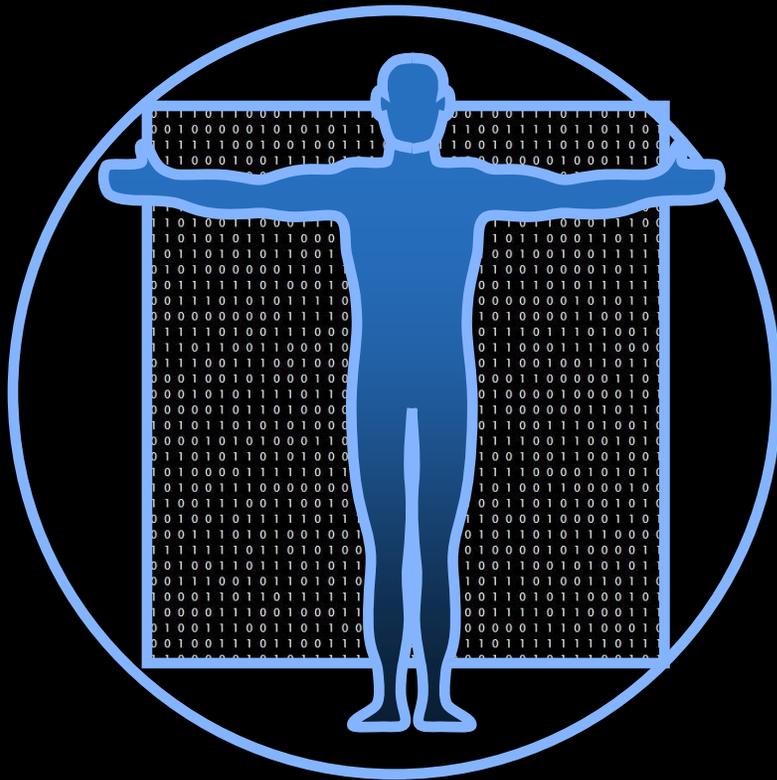


Secretary's Advisory Committee on Genetics, Health and Society

Session on Personal Genome Services
July 8, 2008

Personal Genomic Information: A Consumer's Perspective

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THE EXPERIMENTAL MAN PROJECT

Genes
Environment
Brain
Body

The Center for Life Science Policy
University of California at Berkeley

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Personalized Medicine

- **PAST**: Focus on the ill and the unhealthy
- **FUTURE**: Focus on the healthy individual -- on prevention and improving health
- I'm not sick (that I know of) and I'm reasonably healthy
- What we're doing is ***predicting an individual's future health***

QUESTIONS

- What were your reasons for pursuing personal genome services?
- What sort of information did you anticipate receiving from these services?
- What tests did you take, and what were your results?
- Were there differences in any overlapping results or the interpretation of results from multiple services?

Questions: Expectations

- What were your reasons for pursuing personal genome services?
 - Journalist
 - Curiosity about technology and information
 - Insight to my future health?
- What sort of information did you anticipate receiving from these services?
 - Low expectations given early phase of science
 - Confirmation that I am well

Questions: Tests and Results

- What tests did you take, and what were your results?
- Were there differences in any overlapping results or the interpretation of results from multiple services?

Genetic Tests

- **SNPS, Insertions, Deletion: ~1.5 Million Genetic Markers**
 - Illumina HumanHap 1 Million SNP/650k SNP/330K SNP
 - Affymetrix Genome-Wide Human SNP Array 6.0
 - Sequenom Mass-Spectrometer (2001-2)
- **Dozens of individual genes sequenced**
 - Quest Diagnostics
 - Myriad
 - Academic Labs
 - Others

Companies, Sites and Labs

2001

(cont.)

deCode Genetics

Sequenom

(Ancestry)

Orchid

Diagnostics

2007-2008

deCode Genetics

Institute

deCodeme

University

2007-2008

DNA Direct

Family Tree

Interleukin

Quest

Myriad

Coriell

Baylor

Costs (Genetic Tests)

- 3 Online Consumer Sites
(Genome-Wide): \$8,500* (David:
\$4500 Family: \$4000)
- Ancestral Testing: \$1400 (4
people)*
- DNA Direct (Myriad BRCA1-
BRCA2): \$3500*
- Quest Diagnostics (15 tests):
TBD (>\$2000?)*
- Other Tests: ~\$5,000*

Participants

- **Mother**, 75, Artist, Rockport, Maine*
- **Father**, 76, Architect, Rockport, Maine*
- **Brother**, 48, Photographer, Brunswick, Maine*
- **David**, 50, Journalist, San Francisco, California
- **Daughter**, 19, College Sophomore, St. Andrews,

Navigenics

Causes: heart attack

Genes are only part of the story. Environment and behavior play a big role. Studies of twins show how much of a condition's cause is hereditary and how much is due to other factors.

What's next

- Get yourself moving, but check with your doctor before beginning an aggressive exercise program.
- Talk to your doctor about checking your blood pressure and cholesterol — and lowering them if they're high.
- If you smoke, stop.

[More: What you can do](#)

What we found

To calculate your estimated lifetime risk, we looked at two places in your genome that are associated with heart attack. At each location, there are two markers, for a total of four possible risk markers. The chart below shows your markers for each of the two places. You have four of the four risk markers we looked for. Each risk marker increases your odds by a different amount — some a little, some a lot.

Location name	Your odds ratio	Maximum odds ratio
G221	~1.72	~1.75
MTHFD11	~1.52	~1.55

The height of the blue bars shows your odds ratio, a measure of the effect of a genetic variant on your odds of developing a condition. The clear bars represent the maximum odds ratio for each location. Roll your mouse over the chart for more information about each location.

[More: Your DNA](#)

Navigenics™ Welcome, GL

Your Results Learn More Sharing Results Genetic Counseling

Overview: Your estimated lifetime risk

0 - 1%	>1 - 10%	>10 - 25%	>25 - 50%	>50 - 100%
Graves' disease You: 0.64% Avg: 0.55%	Psoriasis You: 5% Avg: 4.0%	Obesity You: 25% Avg: 34%	You have no results in this range	Heart attack You: 62% Avg: 42%
Multiple sclerosis You: 0.40% Avg: 0.30%	Colon cancer You: 5% Avg: 6%	Diabetes, type 2 You: 21% Avg: 25%		
Crohn's disease You: 0.37% Avg: 0.58%	Alzheimer's disease You: 4.4% Avg: 9%	Prostate cancer You: 17% Avg: 17%		
Macular degeneration You: 0.36% Avg: 3.1%	Restless legs syndrome You: 2.4% Avg: 4.0%	Osteoarthritis You: 14% Avg: 18%		

- 17 traits
- Disease markers only
- Founded by geneticist and physician
- Major venture backing, Google
- Counseling offered
- \$2500

deCodeme

deCODE ME

You have been genotyped!

Use deCODEme to

- myGENE profile
- myCHARACTERISTICS
- myANCESTRY

myCODE

- Analysis
- My Friends
- My Settings
- Orders
- Advanced

deCODE ME

gene profile

select a trait

myCODE

- Analysis
- Gene Profile
- Summary report
- Characteristics
- Ancestry
- Compare Me

traits

- Abdominal Aortic Aneurysm
- Age-related Macular Degeneration
- Alzheimer's Disease
- Asthma
- Atrial Fibrillation
- Breast Cancer
- Celiac Disease
- Colorectal Cancer
- Crohn's Disease
- Exfoliation Glaucoma
- Heart Attack
- Hemochromatosis
- Intracranial Aneurysm
- Lactose Intolerance
- Lung Cancer
- Multiple Sclerosis
- Obesity
- Peripheral Arterial Disease
- Prostate Cancer
- Psoriasis

deCODE ME

heart attack

risk summary

your type (0.87) | average (1)

0.542 | 1.39

According to the selected literature, the relative genetic risk calculated from your genotype for males of European ancestry is 0.87. This corresponds to a 42.4% lifetime risk of heart attack, sudden cardiac death, and angina, which is 13% less than for males of European ancestry in general. Note that these calculations may not include all risk factors.

The lifetime risk of your type
It is estimated that 42 of every 100 males of European ancestry with your genotype variants develop this disease in their lifetime.

42.4%

The average lifetime risk
On average, about 49 of every 100 males of European ancestry develop this disease in their lifetime.

49.0%

- 25 diseases, 6 traits
- Disease, attributes, ancestry
- deCode is drug and gene discovery company
- No counseling offered
- \$1000

23andme

A screenshot of the "Your Genetic Data" section for David Duncan. It shows a grid of avatars representing other users, with 3 out of 100 people of European ethnicity sharing the same genotype for a heart attack between ages 45 and 54. It also includes an "Average" section showing 2.5 out of 100 people and a "Genes vs. Environment" section stating that 38-57% of heart attack death is attributable to genetics.

Your Genetic Data

Show information for **David Duncan** assuming **European** ethnicity

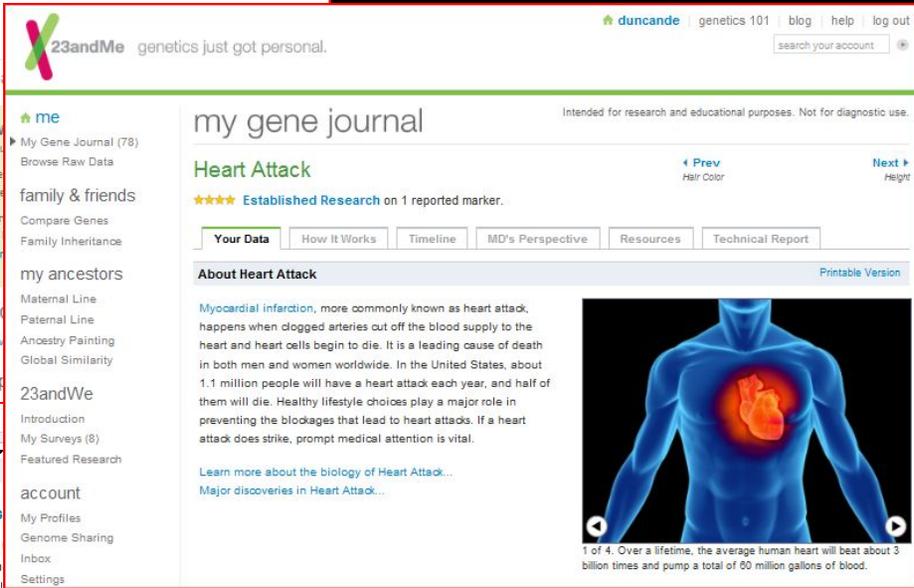
David Duncan
3 out of 100
people of European ethnicity who share David Duncan's genotype will get Heart Attack between the ages of 45 and 54.

Average
2.5 out of 100
people of European ethnicity will get Heart Attack between the ages of 45 and 54.

Genes vs. Environment

38-57% Attributable to Genetics

The **heritability** of death from a heart attack is estimated to be 38% for women and 57% for men. This means that genetic factors contribute slightly less to this condition than **environmental factors** in women, but contribute slightly more in men. Genetic factors that play a role in heart attack include both unknown factors and known factors such as the SNPs we describe here. Other factors that increase your risk include being older, being male, being African-American, smoking, having high blood cholesterol or high blood pressure, physical inactivity, being overweight, having diabetes, alcohol use, and stress. ([sources](#))



- 78 traits
- Diseases, attributes, ancestry
- Web 2.0 company, Google
- Rating system
- Counseling not offered
- \$1000

Two Other Approaches

- **DNA Direct**

- Online ordering and results, physician signs orders
- Offers only individual tests in common use by physicians
- Counseling before and after
- Rich information, including pros and cons of testing

- **Coriell Institute**

- Genome-wide data (Affymetrix)
- 15 or so diseases, website
- Nonprofit: free for 10,000-100,000 people

Sample Results

Red: risks over 1.5 times normal
Orange: risks over 1.2 time normal
 Black: Average or normal risk
Yellow: Between .5 and .99 times normal
Green: Protective SNP or risk factor below .5

Age-Related Macular Degeneration

Trait	Gene	Marker	Results	Risk*	Source	Life Risk* DED
Age-Related	PLEKHA1/ARM	rs932275			deCodeme	Ave 1.1%
Macular	S2 CFH	rs1329428	GG G AA	0.68	deCodeme	8.0%
Degeneratio	CFH	rs10737680	A	0.20	Navigenic	0.36% 3.1%
n	LOC387715	rs10490924	CC T	1.0	Navigenic	
	CFB	Rs541862	GG T	1.0	Navigenic	
	LOC387715	rs3750847	TT	6.98	23andme	0.19%
	CFH	rs1061147	CC A	0.46	23andme	1.2%
			CC	0.34		

*Sites use different methods for determining risk factors.

More Results: Comparing 3 Sites

Diabetes Type II

- 19 Different SNPs
 - 23andme: 9 – Navigenics: 11 – deCodeme: 10
- 15 Different Genes
- Range of SNP risk factors: 0.82 – 2.61
 - Lifetime Risk: 23andme: 16.8% – Navigenics: 21% – deCodeme: 18.8% – Average for U.S. Male: 25%
- 4 SNPs on all 3 sites (2 of 4 risk factors consistent)
- 4 SNPs on 2 out of 3 sites (4 out of 4 risk factors consistent)

Is Data Consistent?

- **Genotyping Results** (CLIA Lab): very consistent among 3 sites (GG or AG is the same)
- **Risk Factor Results**: mostly consistent
- **Risk Factors by Disease, regardless of site**: not always consistent (mix of high, med and low)

Heart Attack Gene Markers

<u>Gene / Locati on</u>	<u>SNP</u>	<u>Risk Vari ant</u>	<u>DED Resul ts</u>	<u>Risk Facto r*</u>	<u>Source</u>	<u>Lifetim e Risk*</u>
CELSR2 +	rs599839	G	AG	.86	deCodeme	42% 49%
9p21	rs101162 77	T	GT	1.0	deCodeme	
9p21	rs133304 9	C	CC	1.72	Navigeni CS	62% 49%
MTHFD1 L	rs692226 9	A	AA	1.53	Navigeni CS	
9p21	rs238320 7	G	GG	1.22	23andme	29.9% 17%

*Risk factors for each site are calculated differently.

Why Different Results?

- Different SNPs/studies used
- Different methods for determining SNP risk
 - deCodeme: Relative Risk
 - 23andme and Navigenics: odds ratios
- Different methods for determining combined SNPs risk/lifetime risk
- Reliance on correlative SNPs

End Result: head scratching,
what does it mean?

Three Generation Study



Heart Attack (rs1075728)

Father
AG

Mother
AG

Alzheimer's (rs4420638)

Father
AG

Mother
AA



David
GG

Brother
AA

David
AA

Brother
AG



Daughter
AG

|
Daughter
AA

Two Brothers

(Rare Diseases vs. Common Diseases)

Disease: Osteogenesis Imperfecta (OI)

Full Sequence: COLA1A and COLA2A

Lab: Peter Byers, University of Washington

Results:

Donald Duncan, 48: Deletion in COLA1A =
Positive for OI

David Duncan, 50: Normal COLA1A = No OI

Q: Should rare diseases be part of
DTC services?

“Recreational” and “Preliminary”

<u>Trait</u>	<u>SNP</u>	<u>Risk</u>	<u>DED</u> <u>Resul</u> <u>ts</u>	<u>Rati</u> <u>ng</u>	<u>Risk</u> <u>Factor</u>	<u>Source</u>
Ancestry	mtDNA	--	Group H	5	European Ancestry	deCodeme /
Bitter Taste	rs71359 8	G=bit ter	CC TT	5 5	No bitter No bitter	Navigeni 23andme CS deCodeme
Intellig ence	rs17268 rs36305 66	T=bit ter	GG	1	Lower IQ	23andme
Avoiding Errors	rs18004 97	A	GG	2	3pts Avoids Errors	23andme
Back Pain	rs20737 11	G	GG	2	Average	23andme
Heroin Addictio n	rs17999 71	G	AG	1	Substantia lly Higher	23andme
Longevit y	rs25420 52	C	CC	1	Higher odds age	23andme
Caffeine	rs76255 1	A	AA	--	100 Rapid Metabolize	23andme

Step 3: Reactions, Thoughts

- Did you alter your behavior in light of test results? If so, how?
 - **One person** – journalist, tested on multiple sites
 - **Not really**... subsequent heart tests
convinced me to alter my diet
 - **Breast cancer data** (high risk SNPs) for

PLUSES OF DTC TESTING

- Insight into personal and societal health
- Personal empowerment
- Will push society (and health industry) to discuss guidelines, ethics, education, and funding
- Opening up new avenues for research impacting individuals and subgroups

MINUSES OF DTC TESTING

- Early days of technology
- Association studies not always applicable to individuals
- Disease and non-disease results mixed
- No standards for validity, risk factors
- Physicians not trained in genetics
- Potential to frighten
- High costs, no insurance (costs

THOUGHTS AND SUGGESTIONS

- Consumers should be free to access their information and buy services
- Encourage discussion
- Early adopters should be part of the experiment - Coriell approach, doctor's first
- Establish standards and guidelines for tests and

THOUGHTS AND SUGGESTIONS

(Cont)

- Crash program to set validation standards, refocus on preventive medicine
- Disease markers should be handled differently; counseling offered
- Physicians in companies should review disease markers, alert consumers of serious findings
- Companies should provide lists

Genetics is just the beginning...

Genes + Environment +
Brain
+ Body

www.experimentalman.com

THE EXPERIMENTAL MAN PROJECT
"I LOVE FOOL'S EXPERIMENTS. I AM ALWAYS MAKING THEM." - CHARLES DARWIN

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THE EXPERIMENTAL MAN PROJECT

A Book, Website and Multimedia Program Exploring what Cutting-Edge Technologies in Personalize Medicine Can Tell Us about Ourselves, Past, Present and Future: Genes, Environment, Brain and Body

EXPERIMENTAL MAN
What One Man's Body Tells Us about His Future, Your Health, and Our Toxic World

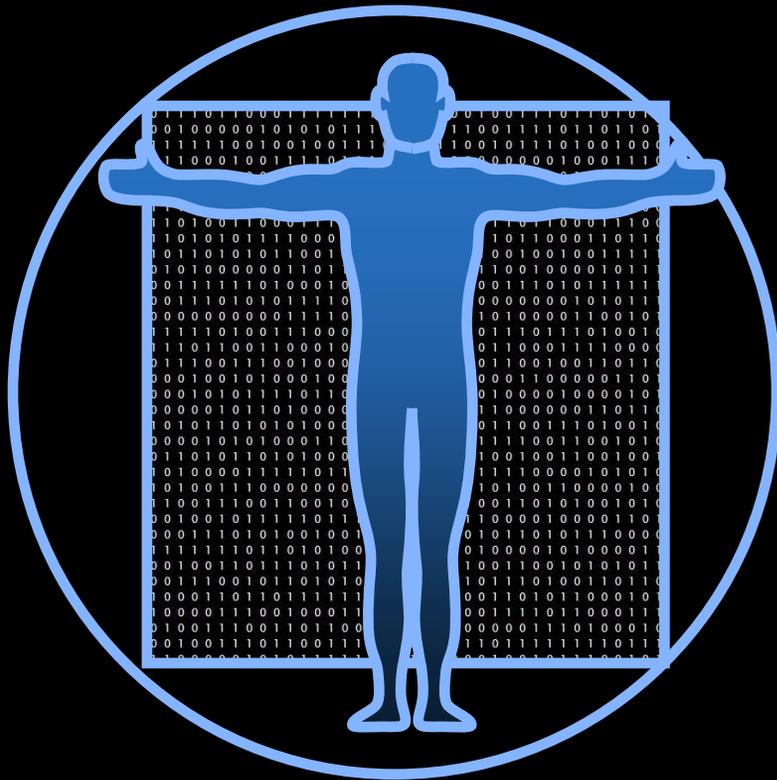
By David Ewing Duncan

Book Due Out from John Wiley & Sons in early 2009.

Also watch for series about Experimental Man on the Today Show, Discover Magazine, and "Biotech Nation" on public radio. Details to follow.

This is a preliminary website that will be added to over the coming months. It will include data from author David Ewing Duncan's tests covering his genes, environment, brain and body, along with commentary, analysis and musings about usefulness and impact of this information on an individual

Center for Life Science Policy UC Berkeley



EXPERIMENTAL MAN

What One Man's
Body Reveals about
His
Future, Your
Health,
and Our Toxic
World

David Ewing
Duncan

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Due Out: March,
2009