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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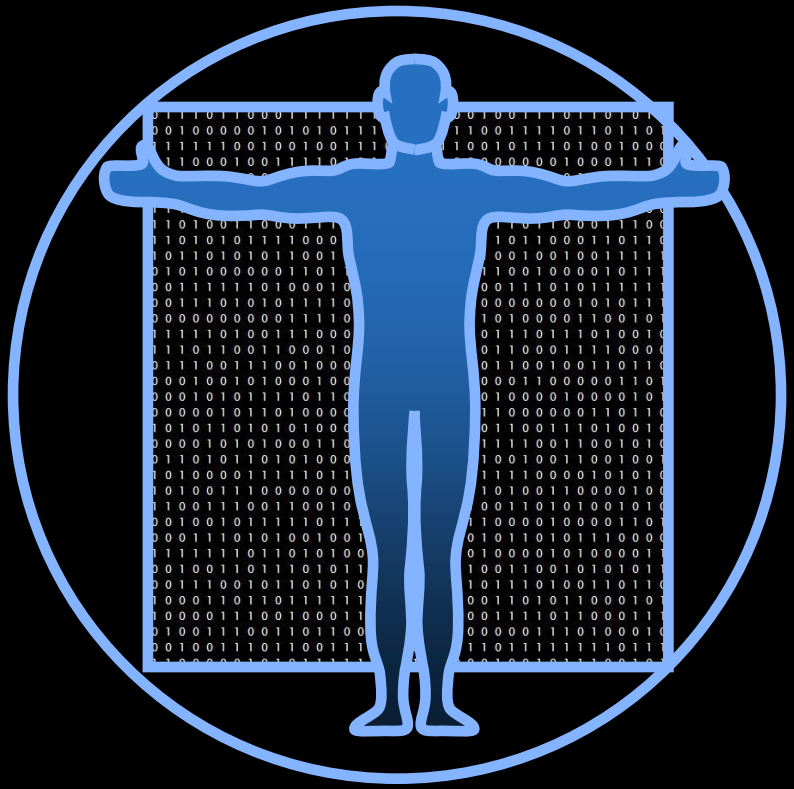


THE EXPERIMENTAL MAN PROJECT

Genes
Environment
Brain
Body

The Center for Life Science Policy
University of California at Berkeley

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
- **Various Full Genome Scans**

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

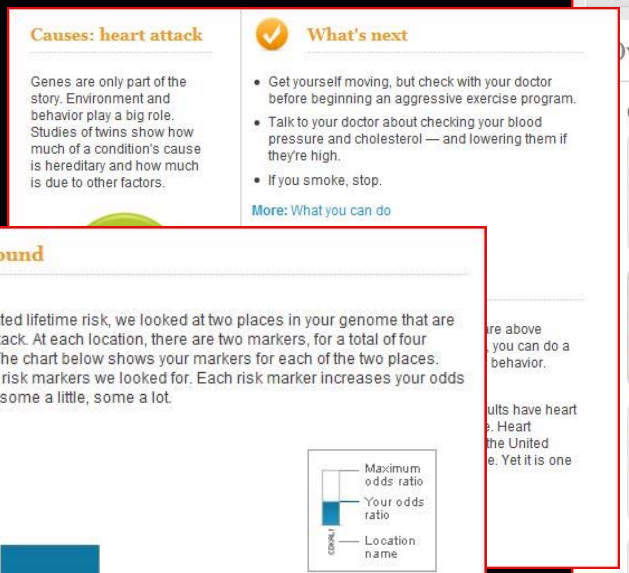
Costs (Genetic Tests)

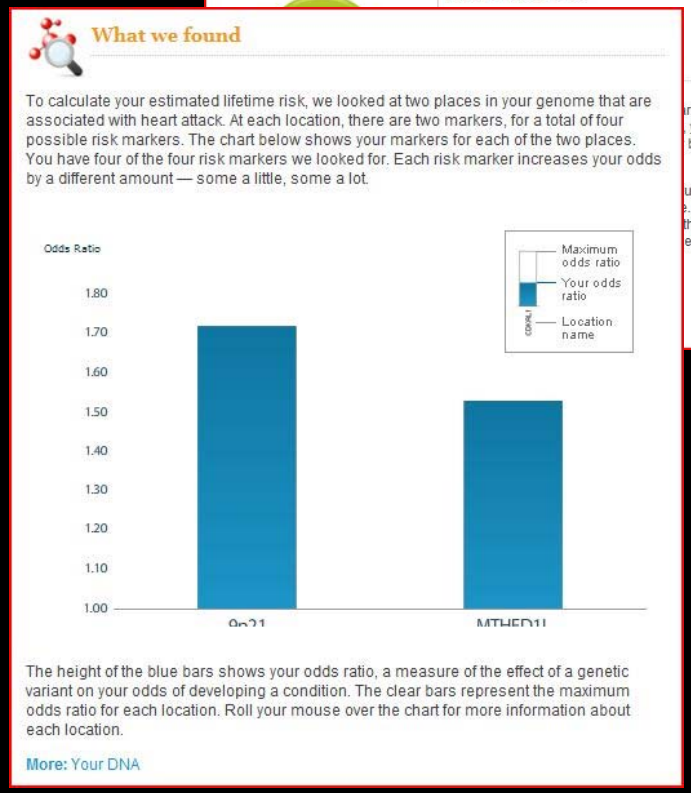
- 3 Online Consumer Sites (Genome-Wide): $8,500* (David: $4500 Family: $4000)
- Ancestral Testing: $1400 (4 people)*
- DNA Direct (Myriad BRCA1-BRCA2): $3500*
- Quest Diagnostics (15 tests): TBD (>$2000?)*
- Other Tests: ~$5,000*

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,

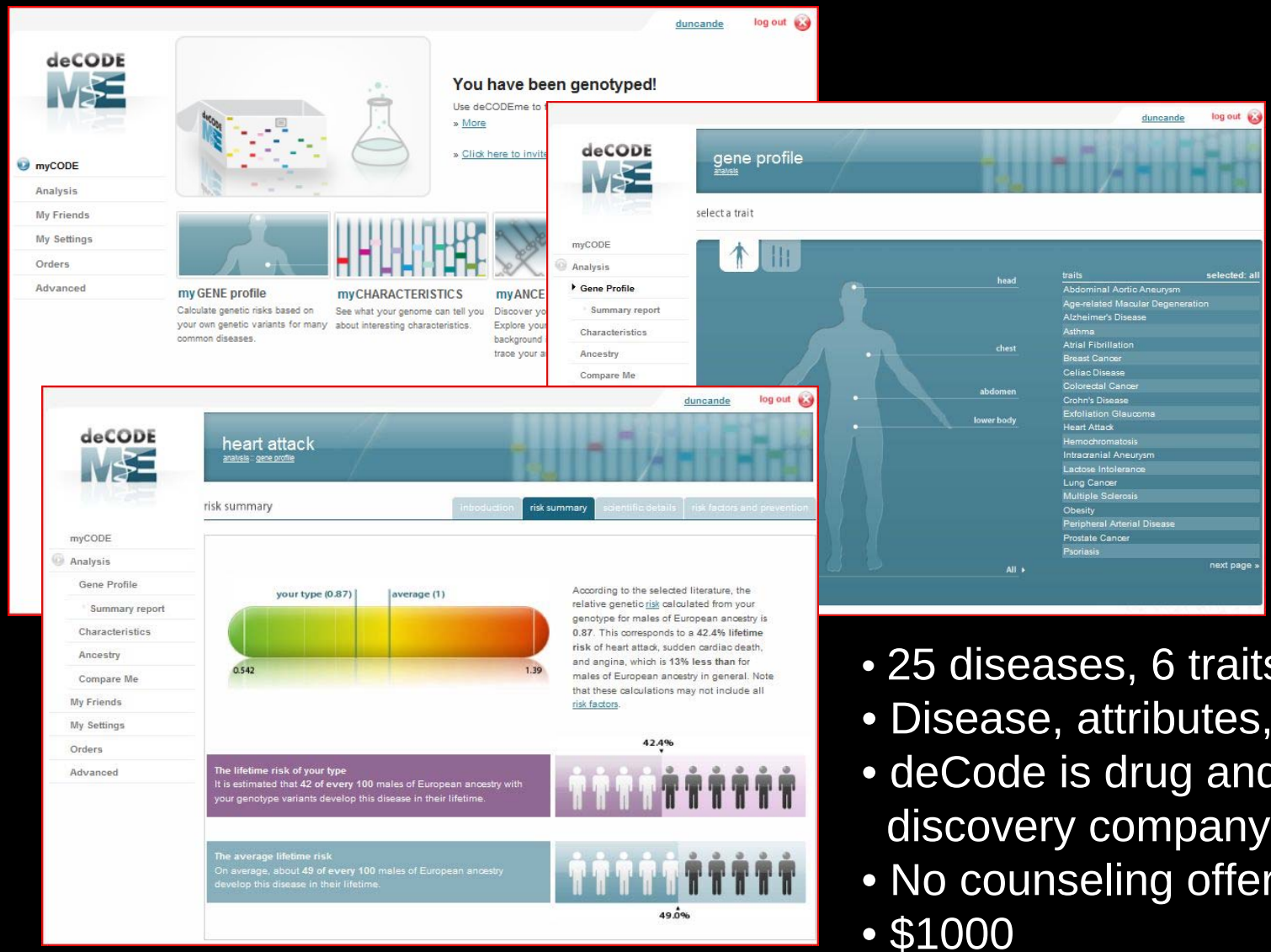
Navigenics





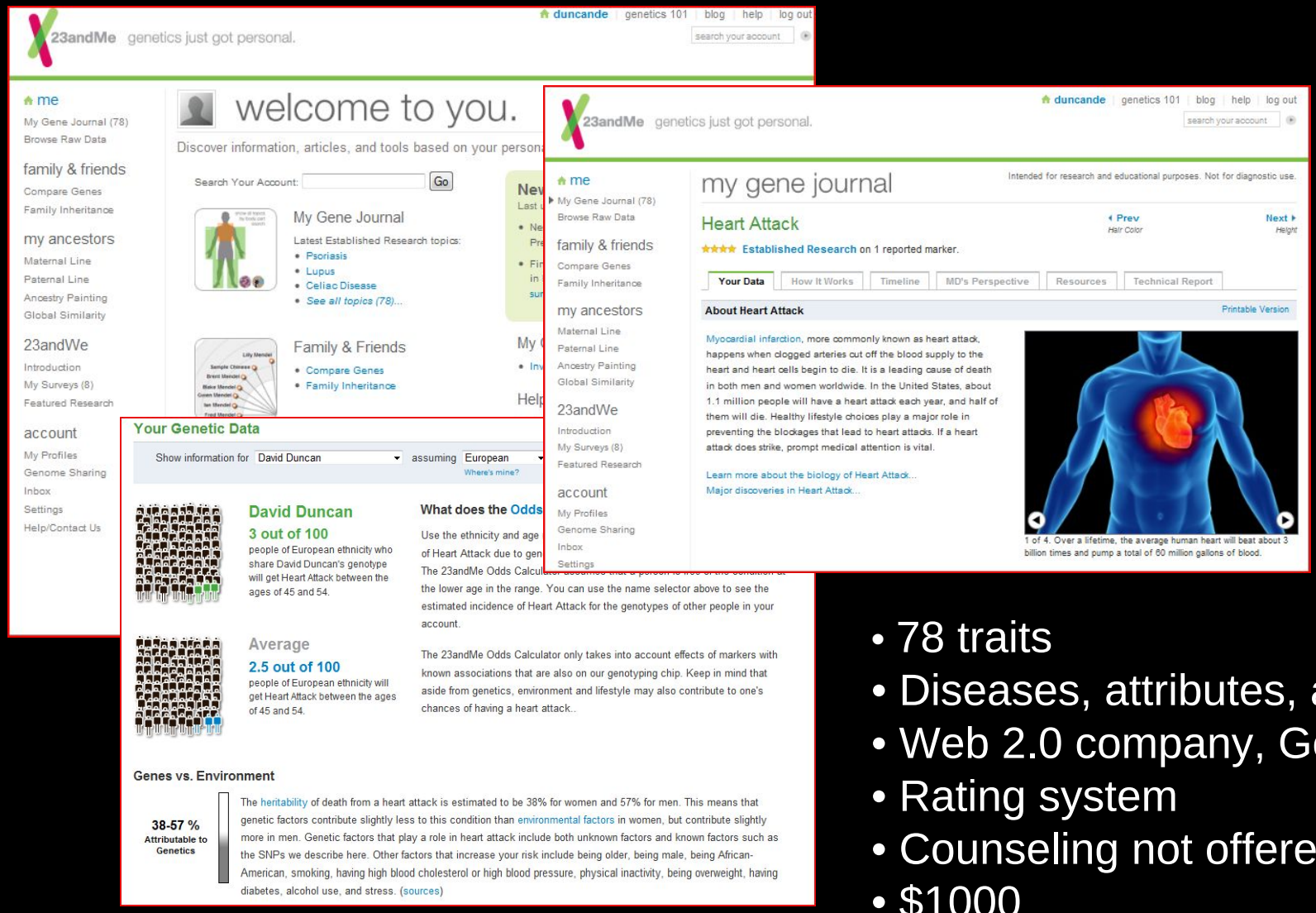
- 17 traits
- Disease markers only
- Founded by geneticist and physician
- Major venture backing, Google
- Counseling offered
- $2500

deCodeme



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

23andme



- 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 Ave
Age-Related Macular Degeneration	PLEKHA1/ARMS2	rs932275	GG		deCodeme	1.1%
	CFH	rs1329428	G AA	0.68	deCodeme	8.0%
	CFH	rs10737680	A	0.20	Navigenics	0.36% 3.1%
	LOC387715	rs10490924	CC T	1.0	Navigenics	
	CFB	Rs541862	GG T	1.0	Navigenics	
	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

Gene / Location	SNP	Risk Variant	DED Results	Risk Factor*	Source	Lifetime Risk*
CELSR2+	rs599839	G	AG	.86	deCodeme	42% 49%
9p21	rs10116277	T	GT	1.0	deCodeme	
9p21	rs1333049	C	CC	1.72	Navigenics	62% 49%
MTHFD1L	rs6922269	A	AA	1.53	Navigenics	
9p21	rs2383207	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)			Alzheimer's (rs4420638)		
	Father	Mother		Father	Mother	
	AG	AG		AG	AA	
	David	Brother		David	Brother	
	GG	AA		AA	AG	
	Daughter			Daughter		
	AG			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 PIC services?

“Recreational” and “Preliminary”

Trait	SNP	Risk	DED Results	Rating	Risk Factor	Source
Ancestry	mtDNA	--	Group H	5	European Ancestry	deCodeme / Navigenics
Bitter Taste	rs713598	G=bitter	CC	5	No bitter	23andme
	rs1726866	T=bitter	TT	5	No bitter	deCodeme
Intelligence	rs3630560	G	GG	1	Lower IQ 3pts	23andme
Avoiding Errors	rs1800497	A	GG	2	Avoids Errors	23andme
Back Pain	rs2073711	G	GG	2	Average	23andme
Heroin Addiction	rs1799971	G	AG	1	Substantially Higher	23andme
Longevity	rs2542052	C	CC	1	Higher odds age 100	23andme
Caffeine	rs762551	A	AA	--	Rapid Metabolizer	23andme

Crush of Data… Chart 24 ft. Long

EXPERIMENTAL MAN
Main Graph - Gene Test Results

High Risk (over 1.5)	Relative Risk (bold)	Ratings: 1 - 5 (5 most useful)
Low Risk (over 1.2)	Odds Ratio (no bold)	1: <100 Population Studied
Average Risk (1.0)		2: 100-1000 Population
Below Average Risk (Below 1.0)		3: 1000-5000 Population
Protective		4: 5000-10,000 Population
		5: >10,000 Population

TRAIT				CRITERIA	DED RESULTS		THREE GENERATION STUDY								LOCATION, POPULATIONS, SOURCES			
Type	Condition	Gene	SNP/Mark	Risk Varian	DED	Risk	Father	Risk	Mother	Risk	Brother	Risk	Daughte	Risk	Sources	Locii	Pop Siz	Rating
I. ANCESTRAL	Ancestry	mDNA	NA	NA	H	*	H	*	H	*	H	*	U5	*	deCodeme	mDNA		
	Ancestry	Y	NA	NA	R1B	*	R1B	*	NA	*	R1B	*	NA	*	deCodeme	Y		
	%European	Auto	NA	NA	*	95	*	93	*	93	*	94	*	95	deCodeme			
	%Asian	Auto	NA	NA	*	3	*	5	*	3	*	4	*	3	deCodeme			
	%African	Auto	NA	NA	*	2	*	2	*	4	*	2	*	2	deCodeme	X		
	%European	X	NA	NA	*	87	*	87	*	91	*	92	*	93	deCodeme	X		
	%Asian	X	NA	NA	*	11	*	10	*	8	*	8	*	5	deCodeme			
	%African	X	NA	NA	*	2	*	3	*	1	*	<1	*	2	deCodeme			
	Orcadia (Scotland)	NA	NA	NA	*	1	*	1	*	1	*	2	*	1	deCodeme			
	French	NA	NA	NA	*	2	*	2	*	2	*	1	*	2	deCodeme			
	Basque	NA	NA	NA	*	3	*	4	*	4	*	5	*	3	deCodeme			
	Tuscan	NA	NA	NA	*	4	*	3	*	3	*	3	*	4	deCodeme			
	Italian	NA	NA	NA	*	5	*	6	*	6	*	6	*	5	deCodeme			
	Russia	NA	NA	NA	*	6	*	5	*	5	*	4	*	6	deCodeme			
II. ATTRIBUTES	Blue Eyes	SLC24A4/T	rs12913832	G (blue)	GG	94.17	*	96.62	*	90.48	*	96.62	*	85.37	SNPedia		*	
	Blue Eyes	OCA2	rs1667394	A (blue)	AA	90	*		*		*		*		deCode			
	Brown Eyes	SLC24A4/T	*	*	*	2.3	*	1.81	*	2.55	*	1.81	*	4.22	*		*	
	Green Eyes	SLC24A4/T	rs7495174	A (blue)	AA	3.52	*	1.58	*	6.96	*	1.58	*	10.41	SNPedia		*	
	Blond Hair	SLC24A4/K	*	*	*	24.21	*	13.28	*	21.3	*	25.65	*	28.58	*		*	
	Brown Hair	SLC24A4/K	*	*	*	74.92	*	22.85	*	77.83	*	73.48	*	70.55	*		*	
	Red Hair	SLC24A4/K	*	*	*	0.87	*	63.87	*	0.87	*	0.87	*	0.87	*		*	
	Height	HMGA2	rs1042725	C	CT	.05 cm	*		*		*		*		Nature Genetics		*	

- Total Markers (so Far): 1000+ (24 feet long when printed out)
- Five Sections: Ancestral, Attributes, Behavioral, Disease, Environment
- 3-Generation Study
- Risk Factors
- Rating System

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

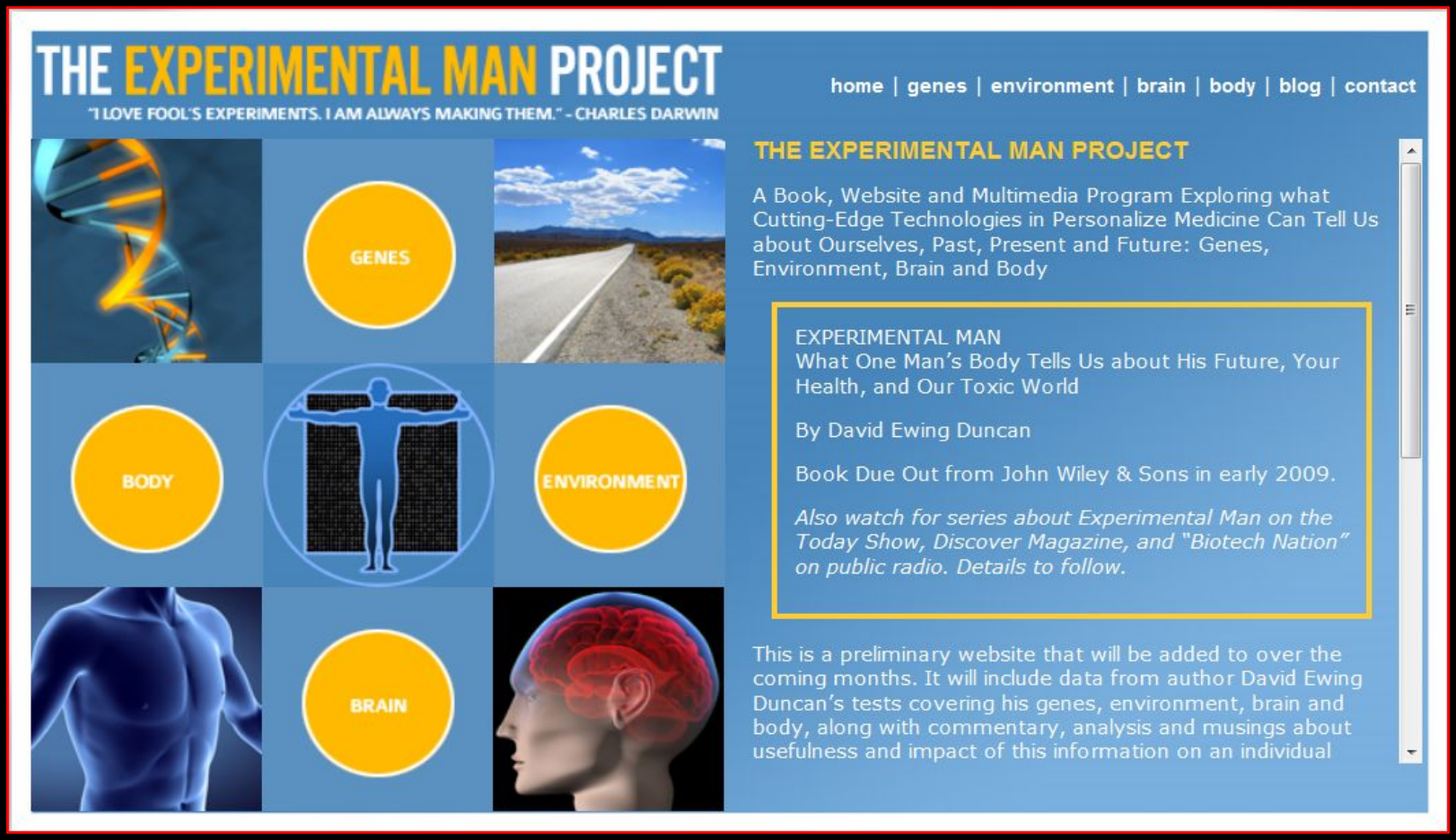
Thoughts and Suggestions (Cont)

- 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

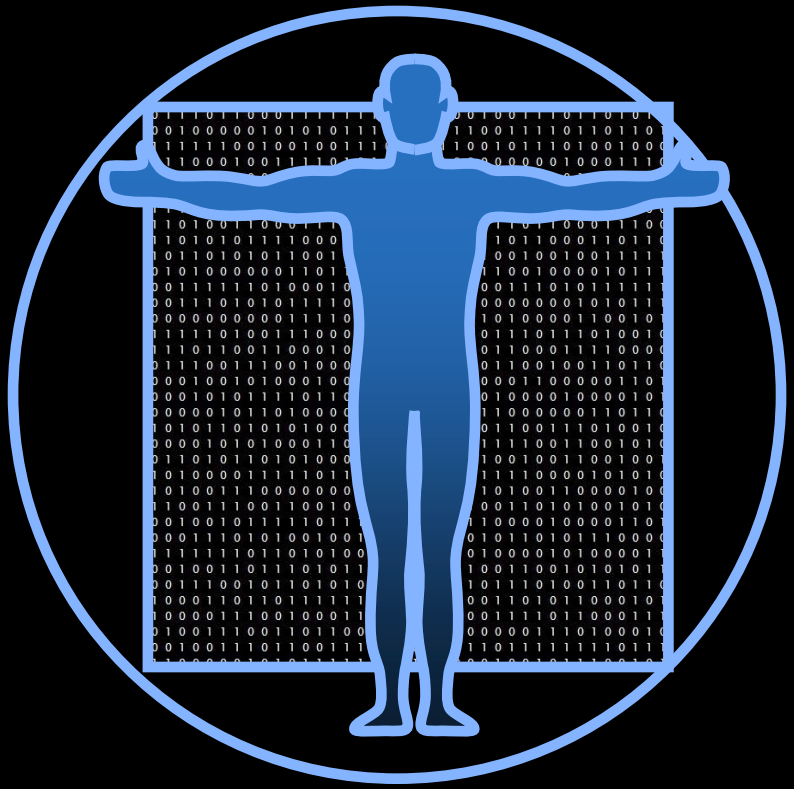
Genetics is just the beginning…

Genes + Environment + Brain + Body

www.experimentalman.com



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

Due Out: March, 2009