Online Direct-to-Consumer Genetic Testing: Implications of the New Business Model

June 29th 2010

Darren Platt
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http://tinyurl.com/2528xrx

Disclaimers:

1) The views presented here are my own and do not in any way represent my past or present employer(s).

2) I have a modest financial stake in a personal genomics company

3) I'm Australian and all Australians are criminals by descent

http://tinyurl.com/2528xrx

My Background

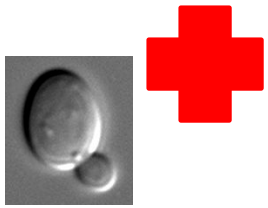
- Ph.D. C.S [Genome mapping]

- Post doc [Human genome project]

- Director of Informatics [Biotech/pharma]

- Head of Informatics [Bio energy genomics]

- Director of Research [Personal Genomics]



- Principal Scientist [Bio energy]

http://tinyurl.com/2528xrx

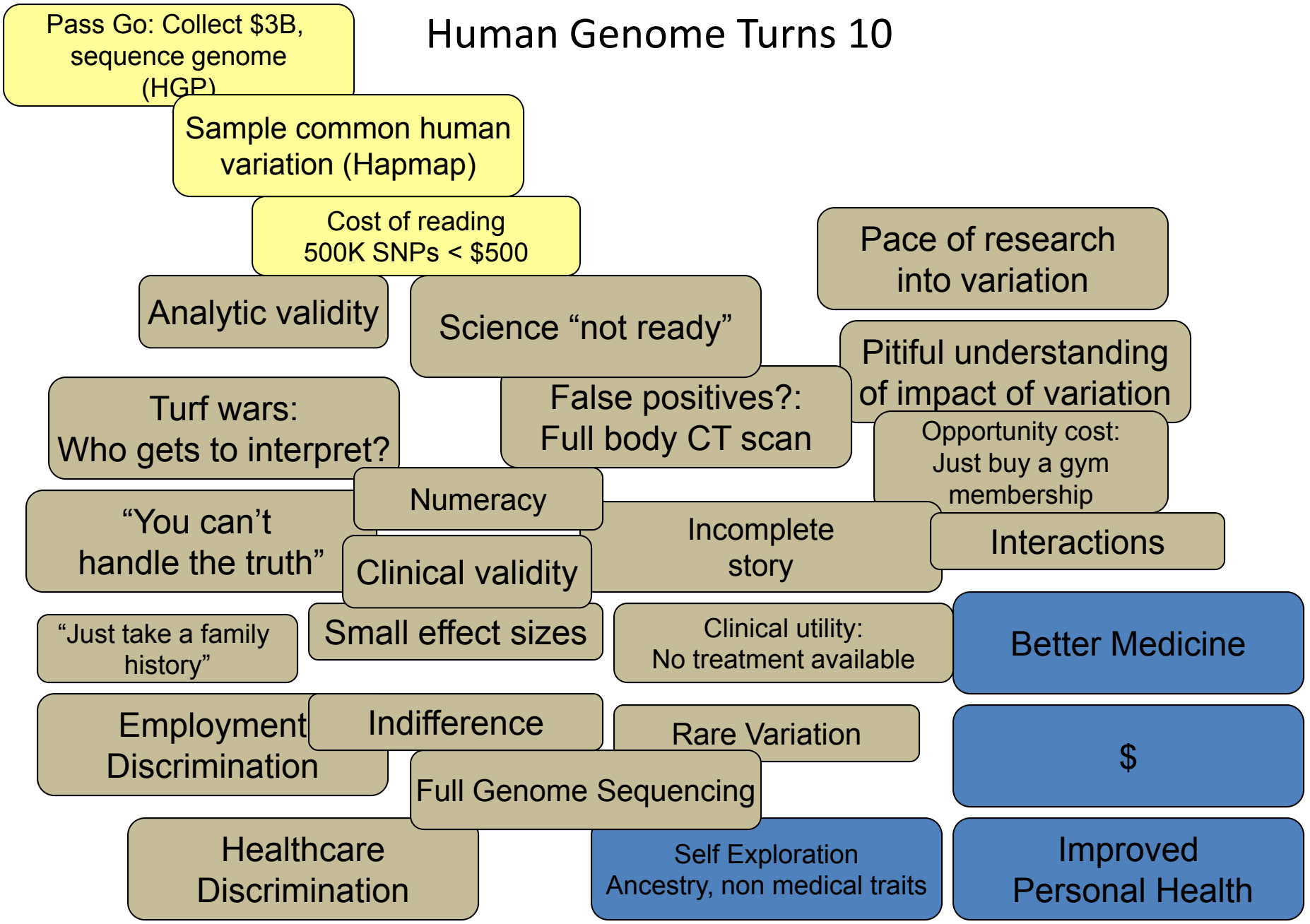
State of the Science

The Business Motivation

The Customer Experience

State of the Science

Human Genome Turns 10



Human Genetic Variation

- Mostly talking today about:
  Single Nucleotide Polymorphisms
  = SNPs or “snips”

TATCTACATCTACTTATCTATCTGA**C**GGCTATAC…

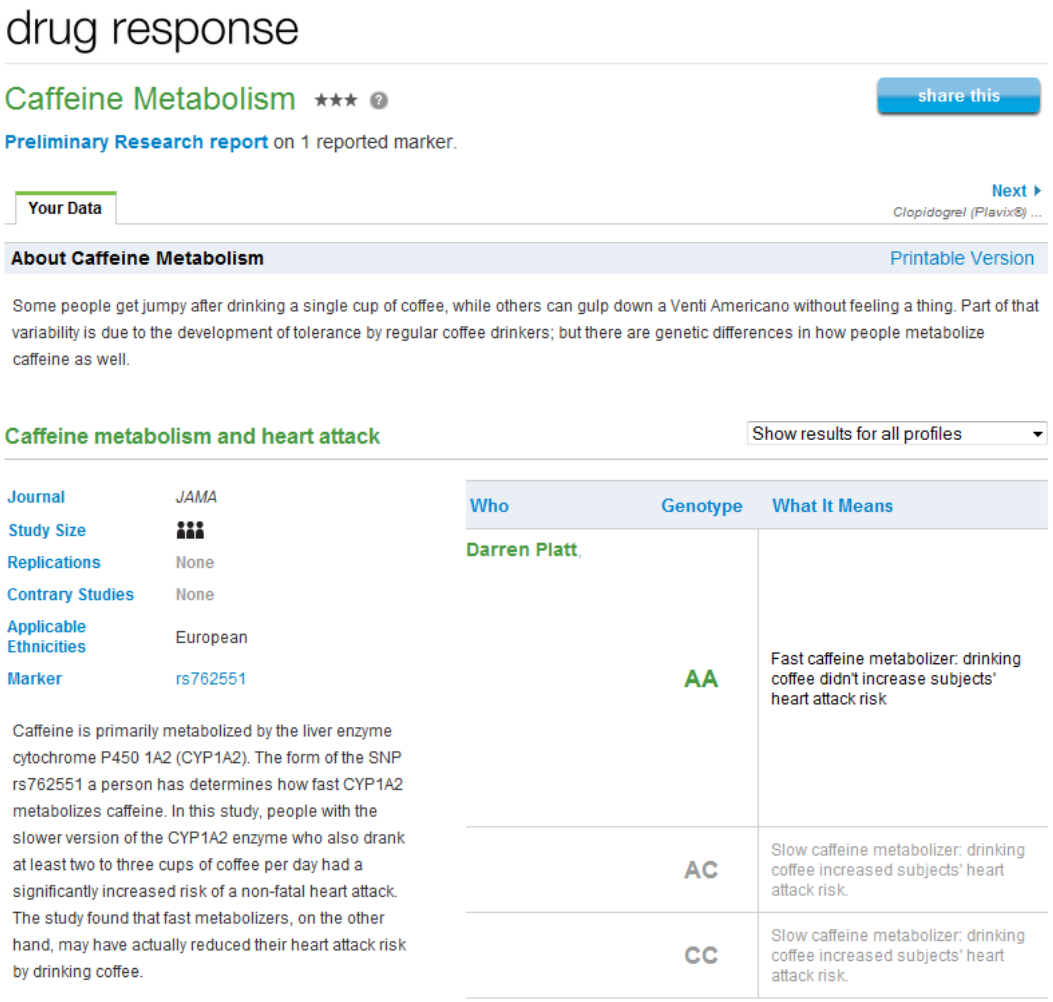
TATCTACATCTACTTATCTATCTGA**T**GGCTATAC…

- Other types of variation exist

SNPs

- Most SNPs have no (known) effect
- The vast majority are unassociated with any disease/trait/characteristic [phenotype]
- Some SNPs have been shown to affect a phenotype through statistical association

Example Trait: Caffeine Metabolism



drug response

Caffeine Metabolism ★★★

share this

Preliminary Research report on 1 reported marker.

Your Data

Next ▸ Clopidogrel (Plavix®) ...

About Caffeine Metabolism — Printable Version

Some people get jumpy after drinking a single cup of coffee, while others can gulp down a Venti Americano without feeling a thing. Part of that variability is due to the development of tolerance by regular coffee drinkers; but there are genetic differences in how people metabolize caffeine as well.

Caffeine metabolism and heart attack — Show results for all profiles

Journal	*JAMA*
Study Size	
Replications	None
Contrary Studies	None
Applicable Ethnicities	European
Marker	rs762551

Caffeine is primarily metabolized by the liver enzyme cytochrome P450 1A2 (CYP1A2). The form of the SNP rs762551 a person has determines how fast CYP1A2 metabolizes caffeine. In this study, people with the slower version of the CYP1A2 enzyme who also drank at least two to three cups of coffee per day had a significantly increased risk of a non-fatal heart attack. The study found that fast metabolizers, on the other hand, may have actually reduced their heart attack risk by drinking coffee.

Who	Genotype	What It Means
Darren Platt,	AA	Fast caffeine metabolizer: drinking coffee didn't increase subjects' heart attack risk
	AC	Slow caffeine metabolizer: drinking coffee increased subjects' heart attack risk.
	CC	Slow caffeine metabolizer: drinking coffee increased subjects' heart attack risk.

https://www.23andme.com/you/journal/pre_caffeine_metabolism/overview/

More Complex Traits

Darren Platt

26.3 out of 100

men of European ethnicity who share Darren Platt's genotype will get Type 2 Diabetes between the ages of 20 and 79.

Average

23.7 out of 100

men of European ethnicity will get Type 2 Diabetes between the ages of 20 and 79.

What does the Odds Calculator show me?

Use the ethnicity and age range selectors above to see the estimated incidence of Type 2 Diabetes due to genetics for men with **Darren Platt**'s genotype. The 23andMe Odds Calculator assumes that a person is free of the condition at the lower age in the range. You can use the name selector above to see the estimated incidence of Type 2 Diabetes for the genotypes of other people in your account.

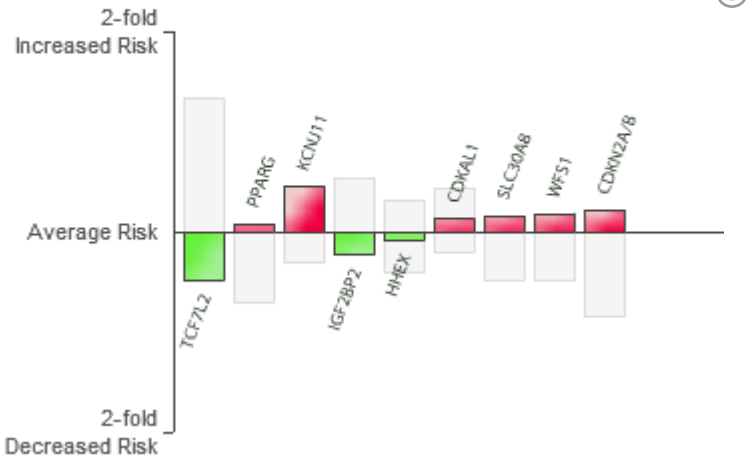
The 23andMe Odds Calculator only takes into account effects of markers with known associations that are also on our genotyping chip. Keep in mind that aside from genetics, environment and lifestyle may also contribute to one's chances of developing type 2 diabetes.

Genes vs. Environment

26 %
Attributable to Genetics

The heritability of type 2 diabetes is estimated to be 26
to differences in risk for this condition than genetic fact
include both unknown factors and known factors such
include obesity, gestational diabetes, giving birth to at l
pressure, abnormal cholesterol levels, physical inactivi
associated with insulin resistance, a history of impaire
history of cardiovascular disease. (sources)

Marker Effects



Potential Problems

- Technical
  - Original research on the association — 1/3 scientific results contradicted
  - Error in Curation of SNP/ literature — DTC firms add value here
  - Genotyping error — Concordance extremely high > 99%
  - Genotype chip design problem — Large populations help with Curation
  - Software quality — Algorithms should be disclosed
  - Data handling steps — Need strong operational expertise
  - Sample handling problems — Occurred recently for 23andMe
  - Incomplete genotyping — Platforms will need to move to whole genome sequencing
- Customer issues
  - Understanding environment vs genetic risk — Users mostly get genes ≠ destiny
  - Relative vs. absolute risk — 1% lower risk could still be very high
  - Incomplete information — Unexplained genetic variation
  - Lack of follow through with professional — No light weight way to get counseling
  - Not understanding limits of current research
  - Numeracy — Need to provide simple interpretation
  - Scientific literacy — Target very simple reading level
  - Follow up testing — Connect users with diagnostic services
- For comparison
  - The Hepatitis C antibody test has a 15%-60% false positive rate in populations where prevalence is < 10%.

The Business Motivation

Good overview of how one (atypical) genome user is applying their genetic data

- Not simply a financial proposition
- Degree of idealism and frustration with pace of research and medical innovation
- Research 2.0, Health 2.0 etc.

http://www.wired.com/magazine/2010/06/ff_sergeys_search/all/1

Business Model

- Customers
  - Pay $25 - $1000 to DTC service, receive sample collection , send saliva to CLIA lab
  - Receive raw genotype, access to curated literature and interpretation of genotype
- CLIA lab
  - Generates genotype service of unnamed sample, destroys sample, sends genotype to DTC firm.
- DTC firm
  - Pairs genotype data with customer account
  - Processes genotype data
  - Curates literature
  - Provides interpretation of genotype in context of literature
  - Provides results of complex algorithms analyzing whole genotype or groups of SNPS
  - Some provide social networking services, ancestry features, connections with counseling services, perform original research
  - Develop drugs?

Other sources of revenue?

- Pharmaceutical companies could
  - Buy population frequency data
  - Buy or sponsor research results
  - Recruit patients
- Academics or Research Foundations could
  - Outsource research [e.g. Parkinson's Inst. & 23andMe]
  - Recruit patients
- Long term?
  - Provide medical diagnostic services to health care providers

23andMe Original Research

23andMe and a New Paradigm for Research

Published by 23andMe under 23andMe and you, news, tomorrow's breakthroughs

Jun 22 2010

As highlighted in Thomas Goetz's new *Wired* article "Sergey's Search*," 23andMe's innovative web-based research platform is pushing Parkinson's disease research ahead at an unprecedented pace. With our database clocking in at 50,000 genotyped customers—a number that grows everyday—we're poised to make exciting discoveries in many other areas.

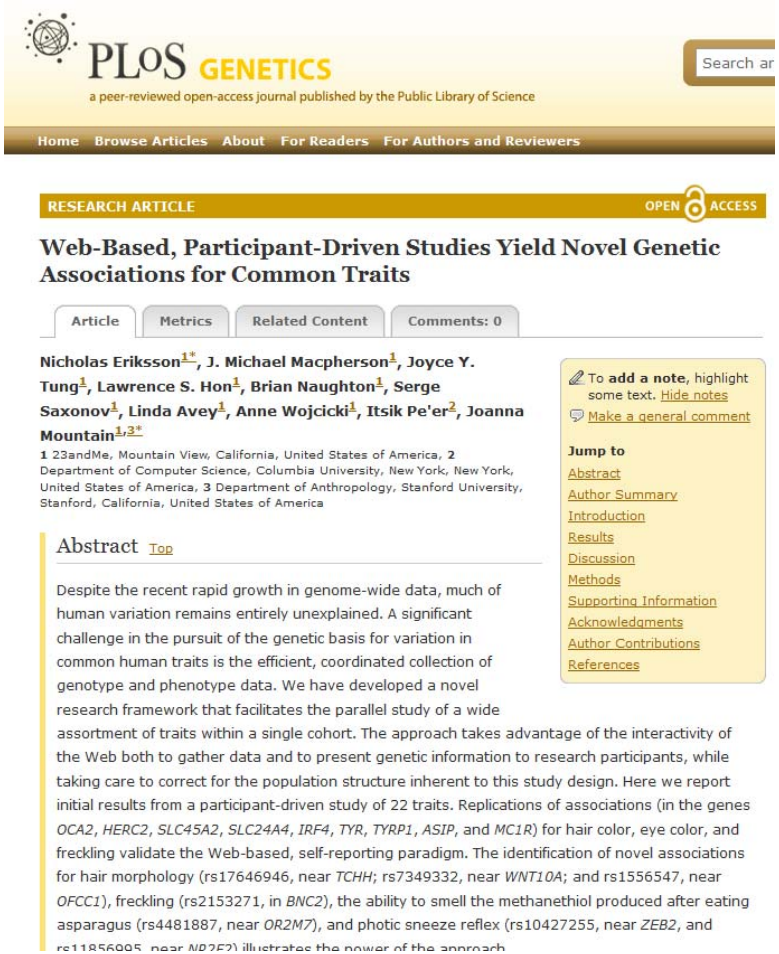
As long as we are tooting our own horn, here are some other numbers we'd like to shout from the rooftops:

- **40** research surveys in progress
- **29,000** customers participating in research…so far
- **9 MILLION** research questions answered
- **650+** genome-wide association studies being run in parallel
- **100s** of genetic associations found – both replications and novel discoveries

- Large scale
- Enabled by web platform

http://spittoon.23andme.com/2010/06/22/23andme-and-a-new-paradigm-for-research/

Web driven research works, Published, Peer reviewed results



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RESEARCH ARTICLE OPEN ACCESS

Web-Based, Participant-Driven Studies Yield Novel Genetic Associations for Common Traits

Article Metrics Related Content Comments: 0

Nicholas Eriksson[1*], J. Michael Macpherson[1], Joyce Y. Tung[1], Lawrence S. Hon[1], Brian Naughton[1], Serge Saxonov[1], Linda Avey[1], Anne Wojcicki[1], Itsik Pe'er[2], Joanna Mountain[1,3*]

1 23andMe, Mountain View, California, United States of America, **2** Department of Computer Science, Columbia University, New York, New York, United States of America, **3** Department of Anthropology, Stanford University, Stanford, California, United States of America

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Make a general comment

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Results
Discussion
Methods
Supporting Information
Acknowledgments
Author Contributions
References

Abstract Top

Despite the recent rapid growth in genome-wide data, much of human variation remains entirely unexplained. A significant challenge in the pursuit of the genetic basis for variation in common human traits is the efficient, coordinated collection of genotype and phenotype data. We have developed a novel research framework that facilitates the parallel study of a wide assortment of traits within a single cohort. The approach takes advantage of the interactivity of the Web both to gather data and to present genetic information to research participants, while taking care to correct for the population structure inherent to this study design. Here we report initial results from a participant-driven study of 22 traits. Replications of associations (in the genes *OCA2*, *HERC2*, *SLC45A2*, *SLC24A4*, *IRF4*, *TYR*, *TYRP1*, *ASIP*, and *MC1R*) for hair color, eye color, and freckling validate the Web-based, self-reporting paradigm. The identification of novel associations for hair morphology (rs17646946, near *TCHH*; rs7349332, near *WNT10A*; and rs1556547, near *OFCC1*), freckling (rs2153271, in *BNC2*), the ability to smell the methanethiol produced after eating asparagus (rs4481887, near *OR2M7*), and photic sneeze reflex (rs10427255, near *ZEB2*, and rs11856995, near *NR2F2*) illustrates the power of the approach

- Replicated known results
- Discovered additional associations
- Raised issues around IRB review and consent

http://www.plosgenetics.org/article/info%3Adoi%2F10.1371%2Fjournal.pgen.1000993

Are DTC services medical in nature?

- Copious disclaimers saying no.
  - … does not provide medical advice, diagnosis or treatment.
  - Description of What the Services Are Not: We Do Not Provide Medical Advice, And The Services Cannot Be Used For Health Ascertainment or Disease Purposes
  - What you see here are not the results of a diagnostic test. These are the results of calculations comparing your genetic sequence to sequences of participants in studies published in the world literature on genetic risk for these diseases.
- Official skepticism
  - Frankly, it blows my mind that someone would be saying that looking at whether you are going to get multiple sclerosis is recreational," says a New York official who spoke on condition of anonymity. Forbes 4/17/2008
  - Action by New York, California officials forced CLIA lab certification
  - Current investigation by FDA claiming DTC services are medical devices

Regulation is Well Intended but …
Not Clear they were doing their Homework

State of California—Health and Human Services Agency
Department of Public Health

Mark B Horton, MD, MSPH
Director

ARNOLD SCHWARZENEGGER
Governor

June 9, 2008

Kari Stefansson, CEO
deCODEme Genetics
Sturlugata 81S-101
Reykjavik, Iceland

Certified mail receipt verification 7004-1160-0003-4426-9920

NOTICE TO CEASE AND DESIST
PERFORMING GENETIC TESTING WITHOUT LICENSURE
OR PHYSICIAN ORDER

Dear Ms. Stefansson,

It has come to the attention of the California Department of Public Health (Department), Laboratory Field Services, that deCODEme Genetics is in violation of California law. Business and Professions (B&P) Code Section 1241 requires that all clinical laboratories in California or receiving biological specimens originating in California for the purpose of performing a clinical laboratory test or examination, possess a clinical laboratory license or registration[1].

deCODEme Genetics is also in violation of B&P Code Section 1288 which prohibits the offering of a clinical laboratory test directly to the consumer without a physician order, unless specifically exempt. Genetics tests are NOT exempt. As such, the test must be ordered by a physician or surgeon.

In order to be granted a California clinical laboratory license, in addition to meeting all other licensure requirements, deCODEme Genetics must provide satisfactory validation documentation to verify the

http://sandberghans.blogspot.com/1999_08_01_archive.html

California requires genetic tests be performed in CLIA certified labs

Pathway Genomics Markets through Walgreens

Los Angeles Times | HEALTH

Booster Shots

ODDITIES, MUSINGS AND NEWS FROM THE HEALTH WORLD

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Direct-to-consumer genetic test kits coming soon to a drug store near you

May 11, 2010 | 1:09 pm

Shoppers who go to the drug store to fill their Plavix prescriptions or pick up a bottle of prenatal vitamins may soon find themselves reconsidering these mundane purchases.

The reason? A new genetic testing kit that will hit the shelves of select Walgreens stores later this month. The test could potentially tell you that taking Plavix increases your risk of heart attack or stroke, or that your baby could inherit a fatal genetic disease.

Companies such as 23andMe and Navigenics have been selling testing kits directly to consumers over the Internet for years. But a San Diego-based start-up firm called Pathway Genomics announced Tuesday that it would offer its Insight Saliva Collection Kits at Walgreens for $20 to $30 (the exact price has not yet been determined).

The kit includes directions for collecting a sample of spit and a pre-addressed, postage-paid envelope in which to ship the sample back to Pathway's lab. Customers would then go to the company's website and order up to three genetic tests.

- "Home brew" or Test Kit?
- Single entity developer/provider tests are more lightly regulated as home brews
- Pathway genomics became a test kit provider by attempting to sell through Walgreens and attracted FDA scrutiny
- Now other DTC firms are under investigation

FDA subpoena

ONE HUNDRED ELEVENTH CONGRESS

Congress of the United States

House of Representatives

COMMITTEE ON ENERGY AND COMMERCE

2125 RAYBURN HOUSE OFFICE BUILDING

WASHINGTON, DC 20515–6115

MAJORITY (202) 225–2927
FACSIMILE (202) 225–2525
MINORITY (202) 225–3641

energycommerce.house.gov

May 19, 2010

Ms. Anne Wojcicki
President
23andMe, Inc.
1390 Shorebird Way
Mountain View, CA 94043

Dear Ms. Wojcicki:

The Committee on Energy and Commerce and its Subcommittee on Oversight and Investigations are examining personal genetic tests sold to consumers over the Internet. Recent press reports suggest that at least one genetic testing company is now seeking to sell these tests in retail locations, despite concern from the scientific community regarding the accuracy of test results.[1]

In order to assist the Committee with its examination of this issue, we ask that you provide the Committee with the following information and documents for the period from January 1, 2007, to the present:

1. A chart listing the conditions, diseases, consumer drug responses, and adverse reactions for which you test;

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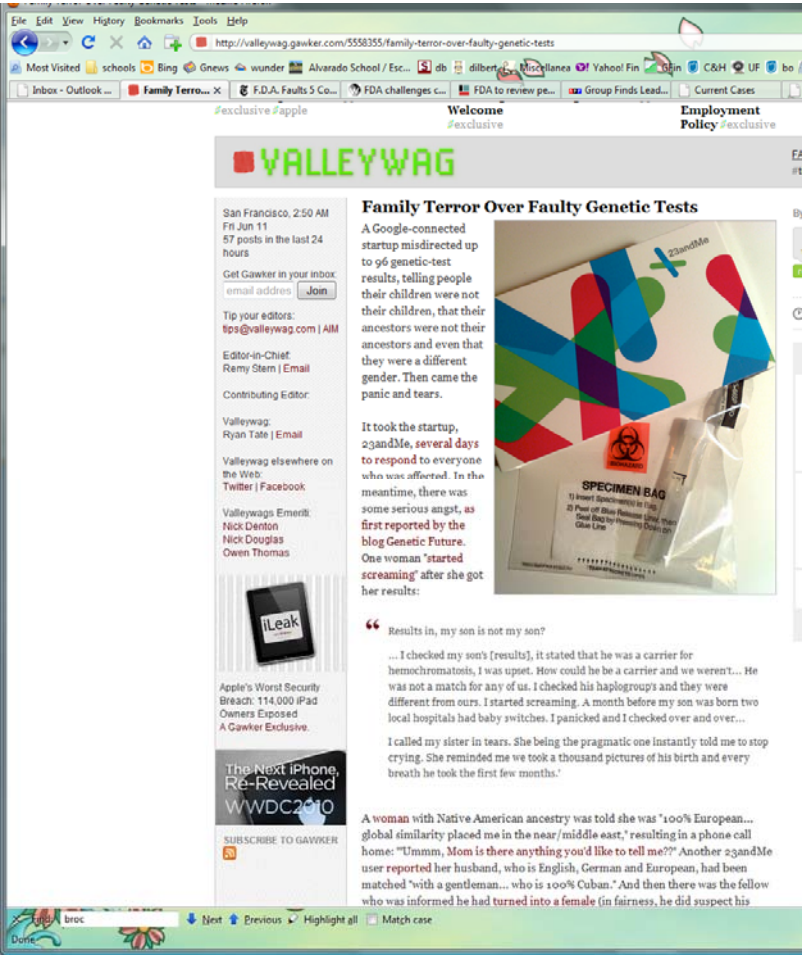
[1] *Start-Up May Sell Genetic Tests in Stores*, The New York Times (May 10, 2010); *Walgreens Delays Selling Genetic Testing Kit*, The New York Times (May 13, 2010).

23andMe mis-tracks 96 samples



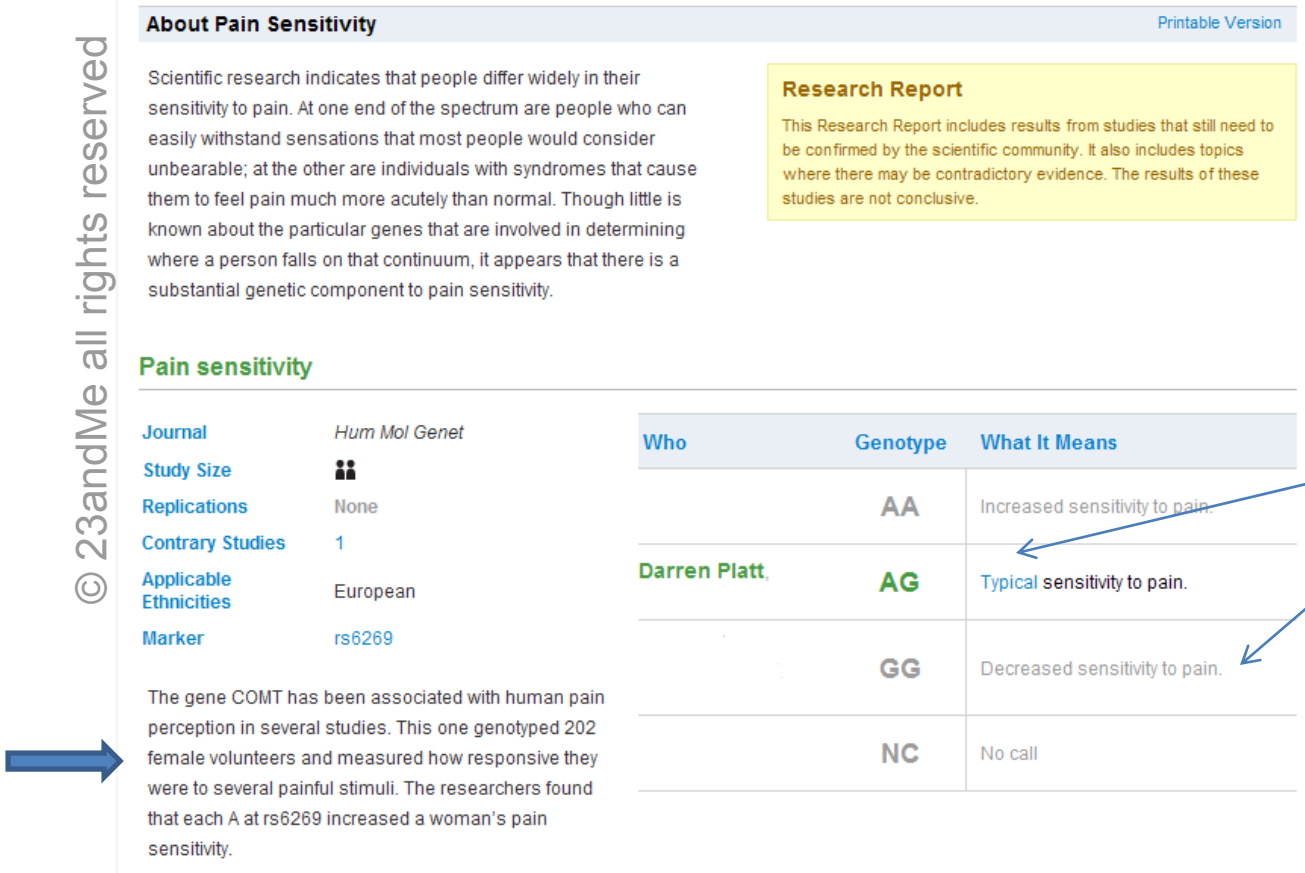
- CLIA lab mis handled a plate of customer samples
- Was quickly (< 2 days) detected and corrected
- Some user distress
- High information content makes detection easy
  c.f 96 mixed cholesterol samples
- New measures in place to prevent this
- Incredibly bad timing

http://valleywag.gawker.com/5558355/family-terror-over-faulty-genetic-tests

The Consumer Experience

Interpretation process

- What is the trait ?
- What is my “score” ?
- What were the alternatives?
- Did I win/lose?
- Is it applicable to me?



About Pain Sensitivity Printable Version

Scientific research indicates that people differ widely in their sensitivity to pain. At one end of the spectrum are people who can easily withstand sensations that most people would consider unbearable; at the other are individuals with syndromes that cause them to feel pain much more acutely than normal. Though little is known about the particular genes that are involved in determining where a person falls on that continuum, it appears that there is a substantial genetic component to pain sensitivity.

Research Report

This Research Report includes results from studies that still need to be confirmed by the scientific community. It also includes topics where there may be contradictory evidence. The results of these studies are not conclusive.

Pain sensitivity

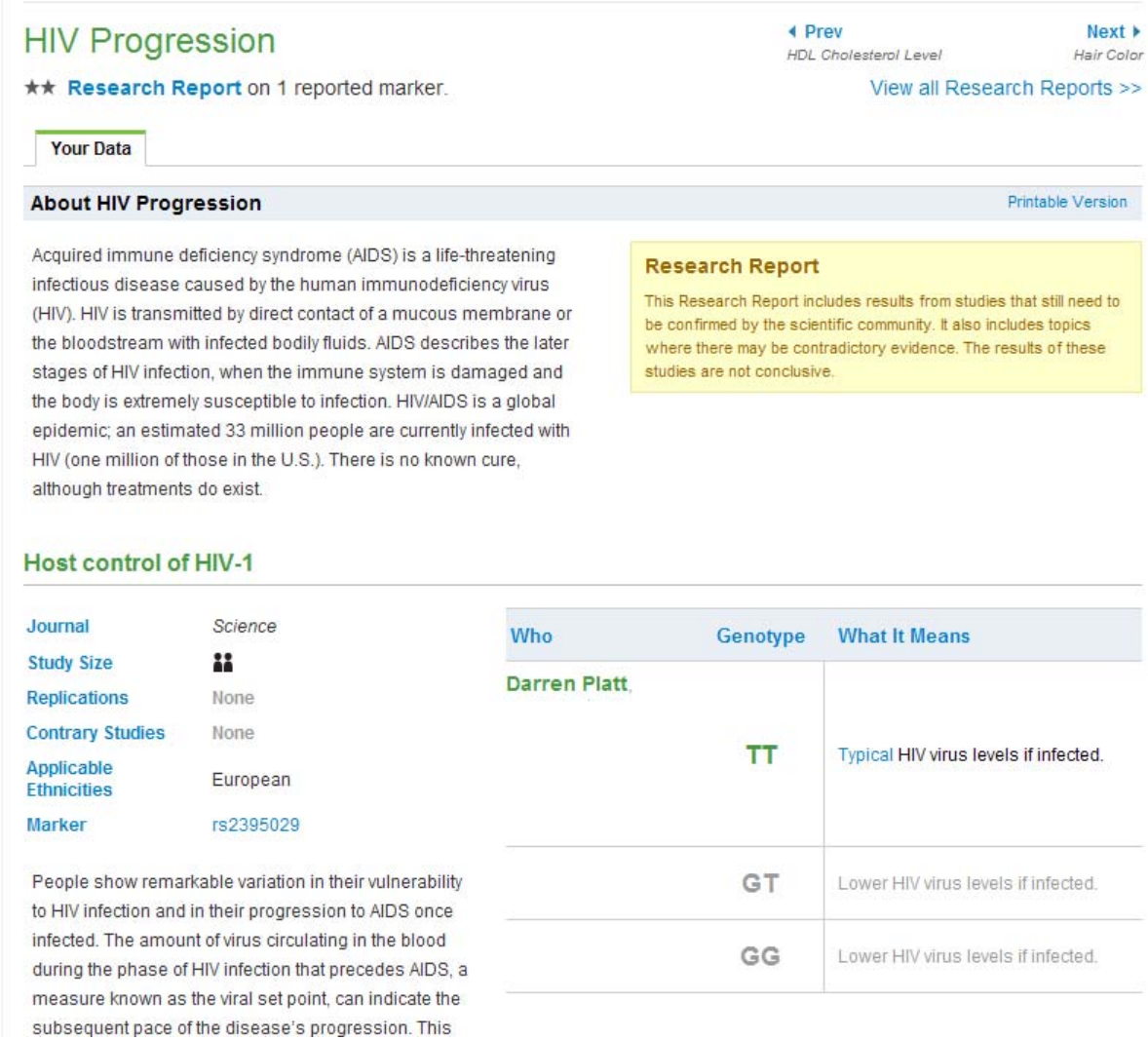
Journal	*Hum Mol Genet*
Study Size	
Replications	None
Contrary Studies	1
Applicable Ethnicities	European
Marker	rs6269

The gene COMT has been associated with human pain perception in several studies. This one genotyped 202 female volunteers and measured how responsive they were to several painful stimuli. The researchers found that each A at rs6269 increased a woman's pain sensitivity.

Who	Genotype	What It Means
	AA	Increased sensitivity to pain.
Darren Platt	AG	Typical sensitivity to pain.
	GG	Decreased sensitivity to pain.
	NC	No call

- Here I am typical
- I guess I would prefer decreased sensitivity

Typical Again..



HIV Progression

◂ Prev
HDL Cholesterol Level

Next ▸
Hair Color

★★ **Research Report** on 1 reported marker.

View all Research Reports >>

Your Data

About HIV Progression Printable Version

Acquired immune deficiency syndrome (AIDS) is a life-threatening infectious disease caused by the human immunodeficiency virus (HIV). HIV is transmitted by direct contact of a mucous membrane or the bloodstream with infected bodily fluids. AIDS describes the later stages of HIV infection, when the immune system is damaged and the body is extremely susceptible to infection. HIV/AIDS is a global epidemic; an estimated 33 million people are currently infected with HIV (one million of those in the U.S.). There is no known cure, although treatments do exist.

Research Report

This Research Report includes results from studies that still need to be confirmed by the scientific community. It also includes topics where there may be contradictory evidence. The results of these studies are not conclusive.

Host control of HIV-1

Journal	*Science*
Study Size	
Replications	None
Contrary Studies	None
Applicable Ethnicities	European
Marker	rs2395029

People show remarkable variation in their vulnerability to HIV infection and in their progression to AIDS once infected. The amount of virus circulating in the blood during the phase of HIV infection that precedes AIDS, a measure known as the viral set point, can indicate the subsequent pace of the disease's progression. This

Who	Genotype	What It Means
Darren Platt	TT	Typical HIV virus levels if infected.
	GT	Lower HIV virus levels if infected.
	GG	Lower HIV virus levels if infected.

- This time not so great..
- Report greatly simplifies application of research but still very complicated
- DTC companies want to responsibly provide a lot of information
- Possibly inhibits ease of understanding for less sophisticated users

My “Scorecard”

HI RIBL

↑ AMD
↓ asthma
↓↓ error avoidance :)
↓ lower lumbar dis

typical odds red hair
20 vs 17 M. Ward

Height → NOT perfect

↓ Breast Cancer
↑ Post caffeine
↓ celiac
↓ colorectal cancer
↓↓ crohn's dis
no CF
↑ dyslexia
↑ exfoliating glaucoma
typical HDL

Heroin addiction typical

↓ lung cancer.

↑ lupus
Breast fed IQ ↑
↓↓ MS

“You Can’t Handle the Truth”

Reasons for seeking genetic susceptibility testing among first-degree relatives of people with Alzheimer disease
Roberts J, et al. Alzheimer Dis Assoc Disord. 2003 Apr-Jun;17(2):86-93.

- Randomized trial of 206 asymptomatic adult children of people with AD, 160 of whom went on to be tested
- Motivation
  - 93.9% contribute to research
  - 87.4% arrange personal affairs
  - 86.8% hope that an effective treatment will be developed
- Best predictor of pursuit of testing, was strong endorsement of need to prepare family

- Argues strongly in favor of scientific testing of assumptions about people’s behaviour e.g Scripps/Navi/Microsoft/Affy longitudinal study

Final Thoughts

- Do I have a fundamental right to read my DNA?
- DTC genomics poses a huge conflict of interest for the medical, ethics and business communities
- Will an imperfect solution be tolerated?
- Encouraging innovation towards more complete medical risk models might be safer than the current ambiguous situation
- Web driven research could dramatically speed genetic research

http://tinyurl.com/2528xrx