Genomics in Society: Genomics, Cellular Networks, Preventive Medicine, and Society

Guest Lecture to UCSD Medical and Pharmaceutical Students
Foundations of Human Biology--Lecture #41
UCSD
October 6, 2010

Dr. Larry Smarr
Director, California Institute for Telecommunications and Information Technology
Harry E. Gruber Professor,
Dept. of Computer Science and Engineering
Jacobs School of Engineering, UCSD
Follow me on Twitter: lsmarr

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Required Reading

- **Quantified Self**
  - www.xconomy.com/san-diego/2010/05/12/how-internet-pionee
- **Future of Personalized Preventive Medicine**
  - www.newsweek.com/2009/06/26/a-doctor-s-vision-of-the-futu
- **Personalized Genomic Sequencing**
  - www.technologyreview.com/biomedicine/25218/
  - www.mercurynews.com/business/ci_15580695
  - http://blogs.forbes.com/sciencebiz/2010/06/03/your-genome-is-coming

Genetics and Society Learning Objectives

- **Explain the relationships between genetics, disease and society**
- **List and explain the major issues concerning genetic testing for predisposition to disease**
- **Explain how measurements of an individual¹s chemical states relate to genetic testing and how both contribute to preventive medicine**
- **Explain how population health systems emerge from individuals' data**

Genetics and Society Learning Objectives

- **Explain the interactions between the genome, cellular networks, systems biology, and emergence of disease states**
- **Explain the difference between Single Nucleotide Polymorphism mapping and complete genomic maps and how each is used in medicine**
- **Present both sides of the debate over keeping a patient¹s genetic information private versus sharing data openly**
- **Vocabulary: SNP, genome, cellular networks, wireless, sensors, system biology, genetic testing, genome sequencers, quantified self**

- **Genetics, Disease, and Society**
- **Measuring the State of Your Body**
- **Genomics, Proteomics, and Cellular Networks**
- **Predictive, Personalized, Preventive, & Participatory Medicine**
- **The Rise of Individual and Societal Genomic Testing-Promise and Concerns**

Genomics is Only One Component for Living a Long Healthy Life

We Will Examine All These

Personalized
Life Extension Conference

October 9-10, 2010
San Francisco Airport Marriott

Strategies and Tactics for a Long Healthy Life



- ✓ Supplements
- ✓ DNA Testing
- ✓ Telomere Protection
- ✓ Blood Testing
- ✓ Finding a Life Extension Doctor
- ✓ Gadgets
- ✓ Inflammation
- ✓ Calorie Restriction & Intermittent Fasting
- ✓ Sleep
- ✓ Stress reduction
- ✓ Self-experimentation
- ✓ Exercise
- ✓ Enhancement & Brain Function
- ✓ Eating
- ✓ Standards of Information Quality
- ✓ Mood

READ MORE

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I am an invited speaker this weekend at:
http://lifeextensionconference.com/

it²

Genetics, Disease, and Society: Inherited Genetics Plus Environmental Variables



Centers for Disease Control and Prevention

Your Online Source for Credible Health Information

Most human disease results from a combination of inherited genetic variations and environmental factors (such as lifestyle, social conditions, chemical exposures, and infections).

Thanks to the genome-based tools now available to public health researchers, we can study how and where disease occurs in populations and families using biological markers (e.g., genes) that can help identify exposures, susceptibilities, and effects.

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www.cdc.gov/genomics/population/

it²

Genomics Plays a Role in 9 of the 10 Leading Causes of Death in the U.S., most Notably Cancer & Heart Disease

Number of deaths for leading causes of death:

- Heart disease: 616,067
- Cancer: 562,875
- Stroke (cerebrovascular diseases): 135,952
- Chronic lower respiratory diseases: 127,924
- Accidents (unintentional injuries): 123,706
- Alzheimer's disease: 74,632
- Diabetes: 71,382
- Influenza and Pneumonia: 52,717
- Nephritis, nephrotic syndrome, and nephrosis: 46,448
- Septicemia: 34,828

Source: Deaths: Final Data for 2007, tables B, D, 7, 30

Leading Causes of Preventable Deaths in the United States in the Year 2000



Cause	Number of deaths resulting
Tobacco Smoking	435,000 deaths or 18.1% of the total deaths
Overweight and Obesity	365,000 deaths or 15.2% of the total deaths.
Alcohol consumption	85,000 deaths or 3.5% of the total deaths.
Infectious diseases	75,000 deaths or 3.1% of the total deaths.
Toxicants	55,000 deaths or 2.3% of the total deaths.
Traffic collisions	43,000 deaths or 1.8% of the total deaths.
Incidents involving firearms	29,000 deaths or 1.2% of the total deaths.
Sexually transmitted diseases	20,000 deaths or 0.8% of the total deaths.
Drug abuse	17,000 deaths or 0.7% of the total deaths.

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Mokdad AH, Marks JS, Stroup DF, Gerberding JL (March 2004). "Actual causes of death in the United States, 2000". JAMA 291 (10): 1238–45. doi:10.1001/jama.291.10.1238. PMID 15010446. www.csdp.org/research/1238.pdf.

it²

Wireless, Clinical, and Home Technologies to Measure & Improve Lifestyle and Other Health-Related Behaviors

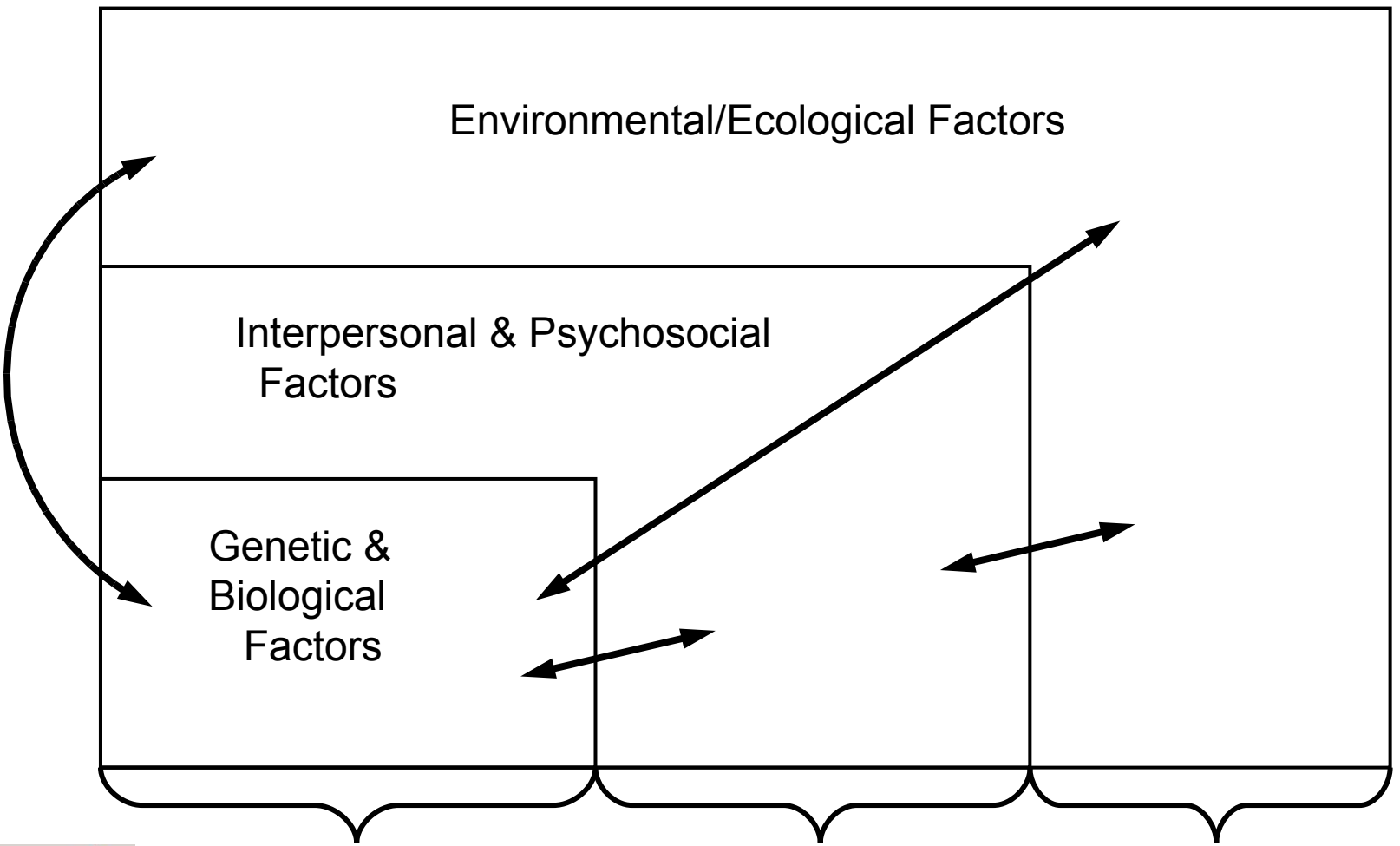
- Healthy Adolescents
- Adolescents Recovering from Leukemia
- Adolescents at Risk for Type 2 Diabetes
- Young Adults to Prevent Weight Gain
- Overweight and Obese Children and Adults
- Depressed Adults
- Post-Partum Women to Reduce Weight
- Adults with Schizophrenia
- Older Adults to Promote Successful Aging
- Exposure Biology Research

Center for Wireless & Population Health Systems: Cross-Disciplinary Collaborating Investigators

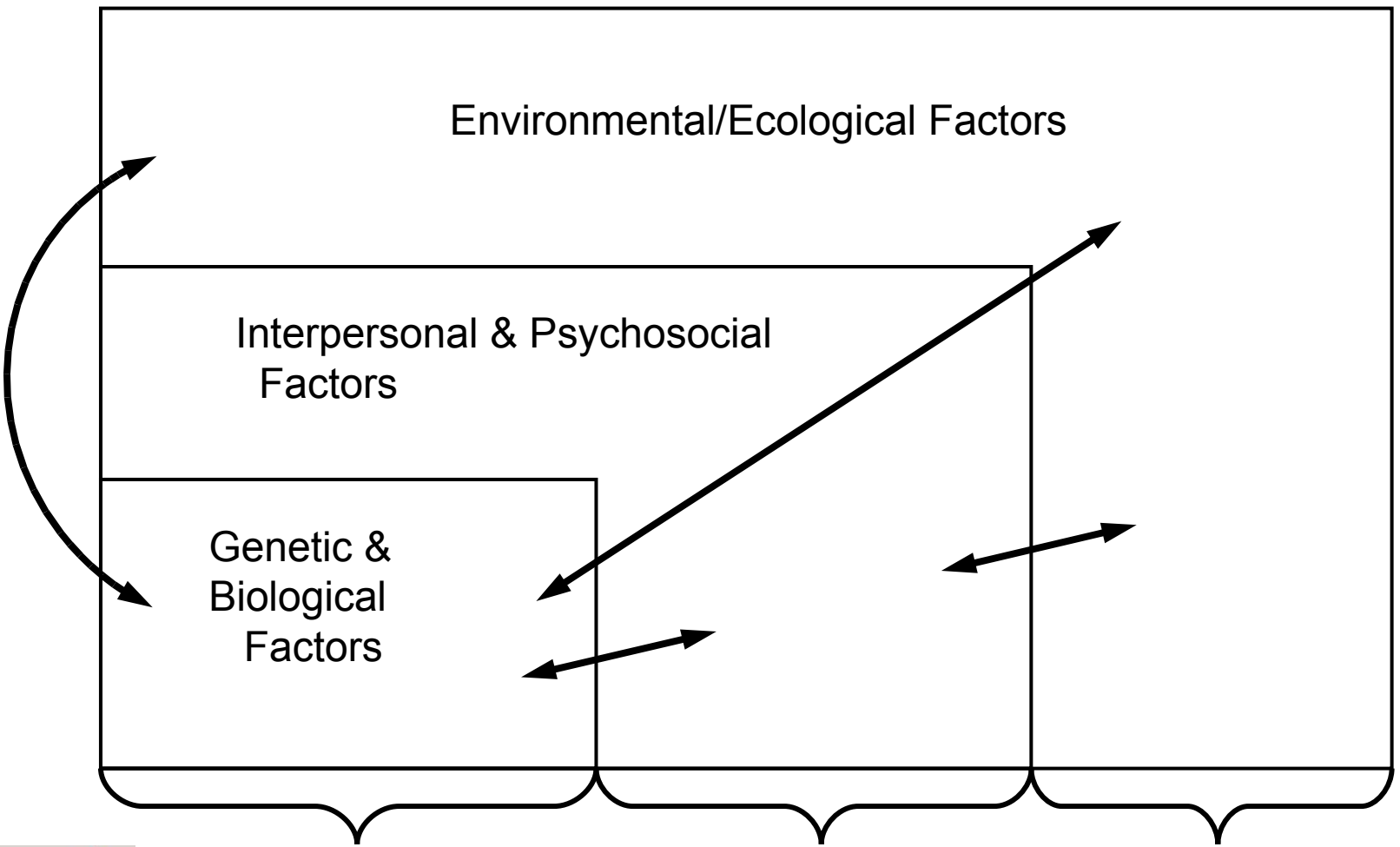
- **UCSD School of Medicine**
  - Kevin Patrick, MD, MS, Greg Norman, PhD, Fred Raab, Jacqueline Kerr, PhD
  - Jeannie Huang, MD, MPH
- **UCSD Jacobs School of Engineering**
  - Bill Griswold, PhD, Ingolf Krueger, PhD, Tajana Simunic Rosing, PhD
- **San Diego Supercomputer Center**
  - Chaitan Baru, PhD
- **UCSD Department of Political Science**
  - James Fowler, PhD
- **SDSU Departments of Psychology & Exercise/Nutrition Science**
  - James Sallis, PhD, Simon Marshall, PhD
- **Santech, Inc.**
  - Sheri Thompson, PhD, Jennifer Shapiro, PhD, Ramesh Venkatraman, MS
- **PhD students and Post-doctoral Fellows (current)**
  - Barry Demchak, Priti Aghera, Ernesto Ramirez, Laura Pina, Jordan Carlson

http://cwphs.ucsd.edu

Center for Wireless & Population Health Systems: Integrative View to Support Interventions



Center for Wireless &Population Health Systems: Developing and Testing Engineering-Based Solutions

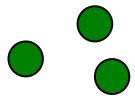


NanoTech, Drug Delivery, Sensors, Body Area Networks (BANs)

BAN-to-Mobile-to-Database, SMS/MMS Social networks

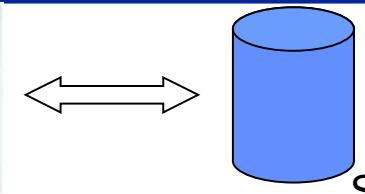
Ubicomp, Location-Aware Services, Data Mining, Systems Sciences

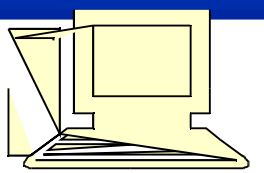
Center for Wireless &Population Health Systems: Mainly, It's All About Sensors



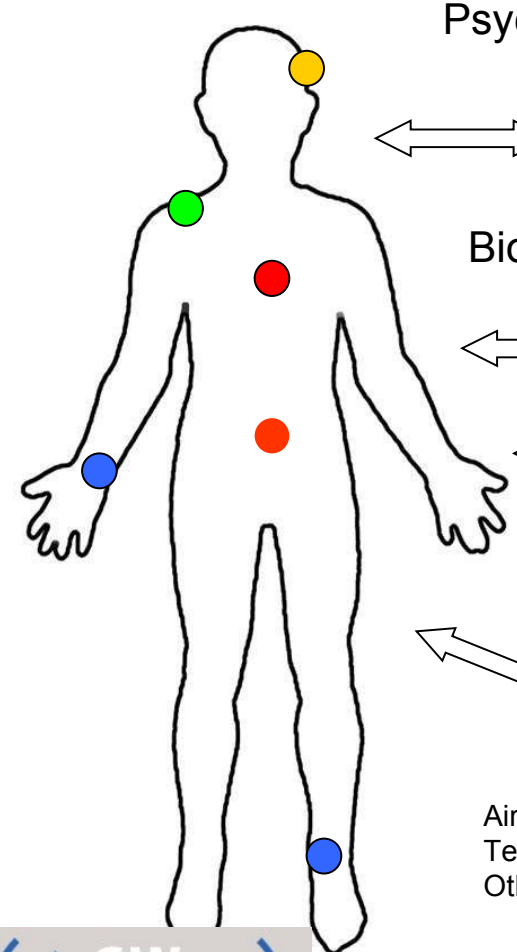
Geocoded data on safety, location of recreation, food, hazards, etc







Sensor data
+
Clinical & Personal Health Record Data
+
Ecological data on determinants of health
+
Analysis & comparison of parameters in near-real time (normative and ipsative)
+
Sufficient population-level data to comprehend trends, model them and predict health outcomes
+
Feedback in near real-time via SMS, audio, haptic or other cues for behavior or change in Rx device



Psychological & Social sensors
Mood, Social network (peers/family)
Attention, voice analysis

Biological sensors
BP, Resp, HR, Blood (e.g. glucose, electrolytes, pharmacological, hormone), Transdermal, Implants

Diet & Physical Activity sensors
Physical activity (PAEE, type), sedentary
Posture/orientation, diet intake (photo/bar code)

Wearable Environmental sensors
Air quality (particulate, ozone, etc)
Temperature, GPS, Sound, Video,
Other devices & embedded sensors

= True Preventive Medicine!

CW PHS
Center For Wireless & Population Health Systems

it2

Measuring the State of Your Body: Learning to "Tune" Your Body Using Nutrition and Exercise

www.xconomy.com/san-diego/2010/05/12/how-internet-pioneer-larry-smarr-lost-20-pounds-by-becoming-a-quantified-self/

HEALTH IT, PEOPLE, WIRELESS

How Internet Pioneer Larry Smarr Lost 20 Pounds by Becoming a "Quantified Self"

Luke Timmerman 5/12/10



2000



2010

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Wireless Sensors Allow Your Body to Become an Internet Data Source

- **Next Step—Putting You On-Line!**
  - Wireless Internet Transmission
  - Key Metabolic and Physical Variables
  - Model -- Dozens of 25 Processors and 60 Sensors / Actuators Inside of our Cars

www.bodymedia.com

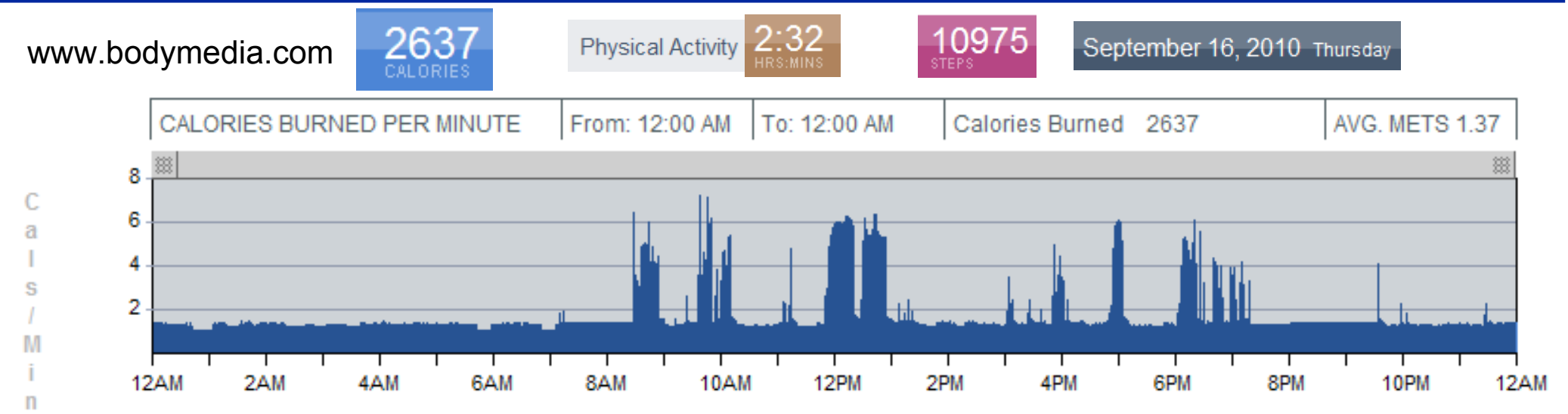


- **Post-Genomic Individualized Medicine**
  - Combine
    - Genetic Code
    - Body Data Flow
  - Use Powerful AI Data Mining Techniques

Nine Years Later I Am Recording My Metabolic Self

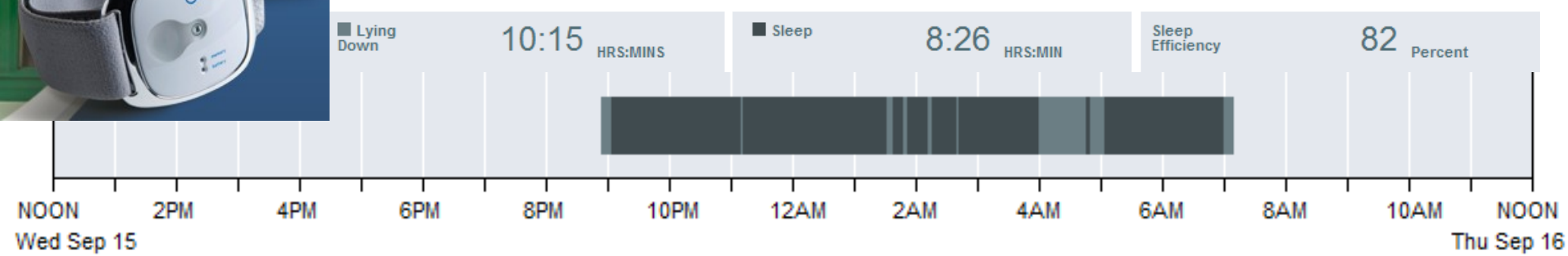
BODYMEDIA® Know your Body. Change your life

www.bodymedia.com





7 Week Ave:
2550 Calories Burned/Day
1:31 hr Physical Activity/Day (>3 METs)
7755 Steps/Day (~3.9 Miles)



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Measure Quantity and Quality of Sleep--
7 Week Ave: 6:55 hrs with 81% Efficiency

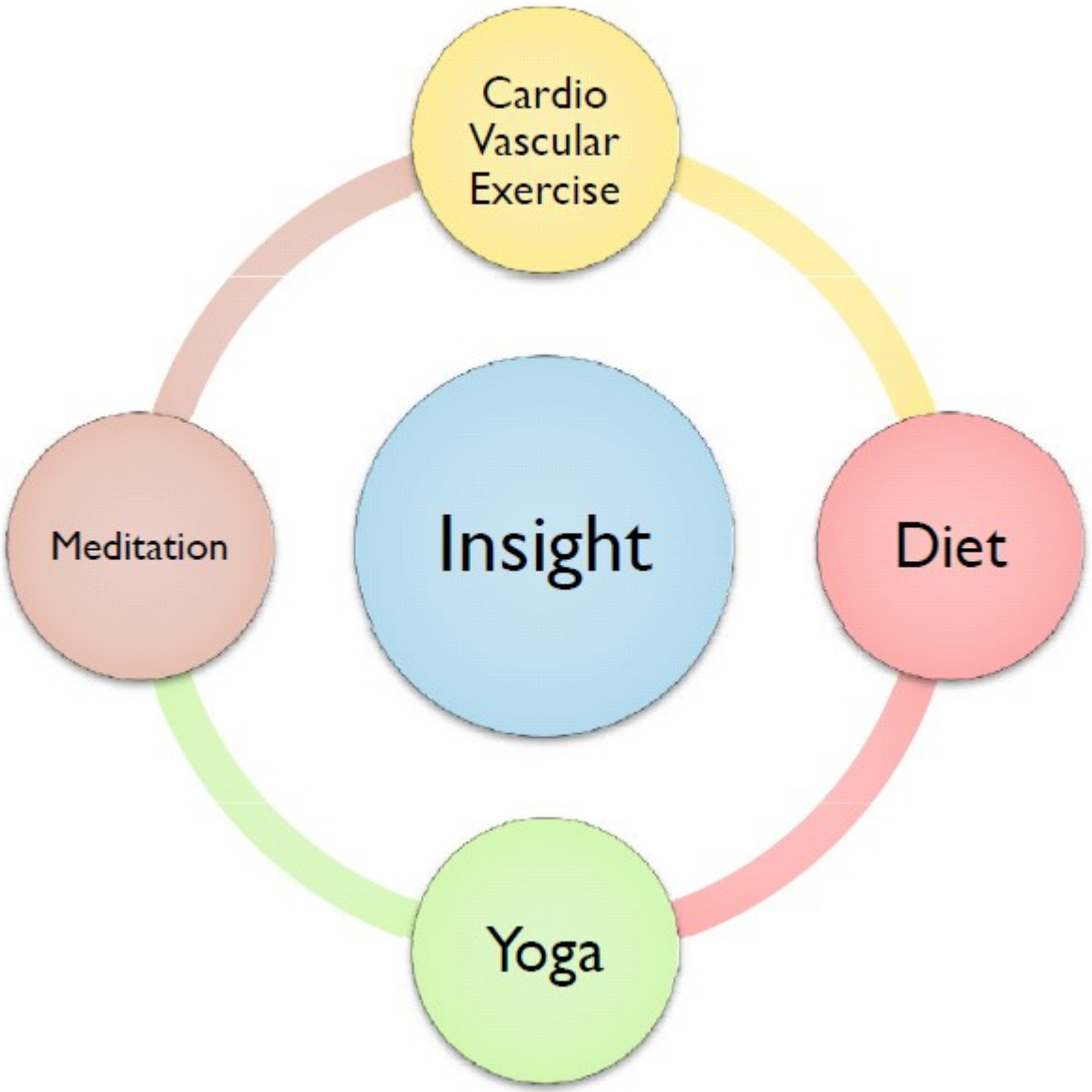
it²

Analyzing Your Food Intake is Critical for"Tuning" Your Body

12 Day Average

calories	fat	carb	protein		fiber	sugar	sodium
kcal	g	g	g		g	g	mg
1441	46	122	80	0	26	53	1358

The Impact on Personal Health from Nutrition, Exercise, Stress Management



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Measuring Key Molecules in the Blood Provides Longer Term Biofeedback

	Mar-08	May-08	Dec-08	Feb-09	Jun-09	Target
LDL	151	103	89	82	86	< 130
HDL	42	42	62	59	71	≥ 40
Triglycerides	223	100	57	81	60	< 150
hsCRP		3.4		0.5	0.7	< 1
Homocysteine		21.5		8.5		< 15
Lipoprotein(A)		62		51.2		< 30 or < 50 or < ?

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Source: Ramesh Rao, Calit2

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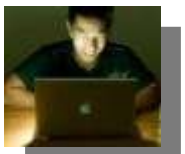
CitiSense:
Air Pollution Case Study

- 158 Million Live in Counties Violating Air Standards
  - Cancer in Chula Vista, CA Increased 140/Million Residents
  - Largely Due to Diesel Trucks and Automobiles
    - Particulates, Benzene, Sulfur Dioxide, Formaldehyde, etc.
- 30% of Public Schools Are Near Highways
  - Asthma Rates 50% Higher There
  - 350,000 – 1,300,000 Respiratory Events in Children Annually
- 5 EPA Monitors in SD Co., 4000 Sq. Mi., 3.1M Residents
  - But Air Pollution Not Uniformly Distributed in Space or Time
  - Hourly Updates to Web Page; Annual Reports in PDF Form
- Indoor Air Pollution is Uncharted Territory
  - Second-hand Smoke is Major Concern
  - Also Mold, Radon

CitiSense -



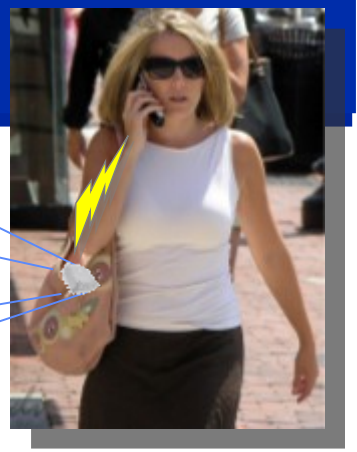
4oz
30 compounds

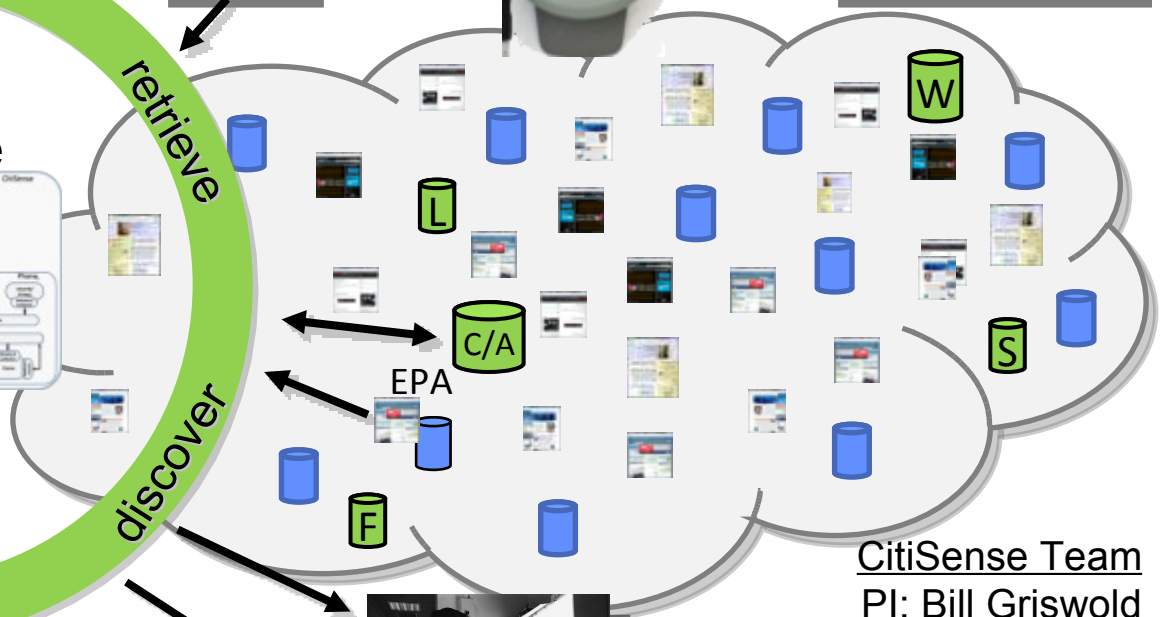


Seacoast Sci.

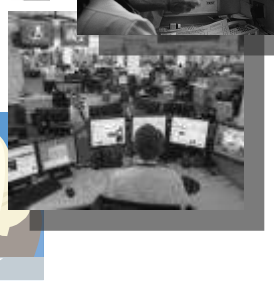


Intel MSP





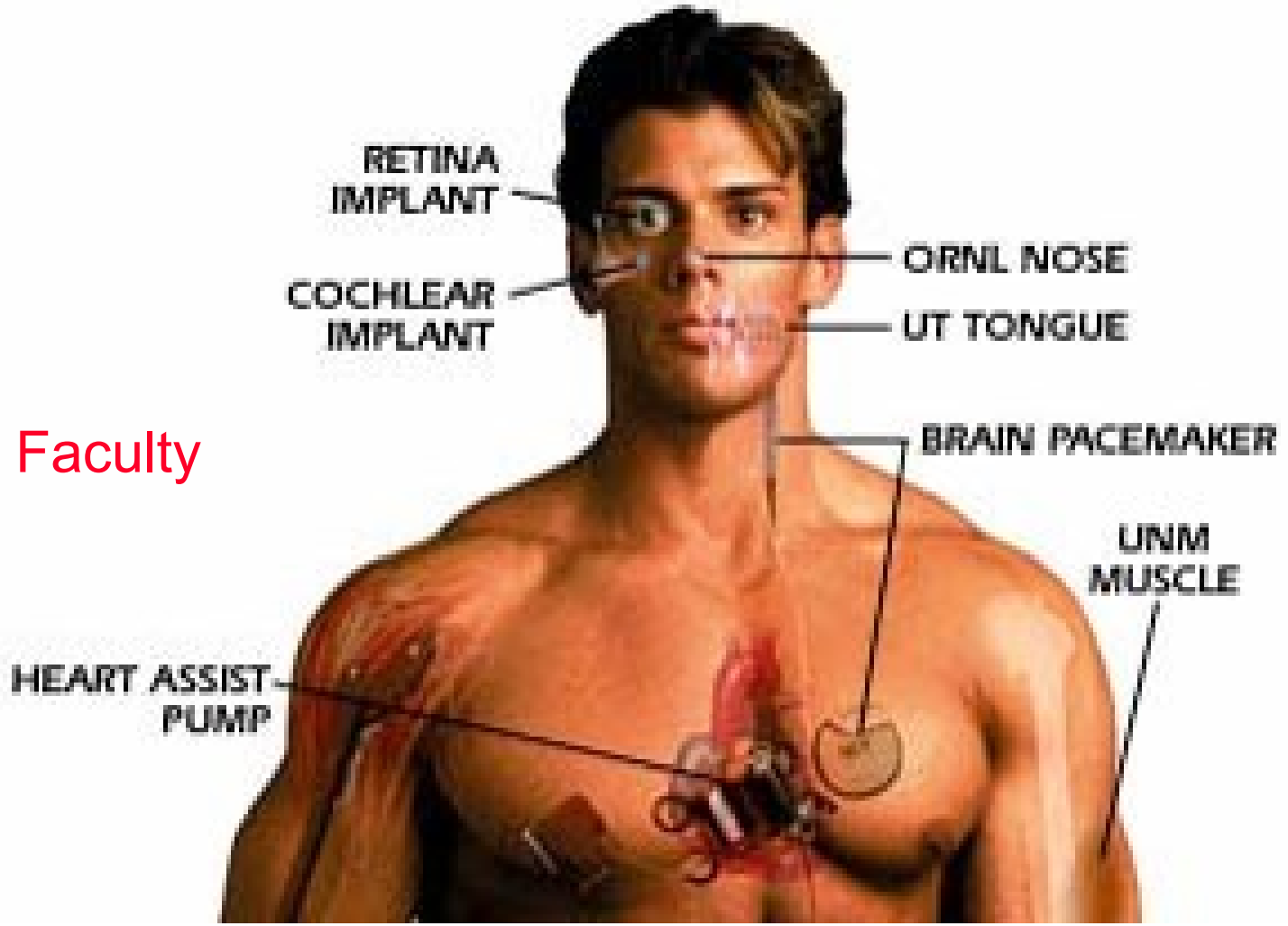




CitiSense Team
PI: Bill Griswold
Ingolf Krueger
Tajana Simunic Rosing
Sanjoy Dasgupta
Hovav Shacham
Kevin Patrick

Lifechips--Merging Two Major Industries: Microelectronic Chips & Life Sciences

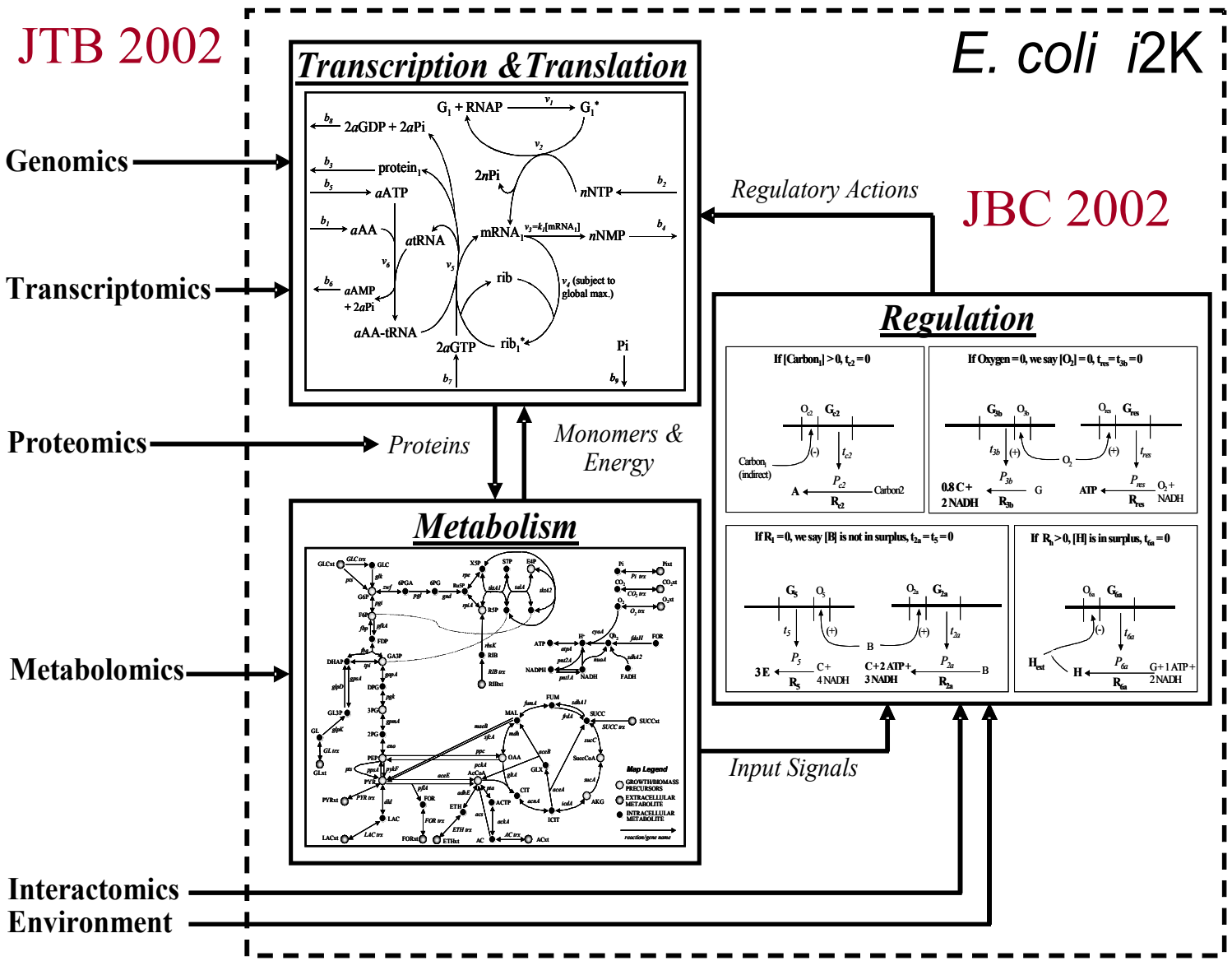
65 UCI Faculty



lifechips
university of california, irvine
www.lifechips.org

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Genomics, Proteomics, and Cellular Networks: Building a Genome-Scale Model of E. Coli *in Silico*



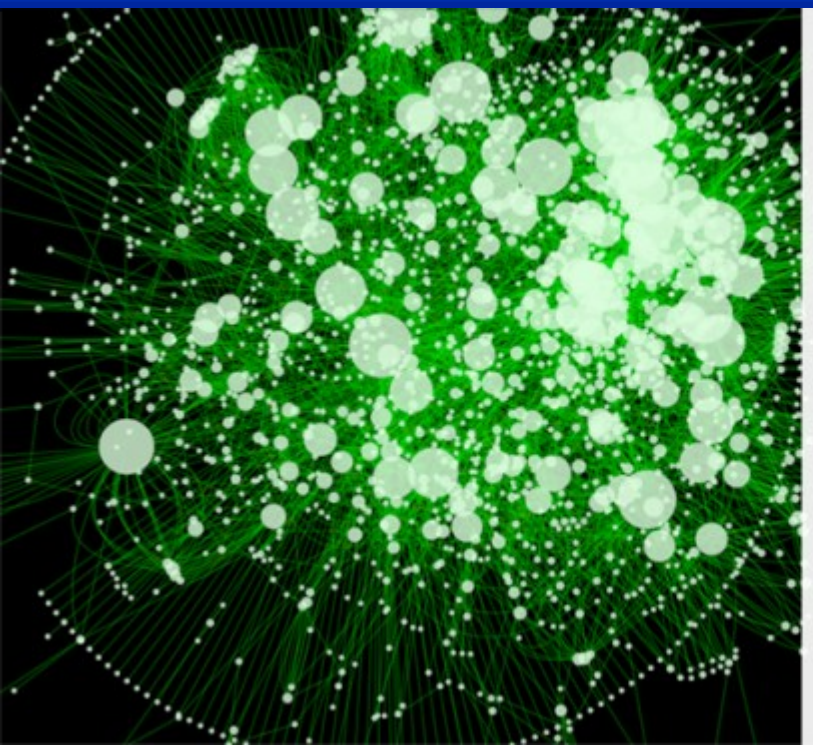
- **E. Coli**
  - **Has 4300 Genes**
  - **Model Has 2000!**

in Silico Organisms Now Available 2007:

- Escherichia coli
- Haemophilus influenzae
- Helicobacter pylori
- Homo sapiens Build 1
- Human red blood cell
- Human cardiac mitochondria
- Methanosarcina barkeri
- Mouse Cardiomyocyte
- Mycobacterium tuberculosis
- Saccharomyces cerevisiae
- Staphylococcus aureus

Source: Bernhard Palsson
UCSD Genetic Circuits Research Group
http://gcrg.ucsd.edu

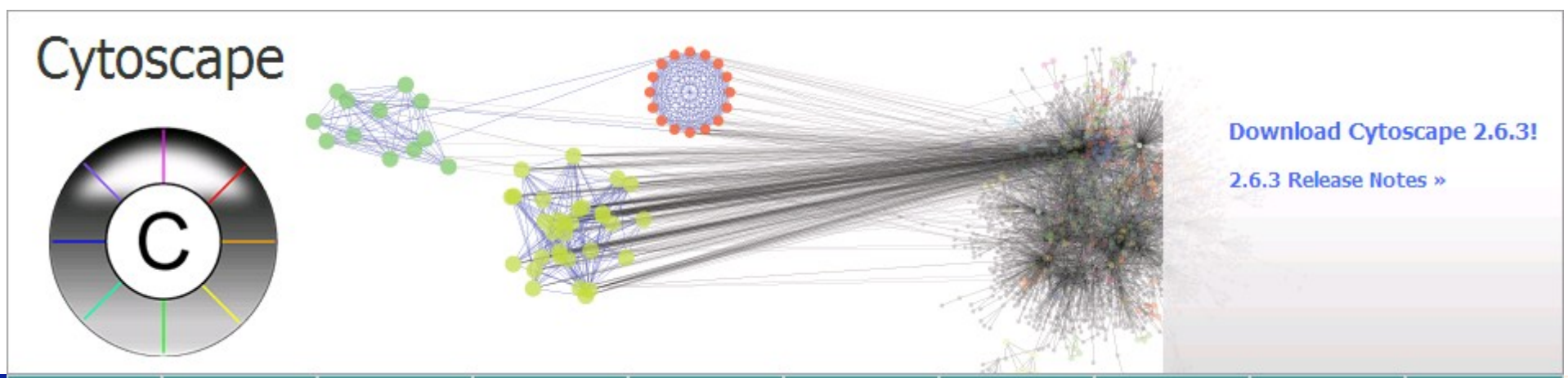
Integrating Systems Biology Data: Cytoscape



Cytoscape

An Open Source Platform for Network Analysis and Visualization

- **OPEN SOURCE Java Platform for Integration of Systems Biology Data**
- **Layout and Query of Interaction Networks (Physical And Genetic)**
- **Visual and Programmatic Integration of Molecular State Data (Attributes)**



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www.cytoscape.org

it²

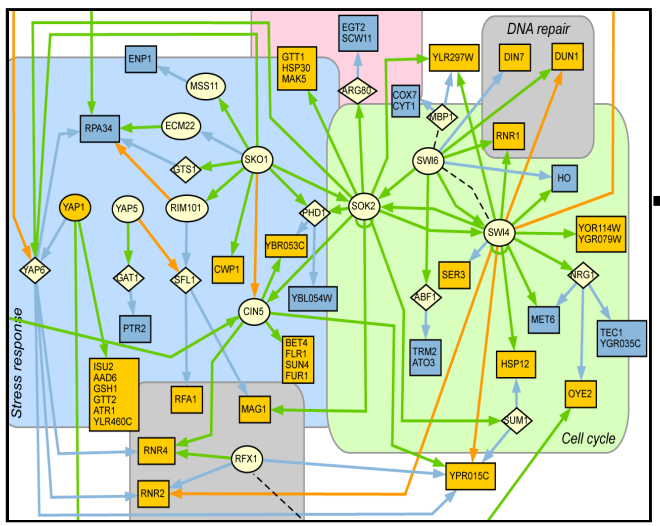
Research in the UCSD Ideker Systems Biology Lab

Network Evolutionary Comparison / Cross-Species Alignment to Identify Conserved Modules

Projection of Molecular Profiles on Protein Networks to Reveal Active Modules

Validation of Transcriptional Interactions With Causal or Functional Links

Alignment of Physical and Genetic Networks



Network-Based Disease Diagnosis / Prognosis

Network-Based Rationale Drug Design

Moving from Genome-wide Association Studies (GWAS) to Network-wide "Pathway" Association (PAS)

Network Assembly from Genome-Scale Measurements

Network Based Study of Disease

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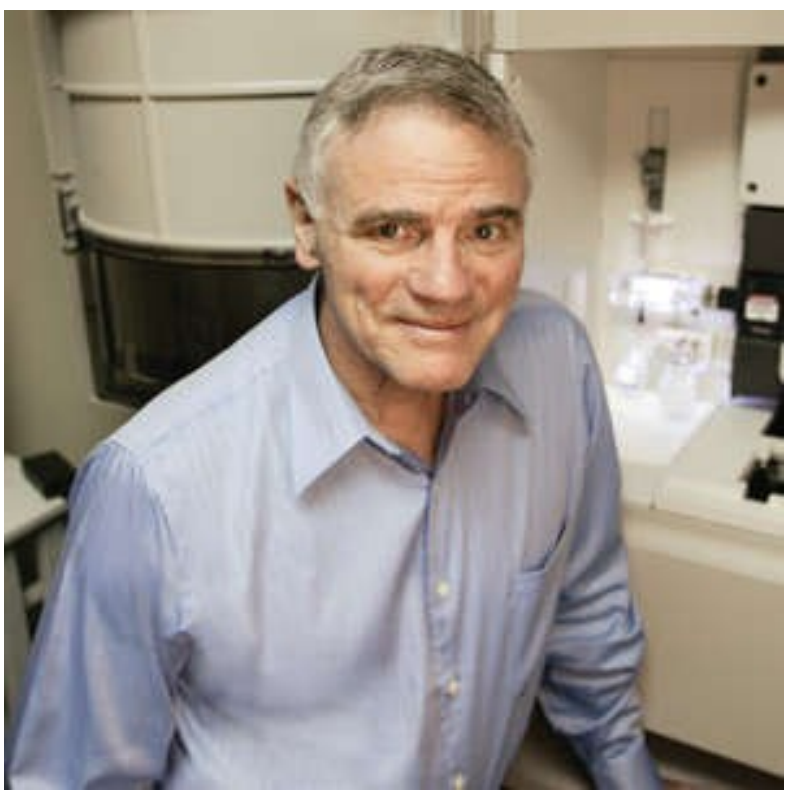
Predictive, Personalized, Preventive, & Participatory Medicine

Newsweek

A Doctor's Vision of the Future of Medicine

Leroy Hood
NEWSWEEK

From the magazine issue dated Jul 13, 2009

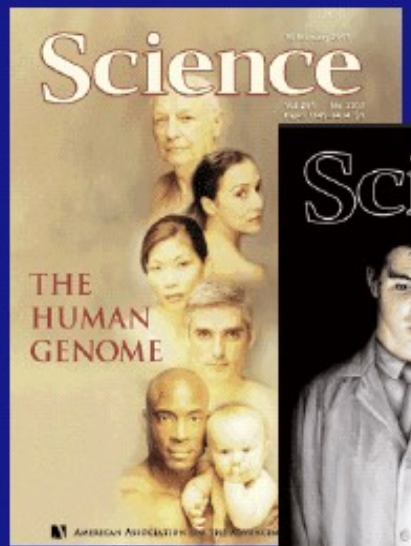


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www.newsweek.com/2009/06/26/a-doctor-s-vision-of-the-future-of-medicine.html

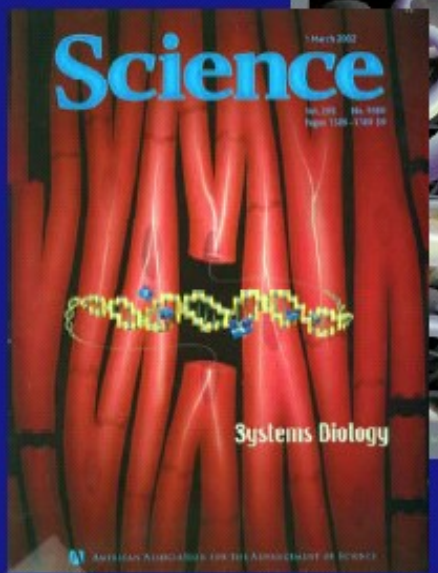
it²

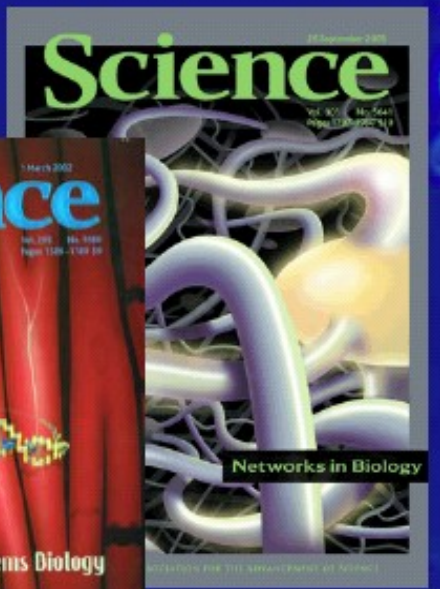
A Grand Convergence





Complexity: Biology is an Information Science

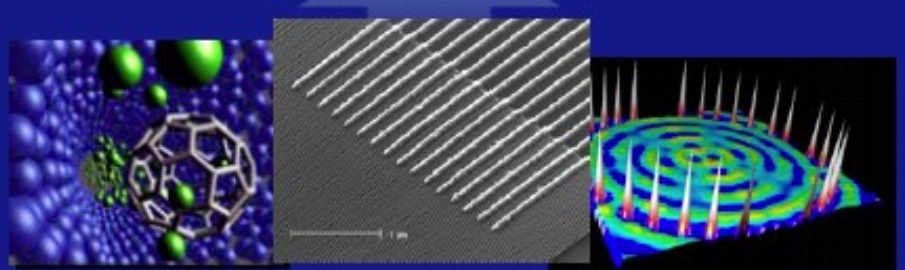




Genetics, genomics

Predictive
Personalized
Preventive
Participatory
Medicine

Systems biology

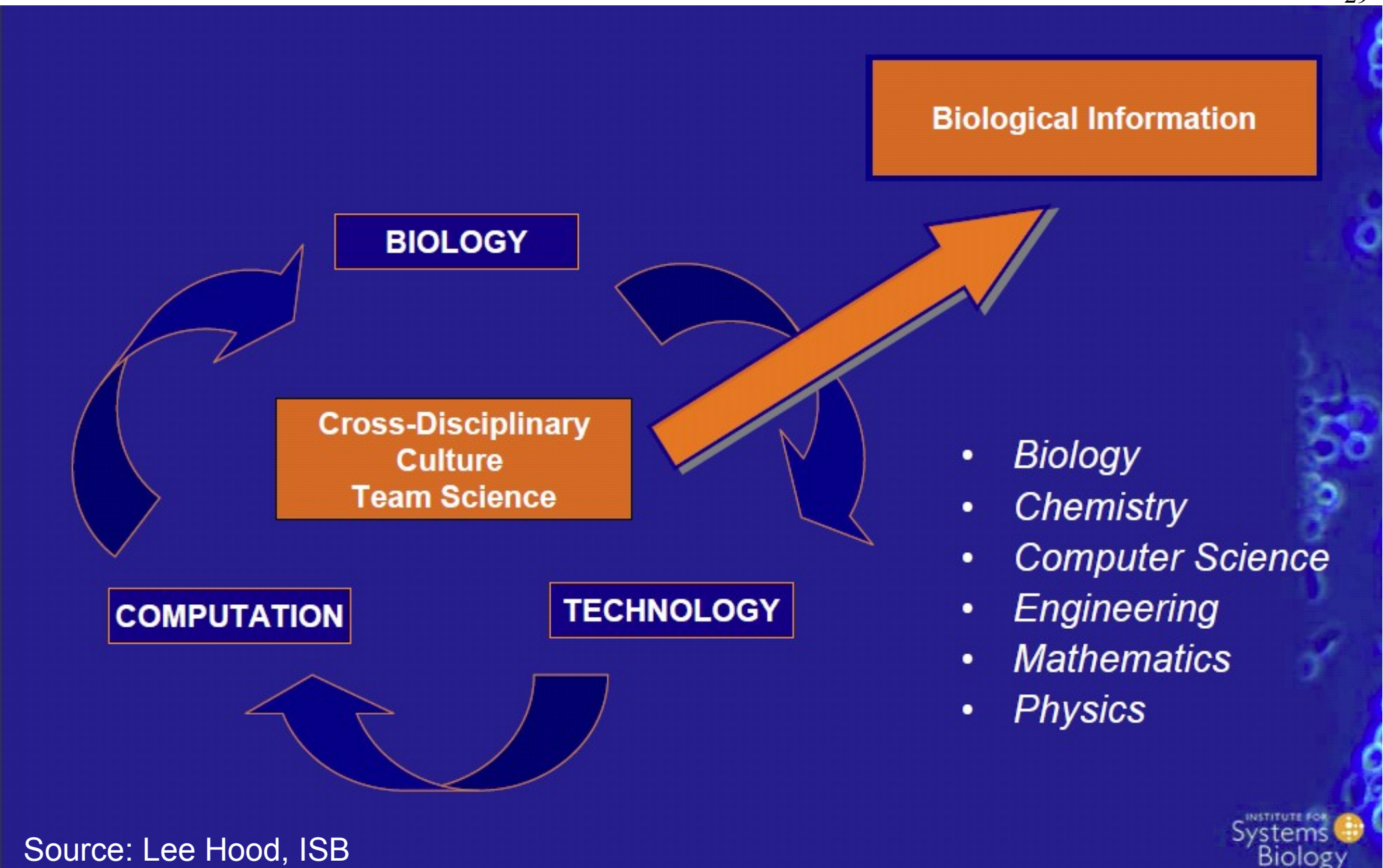


Nanotechnology

Source: Lee Hood, ISB

INSTITUTE FOR Systems Biology

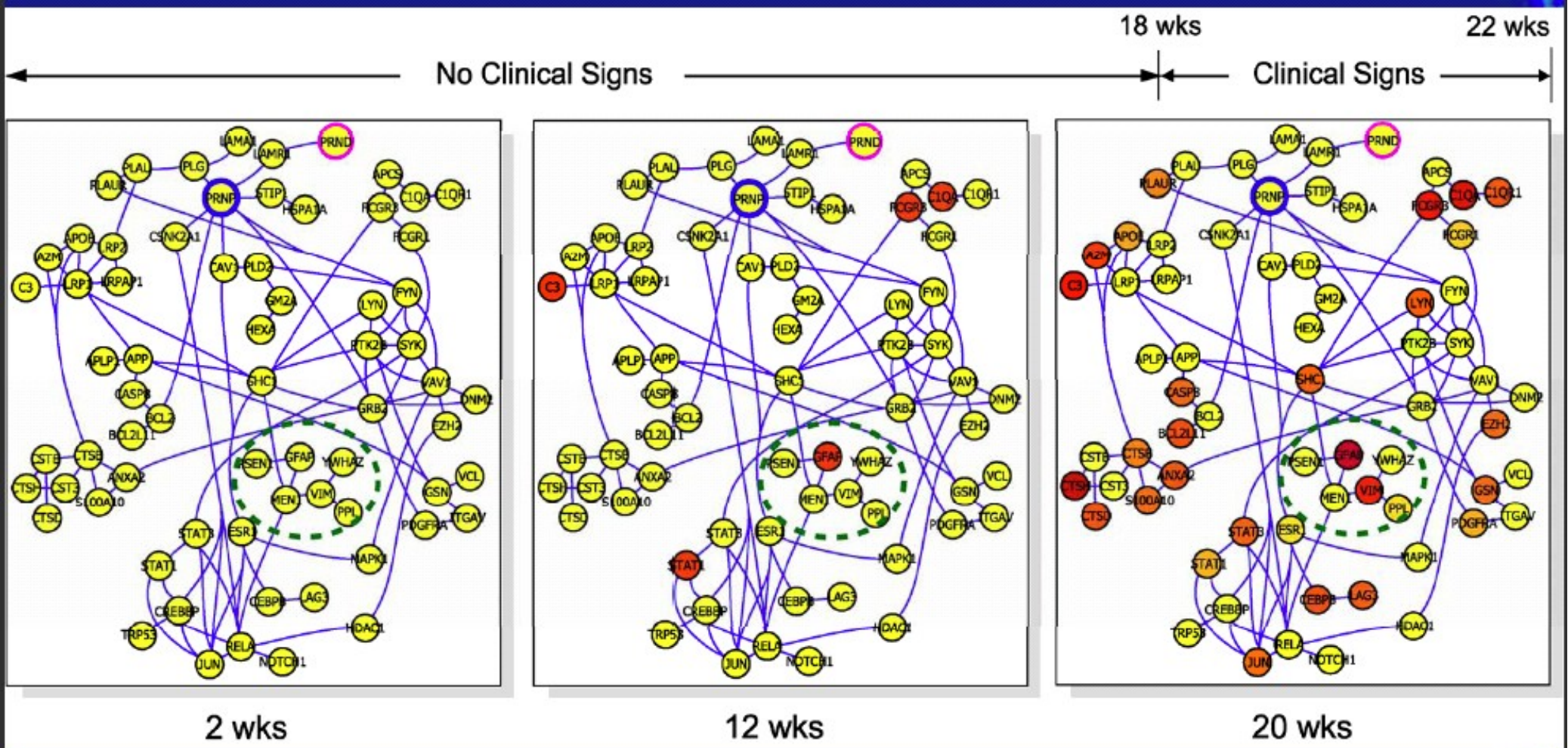
Use Biology to Drive Technology and Computation. Need to Create a Cross-disciplinary Culture



Source: Lee Hood, ISB

INSTITUTE FOR Systems Biology

Disease Arises from Perturbed Cellular Networks: Dynamics of a Prion Perturbed Network in Mice

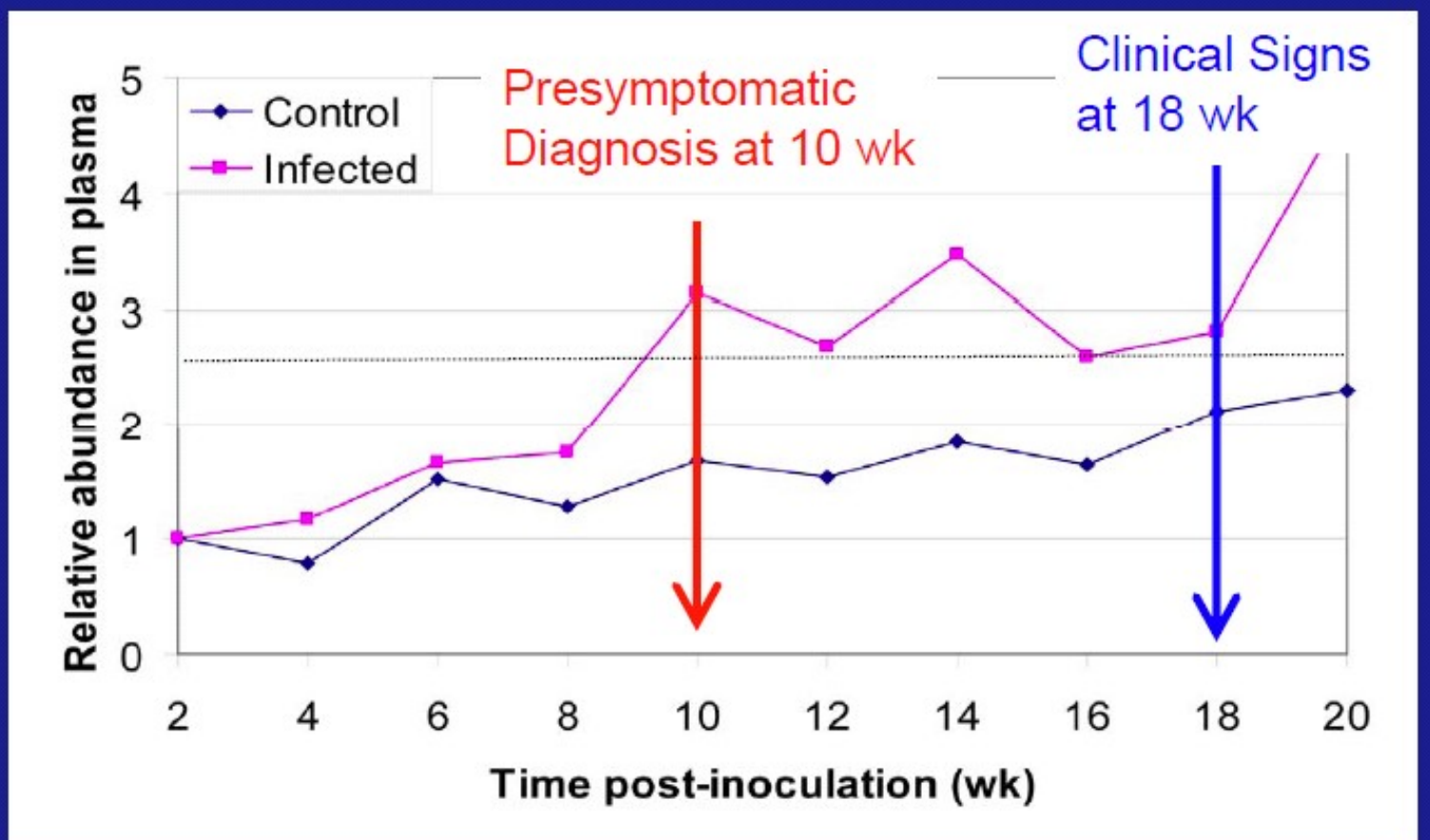


Source: Lee Hood, ISB

Institute for Systems Biology

Increasing Abundance of Protein A for Prion-Infected Blood Samples

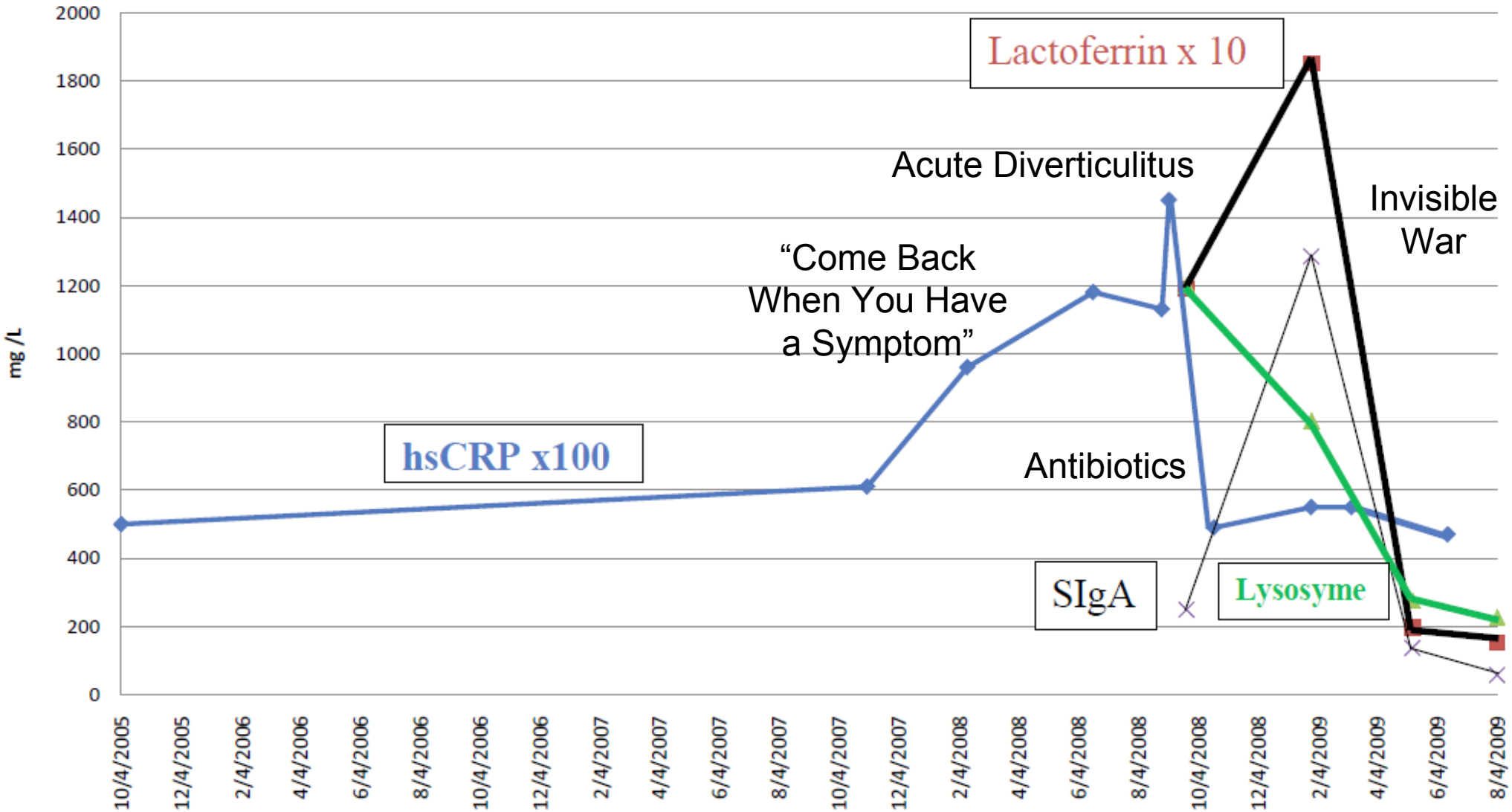
Dynamic change in relative abundance of "Protein A"



Source: Lee Hood, ISB

INSTITUTE FOR Systems Biology

Current Medical Care Relies on "Symptoms," Not Preventive Quantitative Measurements



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Organ-Specific Blood Proteins Will Make the Blood a Window into Health and Disease

Source: Lee Hood, ISB

- **Perhaps 50 Major Organs or Cell Types**
  - **Each Secreting Protein Blood Molecular Fingerprint**
- **The Levels of Each Protein in a Particular Blood Fingerprint Will Report the Status of that Organ**
  - **Probably Need Perhaps 50 Organ-Specific Proteins Per Organ**
- **Will Need to Quantify 2500 Blood Proteins from a Drop of Blood**
  - **Use Microfluidic/Nanotechnology Approaches**

Key Point: Changes in The Levels Of Organ-Specific Markers Can Assess Virtually All Disease Challenges for a Particular Organ

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The Rise of Individual and Societal Genomic Testing-Promise and Concerns

Technology PUBLISHED BY MIT Review

How Personal Genomics Could Change Health Care

The select few who have had their genomes sequenced learn to use that information for health care.

By Emily Singer

FRIDAY, APRIL 30, 2010

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www.technologyreview.com/biomedicine/25218/

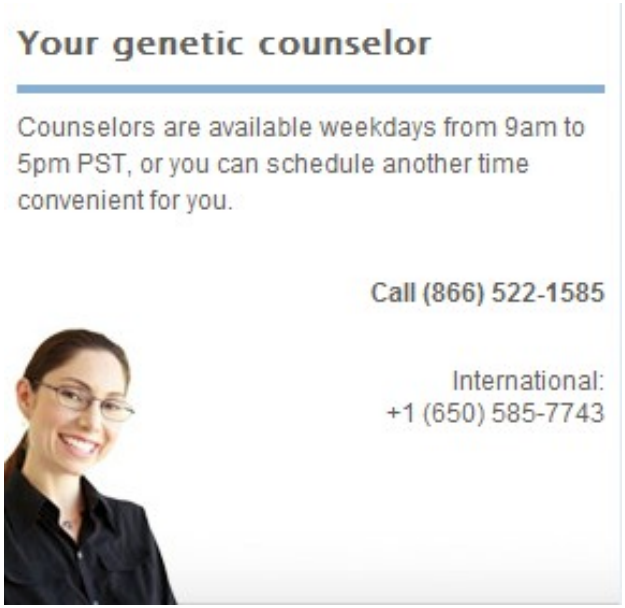
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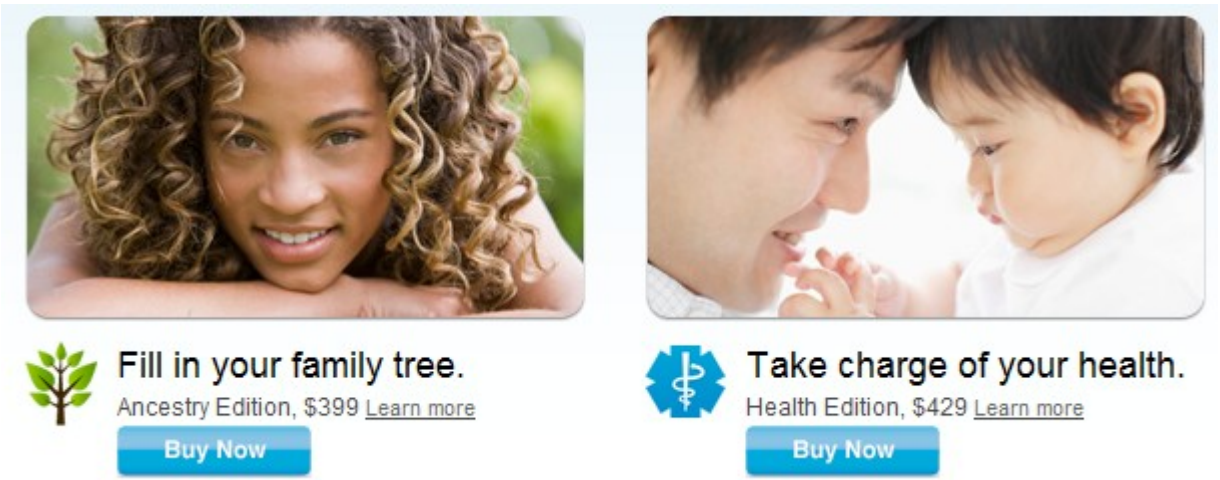
Single Nucleotide Polymophisms (SNPs)

www.ornl.gov/sci/techresources/Human_Genome/faq/snps.shtml#snps

- **DNA sequence variations that occur when a single nucleotide (A,T,C,or G) in the genome sequence is altered**
  - **Example: DNA sequence AAGGCTAA to ATGGCTAA**
- **For a variation to be considered a SNP, it must occur in at least 1% of the population**
- **SNPs make up about 90% of all human genetic variation**
- **SNPs occur every 100 to 300 bases along the 3-billion-base human genome**
- **Many SNPs have no effect on cell function, but scientists believe others could predispose people to disease or influence their response to a drug**

The Promise and Controversy of Personal SNP Genomics





Navigenics, 23andMe slammed in government report

By Steve Johnson
sjohnson@mercurynews.com
Posted: 07/22/2010 09:18:19 PM PDT
Updated: 07/24/2010 04:06:35 AM PDT

Silicon Valley MercuryNews.com

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www.mercurynews.com/business/ci_15580695

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Risk of Disease Results From SNPs Mainly Reveal Average Risks – Are They Consistent?



0 - 1%	>1 - 10%	>10 - 25%	>25 - 50%	>50 - 100%
Graves' disease You: 0.93% Avg: 0.55%	Lung cancer You: 8% Avg: 8%	Prostate cancer You: 17% Avg: 17%	Osteoarthritis You: 44% Avg: 40%	You have no results in this range
Glaucoma You: 0.78% Avg: 1.1%	Colon cancer You: 6% Avg: 6%	Diabetes, type 2 You: 12% Avg: 25%	Heart attack You: 38% Avg: 42%	
Macular degeneration You: 0.74% Avg: 3.1%	Psoriasis You: 6% Avg: 4.0%		Obesity You: 32% Avg: 34%	

You: 1.7%
Avg. 3.0%

You: 22.4%
Avg. 11.4%

You: 14.7%
Avg. 23.7%

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However, SNP Indications of Adverse Drug Side Effects May Be Quite Useful

Navigenics

23andMe

Side Effects

Drug	Your Risk	Side Effect	
Abacavir (Ziagen®) Used to treat HIV infection	High Risk	Severe allergic reaction, including fever, rash, and nausea	Increased Risk
Floxacillin (Floxapen®) Used to treat infections	High Risk	Severe liver toxicity, leading to liver damage	Greatly Increased Risk

I Would Definitely Not Take Either!

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The Cost for Full Human Genome Sequencing is Exponentially Decreasing

Forbes

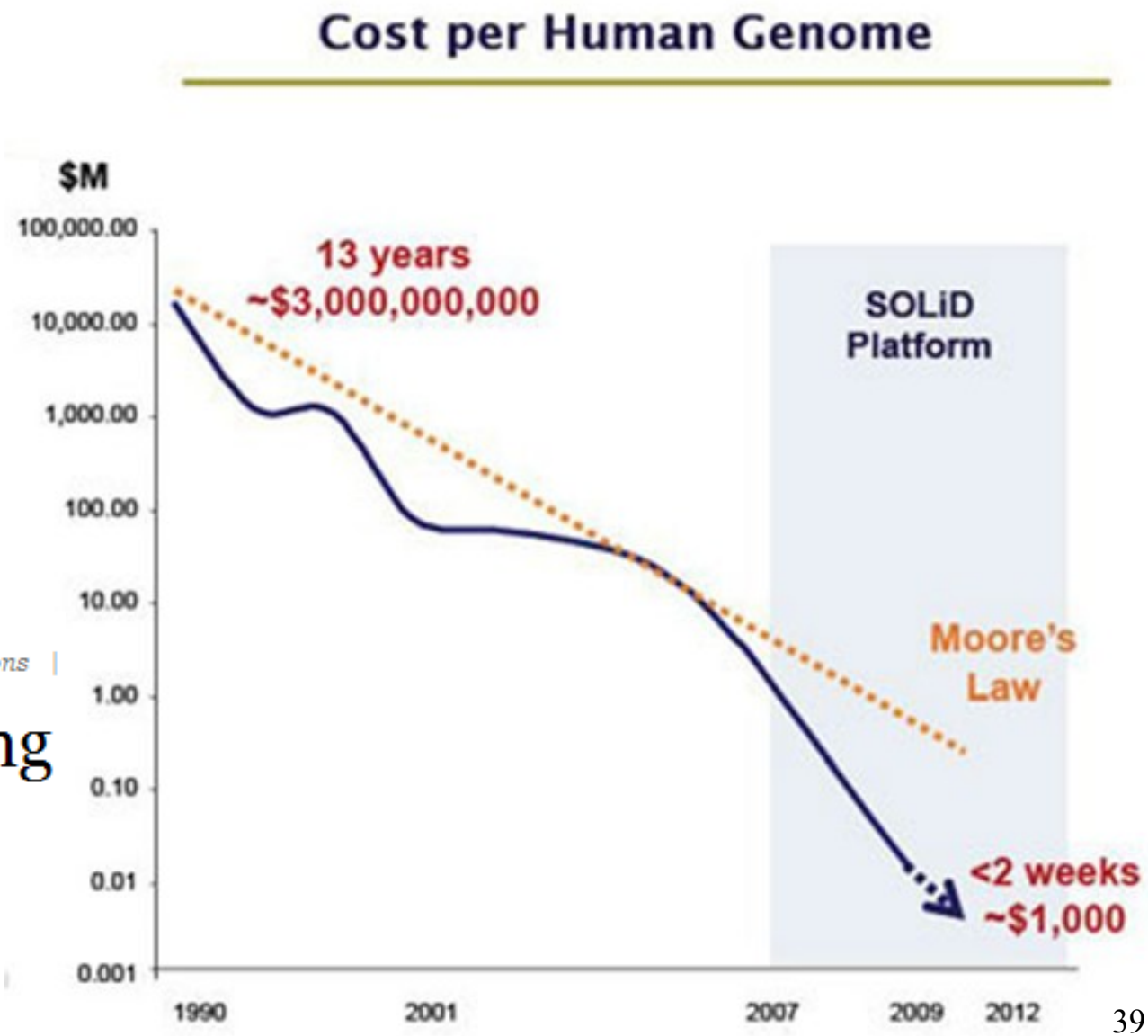


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Your Genome Is Coming

posted by **MATTHEW HERPER**



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http://blogs.forbes.com/sciencebiz/2010/06/03/your-genome-is-coming/

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The Promise of Whole Genome Sequencing Combined with Family Testing

Science 30 April 2010:
Vol. 328. no. 5978, pp. 636 - 639
DOI: 10.1126/science.1186802

REPORTS

Analysis of Genetic Inheritance in a Family Quartet by Whole-Genome Sequencing

Jared C. Roach,[1,*] Gustavo Glusman,[1,*] Arian F. A. Smit,[1,*] Chad D. Huff,[1,2,*] Robert Hubley,[1] Paul T. Shannon,[1] Lee Rowen,[1] Krishna P. Pant,[3] Nathan Goodman,[1] Michael Bamshad,[4] Jay Shendure,[5] Radoje Drmanac,[3] Lynn B. Jorde,[2] Leroy Hood,[1,†] David J. Galas[1,†]

- **We analyzed the whole-genome sequences of a family of four, consisting of two siblings and their parents.**
- **Both offspring in this family have two recessive disorders: Miller syndrome, for which the gene was concurrently identified**
- **Family-based genome analysis enabled us to narrow the candidate genes for both of these Mendelian disorders to only four.**
- **Our results demonstrate the value of complete genome sequencing in families.**

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www.sciencemag.org/cgi/content/abstract/328/5978/636?rss=1

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Should You Keep Your Health Data Private or Share to Gain the Most Knowledge?

U.S. Department of Health & Human Services
HHS.gov *Improving the health, safety, and well-being of America*

The Health Insurance Portability and Accountability Act of 1996 (HIPAA) Privacy and Security Rules

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Trusera is an online health network platform where you can find and share real-world experiences. Share your story and experience the Power of Been There™.

patientslikeme®

Share Your Health Profile

By openly sharing your health profile with the community, you can learn more about yourself while helping other patients like you.

Social Networks and Health NEXT

Medicine 2.0 #10 – Medicine and the Second Generation of Internet-based Services

by Walter Jessen

Quantified Self
tools for knowing your own body and mind

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