Evolution of Direct-to-Consumer Genetic Testing: Present and Future Markets

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August 31, 2009

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The Current State of Affairs

- "If we postpone until we have more information, we are not taking advantage of what we know" -- *K. Steffansson*
- "We all know we are going to die, but don't worry about it. Why not have the same response to personal genetic information?" -- *S. Pinker*
- The revolution will have a great impact on the medical community. When a consumer arrives at the doctor's office to get help interpreting the genomic information, the doctor is likely to respond "What's a SNP?" -- *The Wall Street Journal*

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How we can use genetics today?

- Take advantage of what we know now – use information to educate, motivate and engage people in the uses of genetics
- These are early days in the clinical utility of genetics in complex diseases
- Report genetically valid results
- Meet/exceed regulatory standards
- Responsible communication/utilization of data
- Education of clients and physicians
- Ensure privacy and security of data
- "Ultimately the translation of advances in genomic research to routine patient care will require an educated patient population and educated health care professionals" Feero, Guttmacher and Collins, 2008; JAMA 299; 1351

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Translating Genetic Discoveries into Medical Practice

- More and more genetic information will become validated and clinically useful, including gene-gene and gene-environment interactions
- DTC companies can provide comprehensive genetic tests to the general population, with information integrated into a PHR
- DTC genetic companies will translate scientific discoveries for the consumer and the physician and help to provide education on the use of genetic information
- Genetic information will play a critical role in the future of medicine
  - Early prediction of risk coupled with preventative action
  - Early detection of disease combined with targeted therapies
  - Early prevention based on novel therapies developed from genetic discoveries

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Personalized Medicine is Making a Difference in the Lives of People

- Kate Robbins
  - Lung cancer
- Doris Goldman
  - Cardiac sudden death
- Jeff Gulcher
  - Prostate cancer

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Pathway Genomics, Corp.

- DTC genetic testing company with on-site lab
- CLIA/CA laboratory licenses, high complexity testing
- World class scientific team of MDs, PhDs, Geneticists, Scientists and Bioinformatics
- Custom genotyping chip with broad genomic coverage: Complex disorders, monogenic diseases, pharmacogenetics and ancestry
- Multiple genotyping platforms used with cross validation of platforms
- Family history and lifestyle questionnaires are used to produce a comprehensive picture of disease risk
- Genetic counselors are used – certain genotype results will prompt automatic counseling session

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Management and Scientific Team

Jim Plante, President/CEO

David Becker, PhD, Chief Scientific Officer, Geneticist

Michael Nova, MD, Chief Medical Officer

Linda Wasserman, MD, PhD, Dir of Clinical Pathology

Neil Howell, PhD Geneticist

Michael Cox, Chief Privacy Officer

Scott Mednick, Chief Marketing Officer

Chris d'Eon, VP Marketing

Jim Woodman, VP Business Development

Edgar MacBean, VP Product Dev &Mgmt

Gemini Bio

NEUROGENETICS, INC.

Scientific Advisory Board

Rudolph E. Tanzi, PhD

Joseph P. and Rose X. Kennedy Professor of Neurology, Harvard Medical School

Director, Genetics and Aging Research Unit, Institute for Neurodegenerative Disease, Massachusetts General Hospital

Christoph Lange, PhD

Associate Professor Department of Biostatistics, School of Public Health, Harvard University

Assistant Professor of Medicine, Harvard Medical School

Hywel Jones, PhD

Founding team of two gene sequencing companies True Materials and ParAllele.

True Materials

DNA Sciences

Stephen L. Wagner, PhD

Founding Scientist, Neurogenetic Pharmaceuti

SIBIA Neurosciences, INC.

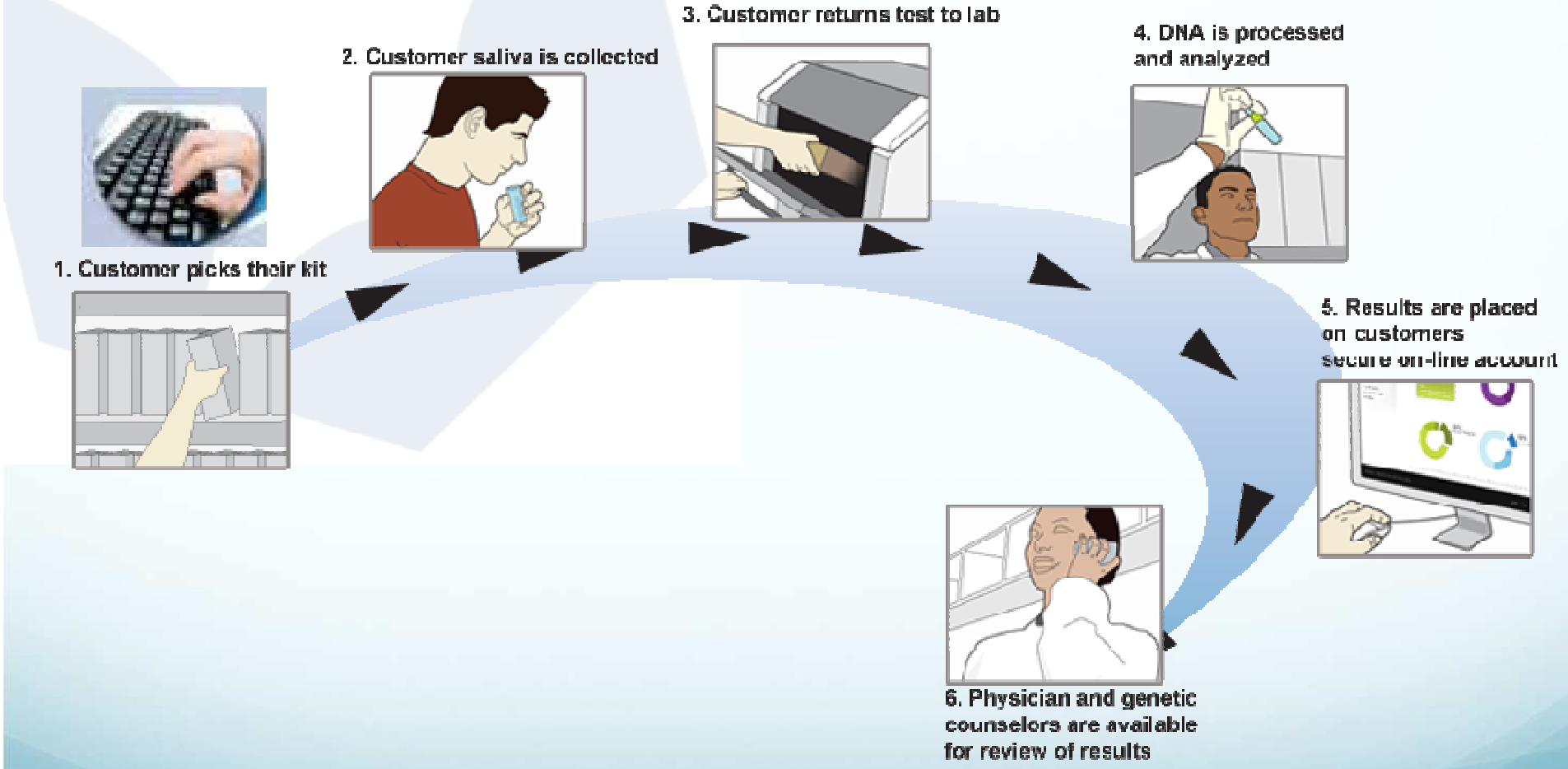
Principal Investigator - University of California San Diego School of Medicine

John C. Reed, MD, PhD

President and Chief Executive Officer, Burnham Institute for Medical Research

Blaine Bettinger, PhD - "The Genetic Genealogist"

The Process at Pathway Genomics



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Pathway Genomics Saliva Collection Kit

- Pathway Genomics-developed
- Simple, easy saliva collection
- Sample container and shipping device included

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Criteria for SNP Selection in Complex Conditions

- **Validated marker = primary and secondary confirmation study**
- **Preliminary research marker = primary study**
- **Primary study**
  - Minimum 1000 cases and 1000 controls
  - Ethnic matching
  - p value, OR significant
  - Can use proxy markers LD=1
- **Secondary study**
  - Minimum 500 cases and 500 controls
  - Same ethnicity as primary study
  - Same allele must show association in the same direction
  - OR significant
- All papers reviewed by PhD and/or MD staff
- One SNP selected per gene/region to avoid duplicating a signal
- We will continue to update the panel and odds ratios as more is known

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Pathway Genomics Reports on 25 of the Most Common Complex Conditions

Complex Diseases - Currently Reported	# of Genes
Age-related macular degeneration	4
Alzheimer's disease, late onset	1
Amyotrophic lateral sclerosis (sporadic)	1
Asthma	2
Atrial fibrillation	1
Breast cancer	11
Colorectal cancer	7
Coronary artery disease	14
Diabetes, Type 1	14
Diabetes, Type 2	20
Glaucoma	1
Hypertension	2
Leukemia	4

Complex Diseases - Currently Reported	# of Genes
Lung cancer	4
Melanoma	4
Multiple sclerosis	11
Myocardial infarction	18
Obesity	4
Osteoarthritis	3
Peripheral arterial disease	1
Prostate cancer	17
Psoriasis	8
Rheumatoid arthritis	13
Systemic lupus erythematosus	13
Ulcerative colitis	10

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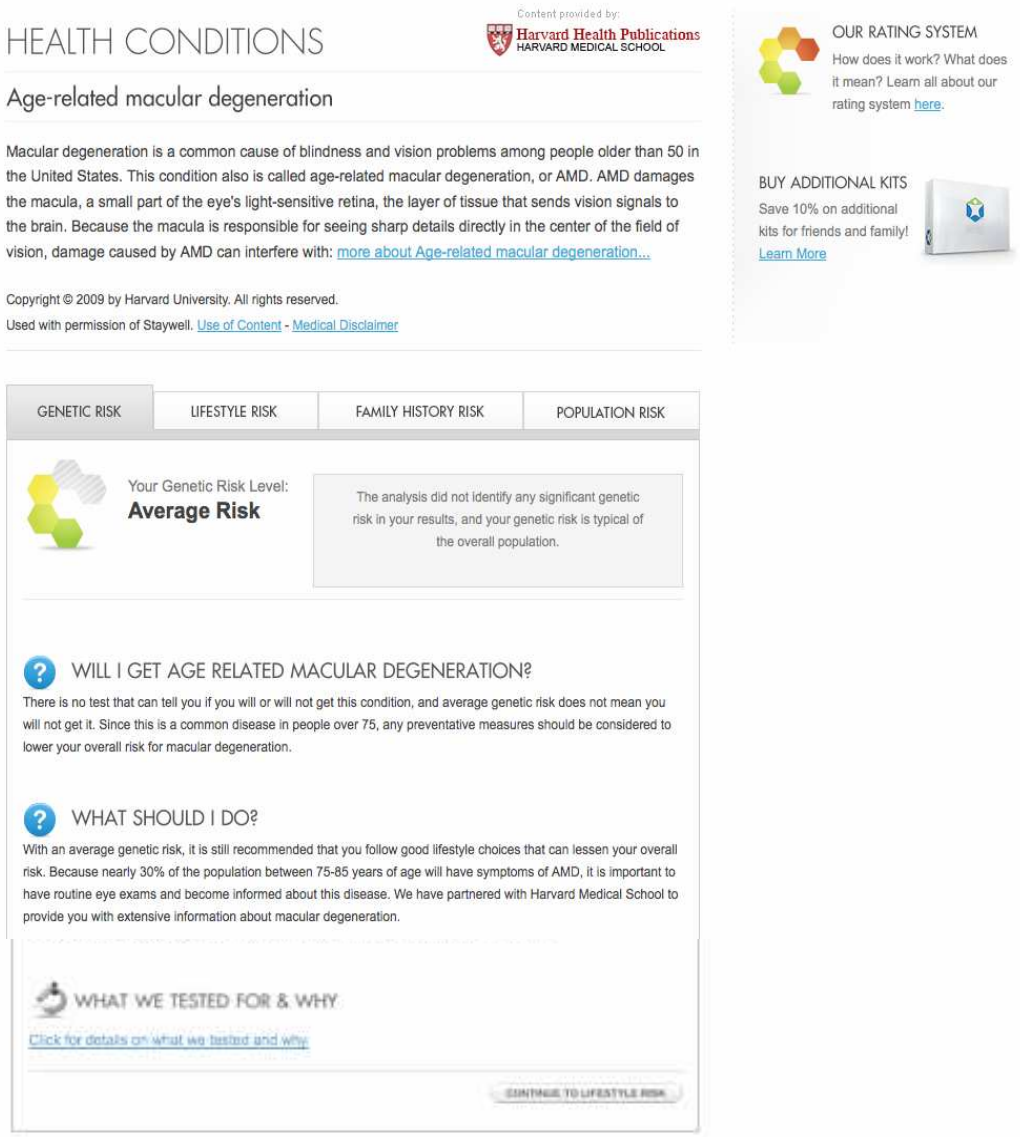
Health Conditions: Age-Related Macular Degeneration



HEALTH CONDITIONS

Content provided by: Harvard Health Publications HARVARD MEDICAL SCHOOL

Age-related macular degeneration

Macular degeneration is a common cause of blindness and vision problems among people older than 50 in the United States. This condition also is called age-related macular degeneration, or AMD. AMD damages the macula, a small part of the eye's light-sensitive retina, the layer of tissue that sends vision signals to the brain. Because the macula is responsible for seeing sharp details directly in the center of the field of vision, damage caused by AMD can interfere with: more about Age-related macular degeneration...

GENETIC RISK | LIFESTYLE RISK | FAMILY HISTORY RISK | POPULATION RISK

Your Genetic Risk Level:
Average Risk

The analysis did not identify any significant genetic risk in your results, and your genetic risk is typical of the overall population.

WILL I GET AGE RELATED MACULAR DEGENERATION?

There is no test that can tell you if you will or will not get this condition, and average genetic risk does not mean you will not get it. Since this is a common disease in people over 75, any preventative measures should be considered to lower your overall risk for macular degeneration.

WHAT SHOULD I DO?

With an average genetic risk, it is still recommended that you follow good lifestyle choices that can lessen your overall risk. Because nearly 30% of the population between 75-85 years of age will have symptoms of AMD, it is important to have routine eye exams and become informed about this disease. We have partnered with Harvard Medical School to provide you with extensive information about macular degeneration.

WHAT WE TESTED FOR & WHY

Click for details on what we tested and why

CONTINUE TO LIFESTYLE RISK

OUR RATING SYSTEM

How does it work? What does it mean? Learn all about our rating system here.

BUY ADDITIONAL KITS

Save 10% on additional kits for friends and family!
Learn More

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AMD: Genetic Details

Age-related macular degeneration

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Genetics Overview

Age and smoking are important risk factors for age-related macular degeneration (AMD). Approximately 30% of people 75 years old or over show signs of AMD. Cigarette smoking increases the risk of AMD two- to four-fold. AMD is more common in white populations than in Hispanic or African-American populations. There is also a strong hereditary component to AMD. In studies with twins, it was estimated that 46% to 71% of the variation in the overall severity of AMD is genetically determined.

Like other late-onset diseases, AMD has early-onset counterparts (monogenic macular dystrophies) that are caused by mutations in single genes. For example, Stargardt disease, which is the most common form of inherited juvenile macular degeneration, is caused by an autosomal recessive mutation in the ABCA4 gene. Like other late-onset diseases, AMD is a complex disease that results from the cumulative effect of mutations in many genes.

In the last five years, variants in the two most important genes that increase the risk of developing AMD have been identified and characterized. These two genes are the complement factor H gene (CFH) on chromosome 1 and the HTRA1 gene on chromosome 10. The study of these genes will give scientists clues to the defects that lead to the development of AMD.

Data Table

Gene/HLA Region	SNP	Your Genotype	Associated Allele	Population Frequency	Odds Ratio	Population Studied	Validated Marker	PubMed ID
C2	rs547154	G/T	T	0.06	0.44	**Caucasian**	Validated	16518403
C3	rs1047286	C/T	T	0.24	1.50	**Caucasian**	Validated	19168221
CFH	rs1061147	A/C	A	0.37	2.34	**Caucasian**	Validated	15870199
HTRA1	rs11200638	G/G	A	0.22	1.00	**Caucasian**	Preliminary	19375943

Molecular details

Pathway Genomics tests for three genes in the complement system: the Y402H mutation in the CFH gene, the IVS10 mutation in the C2 gene and the R102G mutation in the C3 gene all which increase the risk of developing age-related macular degeneration (AMD). In addition, we also test for a promoter mutation in the HTRA1 gene.

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Recessive Monogenic Disorders Covered by Pathway Genomics

Recessive Monogenic Disorders - Carrier Status Determination		
Ashkenazi Jewish disorders	**Inborn errors of metabolism**	**Blood disorders**
Bloom syndrome	3-methylcrotonyl-CoA carboxylase deficiency	Factor XI deficiency
Canavan disease	Biotinidase deficiency	Hemochromatosis
Congenital hypothyroidism	Galactosemia	Hemoglobin C diseases
Cystic fibrosis	Glutaric acidemia I	Hemoglobin E diseases
Factor XI deficiency	Glycogen storage disease type Ia	Sickle cell diseases
Familial dysautonomia	HMG-CoA lyase deficiency	Thalassemia - beta
Familial Mediterranean fever	Medium-chain acyl-coA dehydrogenase deficiency	
Fanconi anemia	Methylmalonic acidemia	**Lysosomal/glycogen storage diseases**
Gaucher disease	Multiple carboxylase deficiency	Bloom syndrome
Glycogen storage disease type Ia	Phenylketonuria	Fabry disease
Hearing loss, nonsyndromic	Propionic acidemia	Gaucher disease
Maple syrup urine disease	Tyrosinemia type I	Glycogen storage disease Ia
Mucolipidosis type IV	Very long-chain acyl-coA dehydrogenase deficiency	Mucolipidosis type IV
Niemann-Pick disease		Niemann-Pick disease
Tay-Sachs disease		Pompe disease
Tay-Sachs pseudodeficiency		Tay-Sachs disease
Thalassemia - beta		

- Where established, PGNX covers ACMG recommended mutation panels for monogenic disorders + more
- Cystic fibrosis (CF): 23 mutations recommended by ACMG (covers 94% of Ashkenazi CF mutations)
  - PGNX covers 23 + 70 rare but recurrent mutations

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Pathway Genomics Tests for Several Pharmacogenetic Markers

Drug Response	Gene
Warfarin sensitivity	CYP2C9; VKORC1
Clopidogrel metabolism	CYP2C19
Abacavir hypersensitivity	HLA*5701
Tamoxifen response	CYP2D6
Methotrexate toxicity	MTHFR
Statin induced myopathy	KIF6
Statin protection against MI	SLOC1B
Caffeine metabolism	CYP1A2
Oral contraceptives and thrombosis	Factor V

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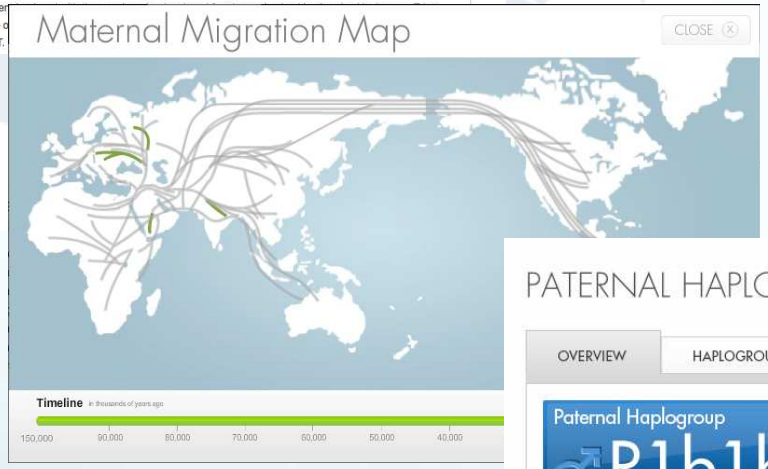

Ancestry
248 Paternal Haplogroups
1200 Maternal Haplogroups
Ancestry Informative Markers
~ 6340 Ancestry Markers
1400 Unique Haplogroups

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Privacy and Security of Client Data is Critical

Privacy = Appropriate Use

Governed by Customer Privacy Policy

- Hired a Chief Privacy Officer (CPO)
- Developed transparent summary and full privacy statements
- Created one page summary matrix fjor easier understanding and compliance
- Website compliance reviews

Security = Privacy Protection

Governed by Internal Information Security Policies

- Administrative, technical and physical controls in place
- Privacy-trained personnel
- HIPAA /HITECH focused, implementing ISO 27002
- “We treat our facility and information as with ‘data center’ level controls

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Pathway Genomics Summary

- Depth and Credibility of Clinical and Scientific Teams, and Advisory Board
- Physicians and Genetic Counselors on Staff
- On Site Laboratory with Federal CLIA / CA State Licenses
- Regulatory Compliance
- 50-90% Lower Cost than other DTC Competitors
- More Genetic Markers Used = Largest # of Disease/Traits Covered
- Custom-designed Chip Containing Numerous Meaningful SNPs
- Custom and Proprietary SNPs assays
- Incorporate use of Family History and Health Questionnaire
- Highly Experienced and Successful Consumer Web Management Team

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Genome Genetic Testing can Provide Benefit Now and in the Future

- "It is pretty clear that the public is afraid of taking advantage of genetic testing. If this continues, the future of medicine that we would all like to see happen stands the chance of being dead on arrival" F. Collins (Former Director, National Human Genome Research Center)
- Informed patients will accelerate the pace of change in medical practice
- Some of the information is actionable today
- At the current pace of scientific endeavor more information becomes actionable each week
- Education on the risks, limitations and benefits is necessary for the consumer and the physician

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Future of DTC Genetics Markets

- The $1000.00 USD genome will be here by 2010
- The complete exome can be sequenced for ~$500.00 USD
- Genotyping will become cheaper - 100,000 markers for $25?
- DNA sequencing will be used for discovery and validation
- Many more markers will be clinically validated and useful
- Inexpensive genotyping will allow for affordable scans for everyone for the majority of the validated causative and meaningful genetic alterations
- DTC genetics companies have the potential to deliver genetic information to the public on a unprecedented scale
- Genetic information and education with responsible communication can have a dramatic impact on future personalized medicine

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