Towards Digitally Enabled Genomic Medicine: the Patient of The Future

Invited Speaker
Hacking Life
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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
http://lsmarr.calit2.net
Calit2 has, for over a decade, had a driving vision that healthcare is being transformed into digitally enabled genomic medicine. To put a more personal face on the "patient of the future," I have been increasingly quantifying my own body over the last ten years. This involves not only non-invasive macro-variables such as weight, pulse, blood pressure, caloric intake and burn, but also invasive blood, saliva, and stool measurements. I currently track over 100 molecular and blood cell types in my blood and dozens of molecular and microbial variables in my stool. Through saliva I have 1 million single nucleotide polymorphisms (SNPs) in my human DNA. My gut microbiome is currently being genetically sequenced. I will show how one can discover emerging disease states before they develop serious symptoms by graphing time series of these key variables. Also I will illustrate the power of multi-variant analysis across all these internal variables. My hope is that by "living in the future" I can be a model for understanding more clearly the new approaches that will arise in wellness and health care.
Calit2 Has Been Had a Vision of “the Digital Transformation of Health” for a Decade

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

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

The Content of This Slide from 2001 Larry Smarr Calit2 Talk on Digitally Enabled Genomic Medicine
The Calit2 Vision of Digitally Enabled Genomic Medicine is an Emerging Reality
From One to a Billion Data Points Defining Me: The Exponential Rise in Body Data in Just One Decade!
I am the Digitally-Enabled “Patient of the Future”: Measuring the State of Your Body and “Tuning” It

I Arrived in La Jolla in 2000 After 20 Years in the Midwest and Discovered I was Pre-Diabetic
Goal: Lose Weight by Changing What & How Much I Eat, While Increasing Aerobic and Weight Bearing Exercise

Exercise is Elliptical and Walking

Gradually Moving to Zone Diet and Regular Exercise

Current Weight 178.6
Blood Pressure 134/73 Pulse 55
Resting Pulse Lowered to 45
Wireless Monitoring Helps Drive Exercise Goals

- 10,731 steps taken
- 8 minutes very active
- 1 hour 55 minutes fairly active
- 3 hours 19 minutes lightly active
- 5.13 miles traveled
- 2,472 calories burned

30 day graph of time active (in hours): lightly active (blue), fairly active (orange), very active (red)

Jan 21 to Feb 20
Quantifying My Sleep Pattern Using a Zeo - Surprisingly About Half My Sleep is REM!

Total Z: 9 hr 31 min
Time to Z: 0 hr 2 min

1% Wake 0:03
6% Deep Sleep 0:37
52% REM 4:59
41% Light Sleep 3:55

Why are these numbers different from the sleep graph above?

REM is Normally 20% of Sleep
Mine is Between 45-65% of Sleep

An Infant Typically Has 50% REM
The Patient of the Future

Internet pioneer Larry Smarr's quest to quantify everything about his health led him to a startling discovery, an unusual partnership with his doctor, and more control over his life.

www.technologyreview.com/biomedicine/39636
Where I Believe We are Headed: Predictive, Personalized, Preventive, & Participatory Medicine

A Doctor’s Vision of the Future of Medicine
Leroy Hood
NEWSWEEK
From the magazine issue dated Jul 13, 2009

Using a “LifeChip”
Quantify ~2500 Blood Proteins,
50 Each from 50 Organs or Cell Types
from a Single Drop of Blood
To Create a Time Series

On-Line Blood, Stool, Urine, & Saliva Tests Are Becoming Routine

25% of All Medical Tests are Conducted Outside the Hospital Laboratory

DirectLabs...putting your health in your hands

State law prohibits direct access laboratory testing in Massachusetts, New York, New Jersey and Rhode Island.

I Track Over 100 Blood Molecules Every Quarter
Goal: Change Your Cholesterol Levels to Lower LDL, Raise HDL, While Lowering Total

- Total: -40%
- LDL: -45%
- HDL: +33%

Began Statin

Raising “Good” HDL Seems Most Difficult
Goal: Lower Ratio of Arachidonic Acid to EPA to Reduce Pro-Inflammatory Potential of Your Cells

Chronically Ill American

Average “Healthy” American

Ideal Range

My Range

“Silent Inflammation”

I take 6 Fish Oil Pills Per Day

Range Source: Barry Sears
My Tests by www.yourfuturehealth.com
Blood Tests I Do Quarterly to Annually
In Addition to Lipids & Omegas

- **Electrolytes**
  - Sodium, Potassium, Calcium, Magnesium, Phosphorus, Boron, Chlorine, CO₂
- **Micronutrients**
  - Arsenic, Chromium, Cobalt, Copper, Iron, Manganese, Molybdenum, Selenium, Zinc
- **Blood Sugar Cycle**
  - Glucose, Insulin, A1C Hemoglobin
- **Cardio Risk**
  - Complex Reactive Protein
  - Homocysteine
- **Kidneys**
  - Bun, Creatinine, Uric Acid
- **Protein**
  - Total Protein, Albumin, Globulin
- **Liver**
  - GGTP, SGOT, SGPT, LDH, Total Direct Bilirubin, Alkaline Phosphatase
- **Thyroid**
  - T₃ Uptake, T₄, Free Thyroxine Index, FT₄, 2ⁿᵈ Gen TSH
- **Blood Cells**
  - Complete Blood Cell Count
  - Red Blood Cell Subtypes
  - White Blood Cell Subtypes
- **Cancer Screen**
  - CEA, Total PSA, % Free PSA
  - CA-19-9
- **Vitamins & Antioxidant Screen**
  - Vit D, E; Selenium, ALA, coQ10, Glutathione, Total Antioxidant Fn.

I Track Over 100 Blood Variables Over Time
But, In Spite of My High Levels of Omega-3s, Blood Measurements Show Chronic Inflammation

Symptom:
Acute Diverticulitis

“Come Back When You Have a Symptom”

Puzzle:
CRP Stays High
High CRP

Arterial Plaque Formation

CRP > 4.2, 5x Risk of Future Heart Disease
Carotid Artery Ultrasound Reveals Artery Wall Thickness Significantly Increasing In Just Two Years

Oct 31 2008

IMT Right: 0.59 mm to 0.73 mm (24% Thicker)

IMT Left: 0.75 mm to 0.84 mm (12% Thicker)

October 14, 2010
Paradox: Anti-Inflammatory Diet, Plus Low LDL, Yet Chronic Inflammation & Plaque Increases

- What Could be the Source of the Chronic Inflammation?
- Started Taking Stool Samples as Well as Blood Samples

Do Not Assume, Always Measure!
Measuring Stool and Blood Markers Revealed Episodic Inflammation Peaks of CRP and Lactoferrin

Stool Tests by yourfuturehealth.com

Colonoscopy December 2010

Colonoscopy May 2006

“Mild Inflammation of Colonic Muscosa”

Inflammatory Psedopolyp Sigmoid Colon

hsCRP Good Range

Lactoferrin Good Range

200
150
100
50
0

hsCRP x 10

Lactoferrin
Latest Data Point Reveals Lactoferrin Spike to Active Crohn’s Disease (CD) Level

Colonoscopy May 2006

Colonoscopy May 2011

Colonoscopy and Biopsies Support CD Diagnosis

Box Shows Previous Size of Graph

Typical Lactoferrin Value for Active Crohn’s
Confirming the Crohn’s Hypothesis:
Finding the “Smoking Gun” with MRI Imaging

I Obtained the MRI Slices
From UCSD Medical Services
and Converted to Interactive 3D
Working With Calit2 Staff and Software
Exploring My Internal Organs in the Calit2 Virtual Reality CAVE Using DeskVOX Software

Photo & DeskVOX Software Courtesy of Jurgen Schulze, Calit2
Autoimmune Diseases
Effect 5-8% of Americans

- Crohn’s Disease
- Ulcerative Colitis
- Rheumatoid Arthritis
- Multiple Sclerosis
- Psoriasis
- Type 1 Diabetes,
- Ankylosing Spondylitis
- Lupus Erythematosus
- Plus Over 70 Others

Despite decades of research, the etiology of Crohn's disease remains unknown. Its pathogenesis may involve a complex interplay between host genetics, immune dysfunction, and microbial or environmental factors.

--The Role of Microbes in Crohn’s Disease
Paul B. Eckburg & David A. Relman
Single Nucleotide Polymorphisms (SNPs) Make Up About 90% of All Human Genetic Variation

Person A

SNPs Occur Every 100 to 300 Bases Along Human DNA

Person B

www.23andme.com Tracks One Million SNPs
I Wondered if Crohn’s is an Autoimmune Disease, Did I Have a Personal Genomic Polymorphism?

From www.23andme.com

Polymorphism in Interleukin-23 Receptor Gene — 80% Higher Risk of Pro-inflammatory Immune Response

SNPs Associated with CD

IL-23 and Autoimmunity: New Insights into the Pathogenesis of Inflammatory Bowel Disease

Clara Abraham¹ and Judy H. Cho¹,² 2009

Section of Digestive Diseases, Departments of Medicine and Genetics, Yale University,
You Are a SuperOrganism: The Human Genome Contains <1% of the Bodies Genes

Human Microbiome Project

There are 10 Times More Bacterial Cells Than of Human Cells in Your Body

http://commonfund.nih.gov/hmp/
Except for E. Coli, My “Good” Cultured Gut Bacteria Collapsed After Antibiotics

Antibiotics: Levaquin & Metronidaloze

Values From yourfuturehealth.com stool test
My cultured dysbiotic bacteria have been flourishing but most gut bacteria cannot be cultured.
My Clostridia Species Were Dropping to Low Values

- Clostridia are primarily responsible for butyrate production, the main energy source for colonic epithelial wall
- Clostridia provide proinflammatory cytokines inhibition in the colonic muscosa

My Butyrate Values Were Very Low

- “Loss of butyrate producers observed here could upset the dialogue between host epithelial cells and resident microorganisms, hence contributing to the development of CD associated ulcerations.”

Next Step: Use Microarray to Measure Time Series of Microbial Diversity

www.secondgenome.com

“Second Genome has developed a sensitive, flexible and robust platform for the identification of microbiome-based signatures for the rapid identification of microbial gut health biomarkers.”

DNA microarray that can identify, within hours, over 50,000 different microbes

LBL’s Gary Andersen and his PhyloChip
Microbial Metagenomics Can Diagnose Disease States

SNPs Associated with CD
Mutation in Interleukin-23 Receptor Gene — 80% Higher Risk of Pro-inflammatory Immune Response

2009 IBD Patients Harbored, on Average, 25% Fewer Microbial Genes than the Individuals Not Suffering from IBD.

Figure 4 | Bacterial species abundance differentiates IBD patients and healthy individuals. Principal component analysis with health status as

A human gut microbial gene catalogue established by metagenomic sequencing

Junjie Qin¹, Ruiqiang Li¹*, Jeroen Raes²,³, Manimozhiyan Arumugam², Kristoffer Solvsten Burgdorf⁴,
First Stage of Metagenomic Sequencing of My Gut Microbiome at J. Craig Venter Institute

Gel Image of Extract from Smarr Sample - Next is Library Construction
Manny Torralba, Project Lead - Human Genomic Medicine
J Craig Venter Institute
January 25, 2012
Publically Sharing Your Genome and Medical Records: Is it Crazy or the Future?

I Have Been Accepted by PGP and Will Speak at GET 2012: My Full Genome (6 Billion Bases) Will Be Sequenced This Year

Personal Genome Project
Posted 06.01.08 | NOVA scienceNOW

The Personal Genome Project, spearheaded by George Church of Harvard's Center for Computational Genetics, aims to recruit 100,000 people willing to offer up their DNA and personal life histories. It's all in an effort to further knowledge of human genetics and why we get—or don't get—diseases.

www.personalgenomes.org
Crowd-Sourcing Health Studies Is Rapidly Growing With More Open Health Data

23andWe begins with you. Learn about yourself while contributing to research.

Genomera
@genomera
Open health studies on the web. Breaking open bottlenecks in health research and discovery with collective data sharing and analysis. The next wave in health.
Mountain View, CA  •  http://genomera.com
From “How Do You Feel?”, to “What Are Your Numbers?”

Where’s There’s Data
There’s Hope
For Further Information
Visit My Portal

http://lsmarr.calit2.net/