P4 Medicine: Catalyzing a Revolution from Reactive to Proactive Medicine

Predictive, Personalized, Preventive and Participatory

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The Grand Challenge of the 21st Century in Science and Technology Is Complexity

- New concepts, strategies and technologies permit biologists to successfully begin to attack biological complexity
  - Biology is an informational science
  - Systems approaches permit one to attack complexity effectively
  - Evolving current and emerging technologies permit the exploration of new areas of data space (and better the old)
  - Computation and mathematical tools permit one to acquire, store, transmit, integrate, mine and create predictive models.

- These approaches will allow us to effectively attack some of society’s most vexing challenges—healthcare (P4 medicine), global health, environment, energy, nutrition, agriculture, etc.
I Participated in Four Paradigm Changes in Biology Leading to P4 Medicine

• Bringing engineering to biology (high throughput biology)
• The human genome project
• Cross-disciplinary biology
• Systems biology

Predictive, Preventive, Personalized, and Participatory medicine (P4 Medicine)

• Each fundamentally changed how we think about biology and medicine.
• Each was met initially with enormous skepticism.
• Each new idea needed new organizational structure.
Features of P4 Medicine

• An informational science
• Data driven—each patient billions of data points—predictive medicine
• Each patient their own control for longitudinally assessing transitions from wellness to disease
• P4 medicine is a driver of new technologies
• P4 medicine will drive an economic healthcare revolution
  – Striking lowering of cost of healthcare
  – Transform the nature of the healthcare industry
  – Global wellness will provide enormous economic benefits
• P4 medicine will be for rich and poor alike
• P4 medicine should be the basis for political healthcare decisions
Contemporary Systems Biology is Predicated on Viewing Biology is an Informational Science
The Flow of Information from DNA to a Human
There are Two Types of Biological Information that Can Lead to Disease

• The digital information of the genome

• The environmental information that impinges upon and modifies the digital information
Two General Biological Structures that Handle Information

- Biological networks capture, transmit, process and pass on information
- Simple and complex molecular machines execute biological functions
Left Index Fingerprints from Identical Twins
Systems Biology—what is it?
Radio Waves → Radio Receiver → Sound Waves
ISB’s View of Systems Biology and Systems Medicine
Institute for Systems Biology
Founded 2000

ISB has 13 faculty and 300 staff
Agenda: Use biology to drive technology and computation. Need to create a cross-disciplinary culture.

- Biology
- Chemistry
- Computer Science
- Engineering
- Mathematics
- Physics
ISB’s 10 Anniversary

ISB 1st in US and 3rd in World for Impact of Papers
A Systems View of Disease
A Systems View of Medicine Postulates that Disease Arises from Disease-Perturbed Networks
Dynamics of a Neurodegenerative (Prion Disease) Network in Mice

Nerve cell death

2 wks

12 wks

20 wks
Differentially Expressed Genes (DEGs) Encoding Known and Novel Prion Disease Phenotypes

- About 300 DEGs encode core prion disease
- About 200/300 DEGs encode known disease pathogenic networks
- 100/300 DEGs encode novel pathogenic networks--the dark genes of prion disease
- Re-engineer disease-perturbed networks with drugs—new approach to drug target discovery and systems diagnosis
A Systems Approach to Blood Diagnostics
Organ-Specific Blood Fingerprints
Making Blood A Window Distinguishing Health and Disease
Why Blood Diagnostics Will Be the Key to P4 Medicine

• Early detection
• Disease stratification
• Disease progression
• Follow therapy
• Assess reoccurrences

Integrated Diagnostics—platform company for P4 medicine
Strategies and Technologies: Exploring New Dimensions of Data Space
Microfluidic Protein Chip:

Assay 2500 Organ-Specific Blood Proteins from Millions of Patients Using a Drop of Blood

• Jim Heath--Caltech
DEAL for *In vitro* molecular diagnostics: *Integrated nanotech/microfluidics platform*

300 nanoliters of plasma

5 minute measurement

Jim Heath, et al
ISB’s Individual Patient Information-Based Assays

- Complete individual genome sequences—predictive health history—will be done sequencing families
- Complete individual genome sequences from a single cell—cancer.
- Complete MHC chromosomal sequence in families—autoimmune disease and allergies
- 200 Actionable SNPs—pharmacogenetics-related and disease-related genes
- Sequence 1000 transcriptomes simultaneously in one DNA sequencing run from single cancer cells to identify quantized cells states and dissect cancer
- 2500 blood organ-specific blood proteins from 300 nanoliters of blood in 5 minutes—twice per year (50 proteins from 50 organs)—wellness assessment.
- Array of 13,000 human proteins—against autoimmune or allergic sera—stratify.
- Analyze 10,000 B cells and 10,000 T cells for the functional regions of their immune receptors—past and present immune responsiveness—follow vaccinations—identify autoimmune antibodies.
- Analyze individual stem (iPS) cells from each individual differentiated to relevant tissues to get important phenotypic information—molecular, imaging and higher level phenotypic measurements.
Predictive, Personalized, Preventive and Participatory (P4) Medicine

- Driven by systems approaches to disease, new measurement (nanotechnology) and visualization technologies and powerful new computational tools, P4 medicine will emerge over the next 10-20 years
P4 Medicine

• Predictive:
  – Probabilistic health history--DNA sequence
  – Biannual multi-parameter blood protein measurements
  – In vivo molecular imaging
P4 Medicine

• **Personalized:**
  – Unique individual human genetic variation mandates individual treatment
  – Patient is his or her own control—longitudinal data
  – Billions of data points on each individual
  – 100s millions patients with billions data points
P4 Medicine

• **Preventive:**
  - Design of therapeutic and preventive drugs via systems approaches
  - Systems approaches to vaccines will transform prevention of infectious diseases
  - Transition to wellness assessment
P4 Medicine

- Participatory:
  - Patient understands and participates in medical choices
  - Physicians trained before P4 will have to understand it
  - Medical community—interconnected and educated
  - Create IT for healthcare to handle billions of patients, each with billions of data points
P4 Medicine Will Transform the Health Care Industry

Will impact the health care system significantly:

- Pharmaceuticals
- Biotechnology
- Diagnostics
- IT for healthcare
- Healthcare industry
- Health insurance
- Medicine--diagnostics, therapy, prevention, wellness
- Nutrition
- Assessments of environmental toxicities
- Academia and medical schools

Fundamentally new ideas need new organizational structures
Digitalization of Biology and Medicine Will Transform Medicine

- Analysis of single molecules, single cells, single organs and single individuals
- A revolution that will transform medicine even more than digitalization transformed information technologies and communications
- Digitization of medicine will lead to dramatically lower healthcare costs
Why the Digitalization of Medicine and P4 (Systems) Medicine Will Reduce Healthcare Costs

- Diagnosis will stratify disease and impedance match drugs
- Re-engineering disease-perturbed networks to normalcy with drugs—new and less expensive strategy for drug target discovery
- Survey wellness with 2500 blood organ-specific protein measurements biannually—50 from each of 50 organs—global early detection
- Technologies exponentially increasing in the number of measurements they can make and decreasing in cost
- Other medical advances arising from mechanistic insights—stem cells, neurodegenerative, aging, vaccines, cancer etc.
P4 Medicine Will Become One of the Most Powerful Public and Private Investments of the 21st Century

• Moving into an information-based economy and society where educated people are the key investment—and their long-term wellness is a critical benefit for increasing productivity.

• P4 medicine will:
  – Predict and prevent disease at the earliest stages
  – Provide the tools for patients to actively participate in optimizing their own wellness
  – Catalyze a new industrial opportunity based on wellness (rather than just disease)
•Analyzing one gene and one small problem at a time

• Systems analysis of biology and medicine--e.g., predictive, preventive, personalized and participatory (P4) medicine

• Technology development

• Pioneer computational tools

• Transferring knowledge to society--joining academics and industry--changing K-12 science education--P4 medicine and society

• Strategic partnerships--for hard scientific problems--P4 medicine--industrial, academic, government, international
ISB/Luxembourg Strategic Partnerships
ISB/Luxembourg Strategic Partnership

• Helping to creating a Center for System Medicine similar to ISB—Rudi Balling Director

• Two collaborative research projects--$100 million over 5 years

• Helping establish biotech industry in Luxembourg—start ups and established companies--integrated personalized medicine company—Integrated Diagnostics
ISB/Ohio State Strategic Partnership
The P4 Medicine Institute
(http://www.P4MI.org)

- Non-profit 501c3
- ISB and Ohio State founding members
- Committed to bringing P4 medicine to patients—initially through two pilot projects—wellness and lung cancer
- Seeking academic and industrial partners who share the P4 vision and have complementary skills/resources
- Bringing on consultants to analyze the societal challenges of P4 medicine—ethics, security, confidentiality, policy, regulation, economics
P4 Medicine Is Personalized Medicine and Far More!

- P4 medicine is medicine of the present/near future.
- P4 medicine is driven by systems approaches to disease and emerging technologies.
- P4 medicine will use measurements to quantify wellness and its transition into disease.
- P4 medicine is revolutionary rather than evolutionary or incremental.
- P4 medicine sees the patient (consumer) as the central focus of healthcare.
- Pilot projects with informational assays in patient groups will be necessary to convince skeptics.
- P4 medicine will restructure the business plans of every sector of the healthcare industry—enormous economic opportunities.
- P4 medicine will be effective, inexpensive and provide enormous economic benefits to economies—readily available to poor and rich.
- The national healthcare debate in the future should be reframed around P4 medicine rather than the old reactive medicine.
Two Comments on the Economic Implications of the Systems Approaches to Big Problems in Biology
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• These opportunities will fuel enormous economic opportunities.
The Flattening of Many Worlds: Strategic Partnerships and the Globalization of Science

The worlds of systems science, technology, health are flattening. Tremendous opportunities for national and international strategic partnerships in science, technology and education to attack “Big Problems”.

- Network of interacting complementary, institutions
  - Training in systems biology and recruiting the best world talent

- Transferring and collaborating on new technologies and computational tools

- Strategic partnerships on systems approaches to biology and P4 medicine

- New patient populations

- New fundraising and commercialization opportunities