Personalized Medicine: Hype or Help?

The Foundation for Community Health
5/20/09

Greg Feero, M.D., Ph.D.
Chief, Genomic Healthcare Branch
National Human Genome Research Institute
National Institutes of Health
DNA IS NOT YOUR DESTINY
THE TESTS THAT CAN FREE YOU
THE VATICAN’S SECRET SCIENCE CLUB
BRAIN TUNE-UP
SMELL YOUR WAY TO HAPPINESS
EINSTEIN’S BLOOPERS
HOW TO GROW A NEW BODY, ONE CELL AT A TIME
Jim Watson receiving his own personal genome sequence on a DVD

May 31, 2007
Keeping Pace with the Times — The Genetic Information Nondiscrimination Act of 2008

Kathy L. Hudson, Ph.D., M.K. Holohan, J.D., and Francis S. Collins, M.D., Ph.D.

Laws and institutions must go hand in hand with the progress of the human mind. As that becomes more consumers from discrimination by health insurers and employers on
1. The Retail DNA Test
By Anita Hamilton

Before meeting with Anne Wojcicki, co-founder of a consumer gene-testing service called 23andMe, I know just three things about her: she's pregnant, she's married to Google's Sergey Brin, and she went to Yale. But after an hour chatting with her in the small office she shares with co-founder Linda Avey at 23andMe's headquarters in Mountain View, Calif., I know some things no Internet search could reveal: coffee makes her giddy, she has a fondness for sequined shoes and fresh-baked bread, and her unborn son has a 50% chance of inheriting a high risk for Parkinson's disease.

Learning and sharing your genetic secrets are at the heart of 23andMe's controversial new service — a $399 saliva test that estimates your predisposition for more than 90 traits and conditions ranging from baldness to blindness. Although 23andMe isn't the only company to offer such products, it is by far the most visible. It announced this week that it had launched a retail DNA test aimed at consumers.
Outline

• A definition and some context.

• The world according to GWAS.

• Challenges ahead.

• Conclusions.
Personalized Medicine

The Personalized Health Care Initiative will improve the safety, quality and effectiveness of healthcare for every patient in the US. By using “genomics”, or the identification of genes and how they relate to drug treatment, personalized health care will enable medicine to be tailored to each person’s needs.

http://www.hhs.gov/myhealthcare/index.html
Genomics

Personalized Medicine
The Health of Our Society

- $2.26 trillion dollars spent on health care in the U.S. in 2007 (16% GDP)

- About equal to the total GDP of France, Italy or the U.K.
OECD “Amenable Mortality”

- Nolte, Health Affairs, Jan. 2008
“More than 4 million hospitalizations potentially could be prevented each year by improving the quality of primary care...

Billions of dollars could also be saved by avoiding the need to hospitalize patients for health problems that, in most cases, can be prevented or if already present, kept stable by high-quality care in physicians' offices.”

AHRQ News and Numbers,
Aug. 2007

*Trends in Potentially Preventable Hospitalizations among Adults and Children, 1997-2004*

“We are installing 10,000 ICDs per month in the U.S.”

Harvard Cardiology Professor
6/2008
We can improve the situation a lot by creating a health care system in the U.S. .......

.... but that will only get us so far ....

.....people still get sick in Andorra.
Chronic diseases!

- More than 90 million Americans live with chronic illnesses.
- Chronic diseases account for 70% of all deaths in the United States.
- The medical care costs of people with chronic diseases account for more than 75% of the nation’s $1.4 trillion medical care costs.
- Chronic diseases account for one-third of the years of potential life lost before age 65.

CDC http://www.cdc.gov/nccdphp/overview.htm#2
We need:

- Better screening methods
- Better strategies for prevention (lifestyle, chemoprevention)
- Better therapies
- Better ways to assess who is at risk
Top 10 Causes of Death 06

1. Diseases of heart *
2. Cancer *
3. Stroke *
4. Chronic lower respiratory diseases *
5. Accidents (unintentional injuries)
6. Alzheimer’s disease *
7. Diabetes mellitus *
8. Influenza and pneumonia *
9. Kidney disease *
10. Septicemia *

CDC 2008
Virtually All Diseases (Except Maybe Trauma) Have a Genetic Component

Cystic fibrosis
Adult onset diabetes
AIDS

Genetic Component
Environmental Component
Can genomics be used to get a handle on chronic disease?
Atoms and DNA: a discovery timeline

- Greeks think about atoms
- Atoms described
- Mendel
- Light bulb
- Electrons described
- DNA structure
- First power plant
- First PC
- WWW
- HGP complete

Year:
- 1800
- 1850
- 1900
- 1950
- 2000
“The sequencing of the human genome was completed in 2003. Since then we’ve been told that we’re living in the "genomic era"—the biggest revolution in human health since antibiotics, some say, and the beginning of scientific, personalised medicine. In the United States we’ve spent about $4bn (£2bn; 2.8bn) since 2000 to fund the National Human Genome Research Institute, so it seems fair to ask what we’ve got for our money.”
Cumulative Pace of Disease Gene Discovery 1981-2005

Number of Genes Associated with Disease

Year

Source: Online Mendelian Inheritance in Man
Glazier et al., Science 298:2345-9, 2002
Are the SNPs correlated with their neighbors?
Mapping the Relationships Among SNPs

Continued Progress in Genotyping Technology

Cost per person (USD)

Affymetrix 500K

Illumina 317K

Illumina 550K

Illumina 650Y

July 2005

Oct 2006

Courtesy S. Gabriel, Broad/MIT
Genome Wide Association Approach to Common Disease: The View from 2008

- Identify an optimum set of 300,000 tag SNPs
- Collect 1000 cases and 1000 controls
- Genotype all DNAs for all SNPs
- That adds up to 600 million genotypes
- In 2002, $10 billion for each disease – completely out of the question
- Genotyping just dropped to $0.0010, so that’s $600,000 for each disease
First quarter 2008

Diseases and Traits with Published GWA Studies
(n = 93, 3/30/09)

- Macular Degeneration
- Exfoliation Glaucoma
- Lung Cancer
- Prostate Cancer
- Breast Cancer
- Colorectal Cancer
- Bladder Cancer
- Neuroblastoma
- Melanoma
- Basal Cell Cancer
- TP53 Cancer Pred’n
- Ac/Ch Lym. Leukemia
- Thyroid Cancer
- Myeloprolif. Synd.
- Infl. Bowel Disease
- Celiac Disease
- Gallstones
- Hirschsprung Disease
- Cleft Palate
- QT Prolongation
- Coronary Disease
- Coronary Spasm
- Atrial Fibrill’n/Flutter
- Stroke
- Intracranial Aneurysm
- Hypertension
- Hypt. Diuretic Rsp.
- Periph. Artery Disease
- Lipids/Lipoproteins
- Warfarin Dosing
- Ximelegatran Adv.Rsp.
- Parkinson Disease
- Amyotrophic Lat.Scler.
- Multiple Sclerosis
- MS Interferon-β Rsp.
- Prog. Supranuc. Palsy
- Tauopathies
- Alzheimer’s Disease
- Var. Creutzfeldt-Jakob
- Cognitive Ability
- Memory
- Hearing, Otosclerosis
- Restless Legs Synd.
- Essential Tremor
- Nicotine Dependence
- Methamphetamine Depend.
- Pain
- Panic Disorder
- Neuroticism
- Schizophrenia
- Sz. Iloperidone Rsp.
- Bipolar Disorder
- Family Chaos
- Narcolepsy
- ADHD
- Personality Traits
- Rheumatoid Arthritis
- RA Anti-TNF Rsp.
- Syst. Lupus Erythem.
- Juv. Idiop. Arthritis
- Osteoarthritis
- Psoriasis
- Kawasaki Disease
- Sarcoidosis
- Pulmonary Fibrosis
- COPD/Lung Function
- CF Severity
- Asthma
- Chr. Rhinosinusitis
- HIV Viral Setpoint
- Type 1 Diabetes
- Type 2 Diabetes
- Diabetic Nephropathy
- End-St. Renal Dis.
- Obesity, BMI, Waist
- IR, Metabolic Traits
- Height
- Osteoporosis
- Age at Menarche
- Male Patt. Baldness
- Fetal Hemoglobin
- Platelet Mass/Volume
- Transferrin Levels
- C-Reactive Protein
- ICAM-1 Levels
- Eosinophil Numbers
- Total IgE Levels
- Urate Levels, Gout
- Protein Levels
- Folate Path. Vitamins
- β-Carotene Levels
- Recombination Rate
- Pigmentation
“There have been few, if any, similar bursts of discovery in the history of medical research...”
2007: The Year of GWA Studies

BREAKTHROUGH OF THE YEAR

Human Genetic Variation

Equipped with faster, cheaper technologies for sequencing DNA and assessing variation in genomes on scales ranging from one to millions of bases, researchers are finding out how truly different we are from one another.

THE UNVEILING OF THE HUMAN GENOME ALMOST 7 YEARS AGO cast the first faint light on our complete genetic makeup. Since then, each new genome sequenced and each new individual studied has illuminated our genomic landscape in ever more detail. In 2007, researchers came to appreciate the extent to which our genomes differ from person to person and the implications of this variation for deciphering the genetics of complex diseases and personal traits.

Less than a year ago, the big news was triangulating variation between us and our primate cousins to get a better handle on genetic changes along the evolutionary tree that led to humans. Now, we have moved from asking what in our DNA makes us human to striving to know what in my DNA makes me me.
Following from GWAS

- **Drug discovery** – novel pathways
- **Treatment selection** – “right drug, right dose”
- **Prognosis** – how will the disease affect you
- **Disease risk prediction** – panels of markers

http://www.genome.gov/26525384
Functional Classification of 782 Index SNPs Associated with Complex Traits

- Missense: 37
- Synonymous: 11
- Intronic: 340
- 5' UTR: 2
- 3' UTR: 11
- miRTS: 6
- 5' (2kb): 22
- 3' (0.5kb): 20
- Intergenic: 354
### Lessons Learned from Initial GWA Studies

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<td>Macular Degeneration</td>
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<th>Signals in Common</th>
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<tr>
<td>Diabetes, Melanoma</td>
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<td>Prostate Cancer</td>
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<td>Breast, Colorectal Cancer; Crohn’s</td>
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<tr>
<td>Type 1 Diabetes</td>
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<td>Celiac Disease</td>
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<td>Crohn’s</td>
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NIH Funds Nine Centers to Speed Application of Powerful New Research Approach

Roadmap Network Will Produce Chemical Probes to Explore New Targets for Therapies

Bethesda, Md., Tues., Sept. 2, 2008 — The funding of a network of nine centers across the country that will use high tech screening methods to identify small molecules for use as probes to investigate the diverse functions of cells was announced today by the National Institutes of Health (NIH). The network — funded at approximately $70 million annually over the four-year production phase — is designed to increase the pace of development and use of chemical (small molecule) probes, which have become invaluable tools for exploring biologic processes and for developing new therapies for disease.

"This network marks a new era in academic and government research as NIH-funded scientists will have access to the tools for rapidly screening hundreds of thousands of small molecules against many novel biological assays at lower costs than previously possible," said Elias A. Zerhouni, M.D., NIH director. "The information generated by this network will be important to developing a greater understanding of biology and its complexity, while hopefully discovering novel approaches to therapies and prevention, especially for rare or neglected diseases."

As genomics research reveals more about the enormous complexity of cell function, new approaches are needed to identify the molecules that play key roles in health and disease.
Following from GWAS

- **Drug discovery** – novel pathways
- **Treatment selection** – “right drug, right dose”
- **Prognosis** – how will the disease affect you
- **Disease risk prediction** – panels of markers
SLCO1B1 Variants and Statin-Induced Myopathy — A Genomewide Study
The SEARCH Collaborative Group*

ABSTRACT

BACKGROUND
Lowering low-density lipoprotein cholesterol with statin therapy results in substantial reductions in cardiovascular events, and larger reductions in cholesterol may produce larger benefits. In rare cases, myopathy occurs in association with statin therapy, especially when the statins are administered at higher doses and with certain other medications.

METHODS
We carried out a genomewide association study using approximately 300,000 markers (and additional fine-mapping) in 85 subjects with definite or incipient myopathy and 90 controls, all of whom were taking 80 mg of simvastatin daily as part of a trial involving 12,000 participants. Replication was tested in a trial of 40 mg of simvastatin daily involving 20,000 participants.

RESULTS
The genomewide scan yielded a single strong association of myopathy with the rs4363657 single-nucleotide polymorphism (SNP) located within SLCO1B1 on chromosome 12 (P = 4×10−9). SLCO1B1 encodes the organic anion-transporting polypeptide OATP1B1, which has been shown to regulate the hepatic uptake of statins. The noncoding rs4363657 SNP was in nearly complete linkage disequilibrium with the nonsynonymous rs4149056 SNP (r2 = 0.97), which has been linked to statin-mediated decreases in SLCO1B1 expression.

Address reprint requests to the SEARCH Collaborative Group at the Clinical Trial Service Unit and Epidemiological Studies Unit, University of Oxford, Richard Doll Bldg., Old Road Campus, Roosevelt Dr., Oxford OX3 7LF, United Kingdom, or at search@ctsu.ox.ac.uk.

*The investigators and institutions participating in the Study of the Effectiveness of Additional Reductions in Cholesterol and Homocysteine (SEARCH) are listed in the Appendix and in the Supplementary Appendix, available with the full text of this article at www.nejm.org. The members of the writing committee (listed in the Appendix) assume responsibility for the overall content and integrity of the article.

This article (10.1056/NEJMoa0801936) was published at www.nejm.org on July 23, 2008.
Molecular Medicine

Genome-wide association scan identifies candidate polymorphisms associated with
differential response to anti-TNF treatment in Rheumatoid Arthritis

Chunyu Liu¹, Franak Batliwalla², Wentian Li², Annette Lee², Ronenn Roubenoff³, Evan
Beckman¹, Houman Khalili², Aarti Damle², Marlena Kern², Robert M. Plenge², Marieke
Coenen⁴, Timothy W. Behrens⁵, Richard Furie⁶, John P. Carulli¹, and Peter K. Gregersen²

¹Biogen Idec, Inc., Cambridge, Mass.; ²The Feinstein Institute for Medical Research,
North Shore L.I.J. Health System, Manhasset, N.Y.; ³The Broad Institute of Harvard and
the Massachusetts Institute of Technology, Cambridge, Mass., ⁴Radboud University
Nijmegen Medical Centre, Nijmegen, the Netherlands. ⁵Genentech Inc., South San
Francisco, CA, 94080, USA ⁶Division of Rheumatology/Immunology/Allergy, North
Following from GWAS

• Drug discovery – novel pathways

• Treatment selection – “right drug, right dose”

• Prognosis – how will the disease affect you

• Disease risk prediction – panels of markers
Chromosome 6p22 Locus Associated with Clinically Aggressive Neuroblastoma


Following from GWAS

- **Drug discovery** – novel pathways
- **Treatment selection** – “right drug, right dose”
- **Prognosis** – how will the disease affect you
- **Disease risk prediction** – panels of markers
Key points about GWAS markers

- Most associations published have very high reproducibility
- Most associations confer small risk increases in isolation (OR 1.2-1.5)
- Combinations of markers can confer very great risk (AMD - 250X with greatest risk combination)

- Missing heritability
April 16, 2009

Genes Show Limited Value in Predicting Diseases

By NICHOLAS WADE

The era of personal genomic medicine may have to wait. The genetic analysis of common disease is turning out to be a lot more complex than expected.

Since the human genome was decoded in 2003, researchers have been developing a powerful method for comparing the genomes of patients and healthy people, with the hope of pinpointing the DNA changes responsible for common diseases.

This method, called a genomewide association study, has proved technically successful despite many skeptics’ initial doubts. But it has been disappointing in that the kind of genetic variation it detects has turned out to explain surprisingly little of the genetic links to most diseases.

A set of commentaries in this week’s issue of The New England Journal of Medicine appears to be the first public attempt by scientists to make sense of this puzzling result.

One issue of debate among researchers is whether, despite the prospect of diminishing returns, to continue with the genomewide studies, which cost many millions of dollars apiece, or switch to a new approach like decoding the entire genomes of individual patients.
NHGRI Funds Next Step in Understanding Biological Roots of Common Diseases

Bethesda, Md., Thurs., July 17, 2008 — The National Human Genome Research Institute, one of the National Institutes of Health, today announced grants expected to total about $31 million over the next four years for research aimed at gaining a better understanding of how specific genetic variants act to influence the risk of diabetes, heart disease, cancer and other common diseases.

Over the past two years, genome-wide association studies (GWAS) have allowed researchers to uncover more than 300 novel genetic variants associated with common diseases. However, the discovery of genetic variants through GWAS research represents just the first step in the challenging process of piecing together the complex biological picture of common diseases. To help speed the process, NHGRI is supporting new research in existing large epidemiology studies, all with a rich range of measures of health and potential disease, and many with long-term follow-up.

The focus of the new research is on how genetic variants initially identified through GWAS research are related to a person's biological and physical characteristics, such as weight, cholesterol levels, blood sugar levels or bone density. Scientists will also examine how non-genetic factors, such as diet, medications and smoking, may interact with genetic factors or each other to influence health outcomes.

"By drawing on the combined strengths of genomics and epidemiology, this innovative program will create a much-needed research resource. The data it generates will save researchers around the world considerable time and energy, accelerating our ongoing efforts to translate genetic findings into new strategies for improving human health," said NHGRI Director Francis S. Collins, M.D., Ph.D.

The information generated by this program will help guide other genomic and epidemiologic studies by defining the potentially wide-ranging effects of genetic differences among people. Additionally, it will lay the groundwork for laboratory experiments in cultured cells and other model systems to identify the precise biological mechanism affected by each genetic variant and how it interacts with other biological and environmental factors. Such information is vital to developing more individually tailored ways of preventing, diagnosing and treating many diseases.
Key points about GWAS markers

• We know little about how the markers perform prospectively
• We know little about interactions with other SNPs and/or the environment
• We know little about diverse populations
• We know little about how this information might affect clinical care
Multiplex Genetic Susceptibility Testing:
A prototype for applied research to inform personalized medicine

Colleen M. McBride, PhD. & Larry Brody, Ph.D.

Research Partners:
National Human Genome Research Institute
Henry Ford Health System
Group Health Cooperative
Cancer Research Network (NCI)
The Spectrum of Genetic Testing

**Accepted**

- Rare disorders: Huntington’s disease
- Prenatal screening: Cystic fibrosis
- Cancer syndromes: BRCA1
- Treatment selection: EGFR/breast cancer

**Expression profiling:**
- Breast cancer

**Genome scans:**
- Complex disease risk

**Pgx:**
- Warfarin metabolism
- Abacavir hypersensitivity

**Dubious**
My Family Health Portrait

A tool from the U.S. Surgeon General

Using My Family Health Portrait you can:

- Enter your family health history.
- Create drawings of your family health history to share with family or health care worker.
- Use the health history of your family to create your own.

Talking with your health care worker about your family health history can help you stay healthy!

Learn more about My Family Health Portrait

Create a Family History

Open a Saved History File

Health Care Providers: Learn how My Family Health Portrait can improve the health of all Americans.

My Family Health Portrait is compatible with most browsers and operating systems. Please see our compatibility statement for more information. My Family Health Portrait Click here if you would like a printable version of My Family Health Portrait.
Translation?
Translating Genomics…

• Genomic discoveries relevant to common disease diagnosis and management are coming at an increasing rate.

• Basic discoveries are leading to the development of clinical applications.

• Ergo, improved healthcare is around the corner!
Figure. “Blue Highways” on the NIH Roadmap

BENCH
- Basic Science Research
  - Preclinical Studies
  - Animal Research

BEDSIDE
- Human Clinical Research
  - Case Series
  - Phase 1 and 2 Clinical Trials
  - Controlled Observational Studies
  - Phase 3 Clinical Trials

PRACTICE
- Clinical Practice
  - Delivery of Recommended Care to the Right Patient at the Right Time
  - Identification of New Clinical Questions and Gaps in Care

TRANSFORMATION TO HUMANS
- T1
- T2
- T3

TRANSFORMATION TO PATIENTS
- T2

TRANSFORMATION TO PRACTICE
- T3

Practice-Based Research
- Guideline Development
- Meta-analyses
- Systematic Reviews
- Phase 3 and 4 Clinical Trials
- Observational Studies
- Survey Research

Dissemination Research
- Implementation Research

“We identified only 1 RCT of a genetic testing intervention for a common condition that measured a clinical outcome.”

- Scheuner et al., JAMA 2008
Translating Genomics...

- Genomic discoveries relevant to common disease diagnosis and management are coming at an increasing rate.
- Basic discoveries are leading to the development of clinical applications.

Mind the gap!

- Ergo, improved healthcare is around the corner!
Who will (pay to) fill the gap?
EGAPP

Evaluation of Genomic Applications in Practice and Prevention

- Non-regulatory
- Independent, non-federal, multidisciplinary Working Group
- Integrate existing processes for evaluation and appraisal
- Minimize conflicts of interest
- Evidence-based, transparent, and publicly accountable
Evaluation of Genomic Applications in Practice and Prevention

Recommendations from the EGAPP Working Group: testing for cytochrome P450 polymorphisms in adults with nonpsychotic depression treated with selective serotonin reuptake inhibitors

The EGAPP Working Group was established in 2005 to support the collection and dissemination of evidence regarding the validity and utility of rapidly emerging genetic tests for clinical and public health practice in the United States.

What's New

- EGAPP Working Group Releases First Recommendation Statement

Evidence based medicine meets genomic medicine

Jim Evans, MD, PhD1, and Muin J. Khoury, MD, PhD2
Hold on to your hats!
NHGRI Seeks DNA Sequencing Technologies Fit for Routine Laboratory and Medical Use

New Grants Drive Development of Rapid, Cost-Effective Sequencing Technologies

Bethesda, Md., Wed., August 20, 2008 — The National Human Genome Research Institute (NHGRI), part of the National Institutes of Health (NIH), today awarded more than $20 million in grants to develop innovative sequencing technologies inexpensive and efficient enough to sequence a person's DNA as a routine part of biomedical research and health care.

"The ability to sequence any individual's genome inexpensively and accurately is the quantum leap needed to usher in an age of personalized medicine, in which healthcare providers will routinely use an individual's genetic code to prevent, diagnose, and treat diseases," said Alan E. Guttmacher, M.D., acting director of the National Human Genome Research Institute.

DNA sequencing costs have fallen dramatically over the past decade, fueled in large part by tools, technologies and process improvements developed as part of the Human Genome project, which culminated in 2003 with the successful effort to sequence the human genome. NHGRI subsequently launched programs in 2004 to accelerate further the development of sequencing technologies and the rate of reduction of genome sequencing cost. Significant progress has been made towards the goal of producing high quality genome sequence of 3 billion base pairs - the amount of DNA found in the genome sequence of humans and other mammals - for $100,000. Ultimately, NHGRI's vision is to cut the cost of whole-genome sequencing to $1,000 or less, which will enable the sequencing of individual genomes as part of routine medical care.
Moore’s Law put to shame

Courtesy of Eric Lander, Broad Institute
International Consortium Announces the 1000 Genomes Project

Major Sequencing Effort Will Produce Most Detailed Map of Human Genetic Variation to Support Disease Studies

Bethesda, Md., Tues., Jan 22, 2008 — An international research consortium today announced the 1000 Genomes Project, an ambitious effort that will involve sequencing the genomes of at least a thousand people from around the world to create the most detailed and medically useful picture to date of human genetic variation. The project will receive major support from the Wellcome Trust Sanger Institute in Hinxton, England, the Beijing Genomics Institute, Shenzhen (BGI Shenzhen) in China and the National Human Genome Research Institute (NHGRI), part of the National Institutes of Health (NIH).

Drawing on the expertise of multidisciplinary research teams, the 1000 Genomes Project will develop a new map of the human genome that will provide a view of biomedically relevant DNA variations at a resolution unmatched by current resources. As with other major human genome reference projects, data from the 1000 Genomes Project will be made swiftly available to the worldwide scientific community through freely accessible public databases.

"The 1000 Genomes Project will examine the human genome at a level of detail that no one has done before," said Richard Durbin, Ph.D., of the Wellcome Trust Sanger Institute, who is co-chair of the consortium. "Such a project would have been unthinkable only two years ago. Today, thanks to amazing strides in sequencing technology, bioinformatics and population genomics, it is now within our grasp. So we are moving forward to build a tool that will greatly expand and further accelerate efforts to find more of the genetic factors involved in human health and disease."

Any two humans are more than 99 percent the same at the genetic level. However, it is important to understand the small fraction of genetic material that varies among people because it can help explain individual differences in susceptibility to disease, response to drugs or reaction to environmental factors. Variation in the human genome is organized into local neighborhoods called haplotypes, which are stretches of DNA usually inherited as intact blocks of information.

Recently developed catalogs of human genetic variation, such as the HapMap, have proved valuable in human genetic research. Using the HapMap and related resources, researchers already have discovered more than 100 regions of the genome containing genetic variants that are associated with risk of common human diseases such as diabetes, coronary artery disease, prostate and breast cancer, rheumatoid arthritis, inflammatory bowel disease and age-related macular degeneration.

However, because existing maps are not extremely detailed, researchers often must follow those studies with costly and time-consuming DNA sequencing to help pinpoint the precise causative variants. The new map would enable researchers to more quickly zero in on disease-related genetic variants, speeding efforts to use genetic information to develop new strategies for diagnosing, treating and preventing common diseases.

The scientific goals of the 1000 Genomes Project are to produce a catalog of variants that are present at 1 percent or greater frequency in the human population across most of the genome, and down to 0.5 percent or lower within genes. This will likely entail sequencing the genomes of at least 1,000 people. These people will be anonymous and will not have any medical information collected on them, because the project is developing a basic resource to provide information on genetic variation. The catalog that is developed will be used by researchers in many future studies of people with particular diseases.
Knome offers sequencing of all of your protein-coding genes for $24,500

Category: exome sequencing • knome • personal genomics
Posted on: May 18, 2009 10:15 AM, by Daniel MacArthur

Personal genomics is a rapidly evolving game, with a clear end goal in sight: offering consumers an accurate, affordable and complete genome sequence, and providing them with tools to dig out the useful nuggets of information contained therein. That goal remains out of reach, and while DNA sequencing technology continues to mature companies in the personal genomics space are offering products at various points on the trade-off curve between information content and cost.

At the low-information/low-cost end, companies such as 23andMe and deCODEme offer cheap (sub-$1000) genome scans looking at between 500,000 and a million sites of common variation throughout the genome. These provide insight into a small fraction of your genome, but include the variants we know the most about (due to the recent explosion of genome-wide association studies, which look for common genetic variants associated with complex disease risk).

Meanwhile, at the other end of the spectrum we have the boutique service offered by Knome - sequencing of the entire human genome, or at least the 85-90% of it that can be reached with current short-read technologies, for the princely sum of close to $100,000. It's difficult to justify this cost given the interpretable information currently obtainable from a genome sequence, but a full genome sequence does offer the possibility of getting insight into rare, severe disease-causing variants lurking in your genome that are largely invisible to genome scans.

Now Knome has launched a new product that provides a substantial chunk of the information value of a whole genome sequence at a quarter of the cost, by focusing exclusively on the 2-3% of the genome that codes for proteins:

Unlike low-priced SNP-based genotyping, which captures genetic changes known as common variants by taking a sample of less than 0.05% of the genome, comprehensive gene sequencing
Coming in January 2010!
Personal Medical Home

The American Academy of Family Physicians believes that everyone should have a personal medical home that serves as the focal point through which all individuals—regardless of age, sex, race, or socioeconomic status—receive acute, chronic, and preventive medical services. Through an on-going relationship with a family physician in their medical home, patients can be assured of care that is not only accessible but also accountable, comprehensive, integrated, patient-centered, safe, scientifically valid, and satisfying to both patients and their physicians.

Conclusions

- Many genetic tests are well established and some are highly predictive. **FOR MANY COMMON CONDITIONS THIS IS NOT YET TRUE!**

- The ultimate benefit of the current crop of discoveries driven by GWAS will likely be in the development of new preventive and therapeutic strategies.

- Family history is a great interim personalized medicine tool for disease risk prediction.

- Think long term....
THANKS

Slides courtesy of:

Francis Collins, address unknown
Alan Guttmacher, NHGRI
Muin Khoury, CDC
Teri Manolio, NHGRI
Colleen McBride NHGRI