The Genie Is Out of the Bottle

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We must not be conservators of the past.
We are the creators of the future.
That future is before us now.

We can take human destiny into our own hands through genetics.
This will be a disruptive change driven by finance rather then idealism or enlightened self interest.

Grant me 3 wishes based on my genetics:
1. That I may make informed life choices.
2. That I find physicians prepared to use this information to guide my therapeutics.
3. That genetic profiles will decrease cost and increase quality of both my health and my therapeutics.

Grant me 3 wishes based on my genetics:

Direct To Consumer (DTC) Genetics
23andme: Testing > 1,000,000 common genetic variants for each person’s profile.
Today 96% white European profiles; hence 10,000 free tests to African Americans.
Unlike most medical studies, participants get their data directly. They are engaged in their information pool and can be proactive in their own health.
Richard YaDeau

14.2 out of 100 men of European ethnicity, who share Richard YaDeau’s genotype, will develop Alzheimer’s disease between the ages 50 and 79.

7.2 out of 100 men of European ethnicity without Richard YaDeau’s profile develop Alzheimer’s disease between the ages of 50 and 79.

Ethnicity and age range are used to estimate an incidence of Alzheimer’s Disease due to genetics of men with Richard YaDeau’s genotype.

Genes vs. Environment

60-80 % Attributable to Genetics

- The heritability of AD is estimated to be 60-80%. This means that genetic factors contribute more to individual differences in risk for AD than environmental factors do.
- Genetic contributions to AD risk include known factors, such as the APOE gene variants we describe in this report.
- Non-genetic risk factors for AD include high blood pressure, high cholesterol, obesity, poorly controlled diabetes, and history of head trauma.

Genotypes Predict Weight Loss Success:
The Right Diet Does Matter

Stanford University School of Medicine

American Heart Association’s Epidemiology and Preventive Medicine Conference

Wall Street Journal, March 4 2010
Stanford study:
- Individuals on genotype-appropriate diets lost 6.8% body weight
- Individuals without a diet genotype match lost 1.4%
- Improvements in clinically related parameters followed weight loss

Grant me 3 wishes based on my genetics:
2. That I find physicians prepared to use this information to guide my therapeutics.

 Profiles in Leukemia
- Acquired mutations accumulate progressively.
- Sub-clones acquire new properties.
- Profiling provides critical diagnostic categorization.
- Survival is be linked to the therapeutic choices based upon this categorization.

Microbial Genomics & Infectious Diseases
- 1554 complete bacterial sequences (virtually all pathogens), 4800 now in progress
- 2675 viral sequences with the influenza virus showing >40,000 strains
- Unique (new) pathogens can be sequenced in < 24 hours

The Black Death, Yersinia Pestis Sequenced. Announced 10/12/2011 
Nature 1347-1351
50 Million Died, ½ of the European Population. Today 2000 deaths per year
Ion Torrent’s “Personal Genome Machine”
“PGM” Desk-top sequencing
- Identifies viral and bacterial pathogens by their genetics.
  Sequence's initial cost: $450
  Time to results: 20-30 minutes
- Already installed in > 500 Physicians’ offices and numerous Emergency Rooms.
MIT conference on Emerging Technologies (EMTech), October 2011
www.Lifetechologies.com

Ion Torrent’s “Personal Genome Machine”
“PGM” Total Sequencing all 3 billion DNA units
- Total sequencing for $1,000
- Results in < 24 Hours.
- Machine capital cost: $149,000
- Drug companies are using gene variants that they can target with drugs.
  BUT who will interpret all of this data?
Life Technologies Corp. 1/10/2012
Jonathan Rothberg @ J.P. Morgan Healthcare Conference

DNA Sequencing to Go

15 minute run time. $900. Technology Review 2/17/2012
www.nanoporetech.com

Genomics and Drug Responses
- Cardiovascular drugs
- Infectious diseases
- Anti-neoplastic drugs
L. Wang M.D. Mayo Clinic,
NEJM March 24 2011; 364:1144-53
Grant me 3 wishes based upon my genetics:

#3. That genetic profiles will decrease the cost and increase the quality of both my health and my therapeutics.

Direct to Consumer
Genome-wide Risk Profiles
- 10% sought professional counseling when they saw their results
- 26% shared them with their physician
- 10% of physicians felt able to use the information from gene testing

C. S. Bloss PhD, Scripps Clinic
NEJM February 10 2011;364:524-34

Direct to Consumer
Genome-wide Risk Profiles
- No significant increase in anxiety, change in dietary fat intake or exercise programs in response to receiving genetic information.

- Results of DTC genetic testing does not affect an individuals health-related behavior.

C. S. Bloss PhD, Scripps Clinic
NEJM February 10 2011;364:524-34

The biggest challenge is in data analysis.

Eric Green, director, The National Human Genome Research Institute
www.technologyreview.com, February 10 2011

“Risk Adopted Therapy”

Consider a vaccine to prevent a specific cancer, e.g. multiple myeloma, by treating patients with the genetic precursors of the disease.

Kenneth Anderson, Dana-Farber Cancer Institute (OncoPep)
www.technologyreview.com May 4 2011
Today hospitals and physicians bring to their patients genetic testing and therapy in a haphazard approach.

There are few institutions that have standardized genetic testing and therapies in order that every appropriate patient would receive them.

First and foremost we will need data-bases to support the storage, recall and management of the genetic code for each individual.

Only 4% of institutions have EMR which can support genetic interpretation and genetic therapy management.

The FDA has 311 approved drugs that are required to have pharmacogenomic information on their labels.

www.fda.gov/drugs/scienceresearch/researchareas/pharmacogenetics/ucm083378.htm

Example:

The most recent label for warfarin (Coumadin) includes a table of starting dose on the basis of the patient’s genetics: (CYP2C9 and VKORC1).

Does your institution check all patients’ genomic signature before anticoagulant therapy?

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<th>Result</th>
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<tr>
<td>rs1057910</td>
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<td>Increased warfarin sensitivity. May require decreased warfarin dose.</td>
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Frequently asked question about genetics:

1. What effect will genetic testing have on my health insurance? (genetic discrimination)

Two acts (GINA Dec. 2009 & PPACA 2014) protect you from health insurers utilizing your genetic data for coverage: rating, increase of premiums, denial of enrollment or exclusions for preexisting conditions.

This legislation does not apply to Life Insurance.

2. Why is genetic testing so expensive when I can get almost all of my genetic markers done by DTC firms for less the $400?

Patents have been awarded for 20%! of the human genome, including your genetic sequences and for methods of testing and analysis. But:

Justice Breyer, (Prometheus:10-1150, 3/20/2012) said “Einstein could not patent his celebrated law that E = mc²; nor could Newton have patented the law of gravity.” Several similar cases are on hold.

A prominent example is Myriad Genetics, BROCA 1 & 2.

Hospitals, physicians and a world of patients need to prepare themselves, their systems and their therapeutic practices to function in an environment of genetic diagnostics and therapies.

I believe genetics will be the unifying resource for a vibrant and successful future throughout the healthcare phenomenon.