochromatosis is associated with a variant in the HFE gene.

*Hereditary hemochromatosis* causes the body to absorb too much iron, which can lead to cancer, heart arrhythmias, and liver cirrhosis. It is one of the most common genetic diseases in Caucasians, and is usually associated with a variant in the HFE gene—about 1/10 Caucasians carry this defect.
Hereditary hemochromatosis is associated with a rare variant in the HFE gene. Combining genome sequencing with our blood chemistry panel allows us to visualize the effect of this rare variant in only 100 individuals, and infer hemochromatosis in two participants after the first round of blood draws. Subsequent bloodletting treatment yielded a reduction in iron levels by the second round to healthy levels. Left untreated, this disorder can lead to liver cancer, diabetes, pancreatic disease and heart disease.
Personalized Dynamical Data Clouds
Growing exponentially over time

By examining only one data type, it was determined that 100% of the 107 Pioneers have actionable traits:

• Hence, virtually every person will have multiple, actionable traits as their data are aggregated and integrated

• These actionable possibilities will change as the environment changes, as reflected by dynamically changing personalized data clouds
ISB Hundred Person Wellness Project – Team

**Project Leadership**
- Leroy Hood, PI
- Nathan Price, PhD, Co-PI
- Sean Bell, Business Director

**Participant Engagement**
- Jennifer Lovejoy, VP Clinical Affairs
- Sandi Kaplan, Wellness Coach
- Craig Keebler, M.D., Study Physician

**Communications**
- Gretchen Sorenson, Consultant
- Hsiao-Ching Chou, Communications Director

**Project Management**
- Sean Bell, Business Director
- Kristin Brogaard, Project Manager
- Sara Mecca, Project Assistant
- Mary Brunkow, Project Coordinator

**Data Analytics**
- Nathan Price, Analytics Lead
- Gustavo Glusman, Genomics
- Andrew Magis, Multi-Omics

**Medical Advisory Board**
- Robert Green, M.D.
- Michael Raff, M.D.
- Sarah Speck, M.D.
Most of the 107 Pioneers have learned two important concepts
Your genome determines your potential but not your destiny. You can control your health.
The Pioneers Realize that They Must Take Responsibility for their Own Wellness (and Disease)

P4 Medicine puts individuals at the epicenter of their own health which will dramatically reduce the cost of healthcare
Opportunities
100K Project: Transforming Healthcare

- Identify vast array of actionable possibilities
- Analytics to optimize wellness and avoid (reduce) disease for each individual patient—optimize human potential
- Create a data base of wellness measurements to mine for the “multiparameter wellness metrics”—define fundamental human features of wellness—physiological and psychological
- Generate a data base from individuals that will allow us to follow early disease mechanisms in the transitions from wellness to disease for major diseases—diabetes, cardiovascular, cancer and neurodegeneration—enable early transition back to wellness
- Drive the development of improved old and new assays and analytics—parallelize, miniaturize, increase throughput, reduce cost, point of contact—digitalization through smart phone format
- Database of wellness and disease transitions catalyze innovation for the wellness industry
- Bring P4 medicine into the healthcare system
  - Improving the quality of healthcare
  - Decreasing the cost of healthcare
  - Promoting innovation in Healthcare
P4 medicine and the 100K project: Societal Implications

- **Digitalize medicine for the individual patient**—Leading to a lowering of healthcare costs and the democratization of healthcare—assays to smart phone.
- **Innovation**—100K database will create many opportunities for start ups and established healthcare industries.
- **Wealth**—the Wellness Industry will far exceed the current disease (healthcare) industry in market cap in 10-15 years. We are creating today the companies that will be the Google and Microsoft of the Wellness Industry.
- **Competition**—Economic advances generally arise from new technologies. Macro and micro inventions. P4 is a macroinvention and will span many microinventions and commercial opportunities.
- **Financial crisis from healthcare**—key is to have individuals take responsibility for their own health.—enormous savings from individuals becoming responsible for their own healthcare.
- **Optimization of human capital**—avoid loss of productivity due to absence from illness or presenteeism. Elevate all individuals to their highest level in their “wellness wells”.

Institute for Systems Biology
Revolutionizing Science. Enhancing Life
The ISB Wellness Project Is Taking Two Directions

• The 100,000 person wellness project—academic—discovery science—pioneer assays (to the smart phone) and pioneer the integrative and modeling analytics—open data--seek Congressional funding

• The company—Wellness Sciences—consumer directed—may really lead the large-scale adoption of P4 medicine and the democratization of healthcare
Take home lessons

- Systems medicine is key to dealing with the complexities of disease leading to new strategies and technologies for diagnostics and therapeutics.
- Systems medicine has reached a tipping point and is enabling a medicine that is predictive, preventive, personalized, and participatory (P4 medicine)—that is very different from contemporary medicine.
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