Genomics and healthcare: Will primary care lead or follow?

Greg Feero, M.D., Ph.D.
Chief, Genomic Healthcare Branch
National Human Genome Research Institute
National Institutes of Health

Outline

- Why primary care and genomics?
- How did we get here?
- Connecting the dots? Not easy…
- Where do we go from here?

"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

http://www.hcup-us.ahrq.gov/reports/statbriefs/sb36.pdf

Chronic disease!

- 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

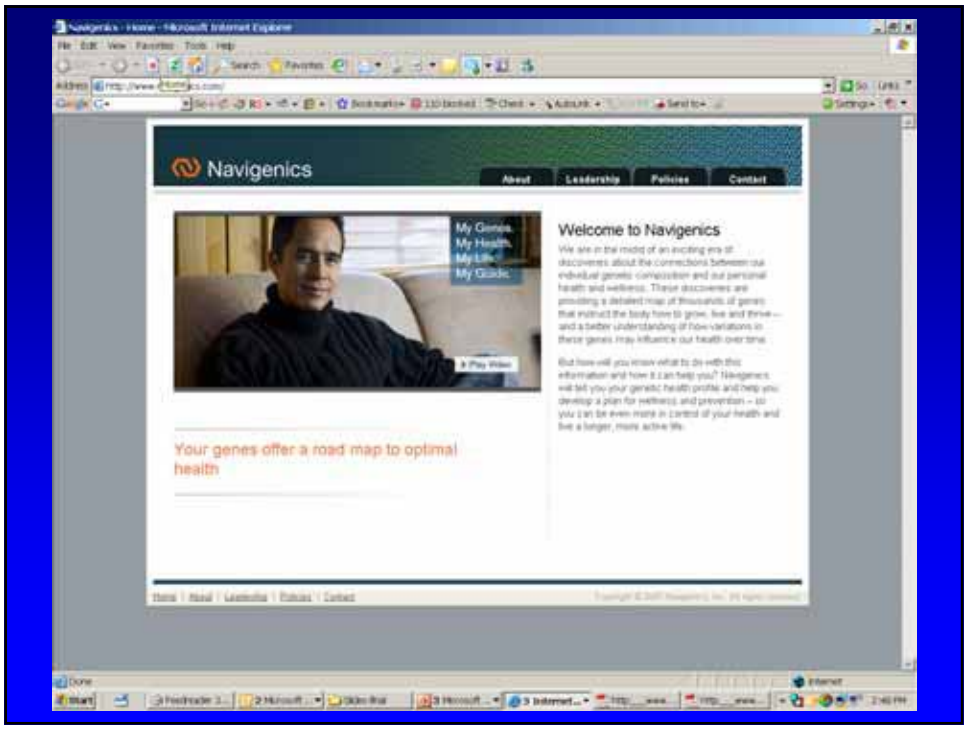
The 10 Leading Causes of Death '02

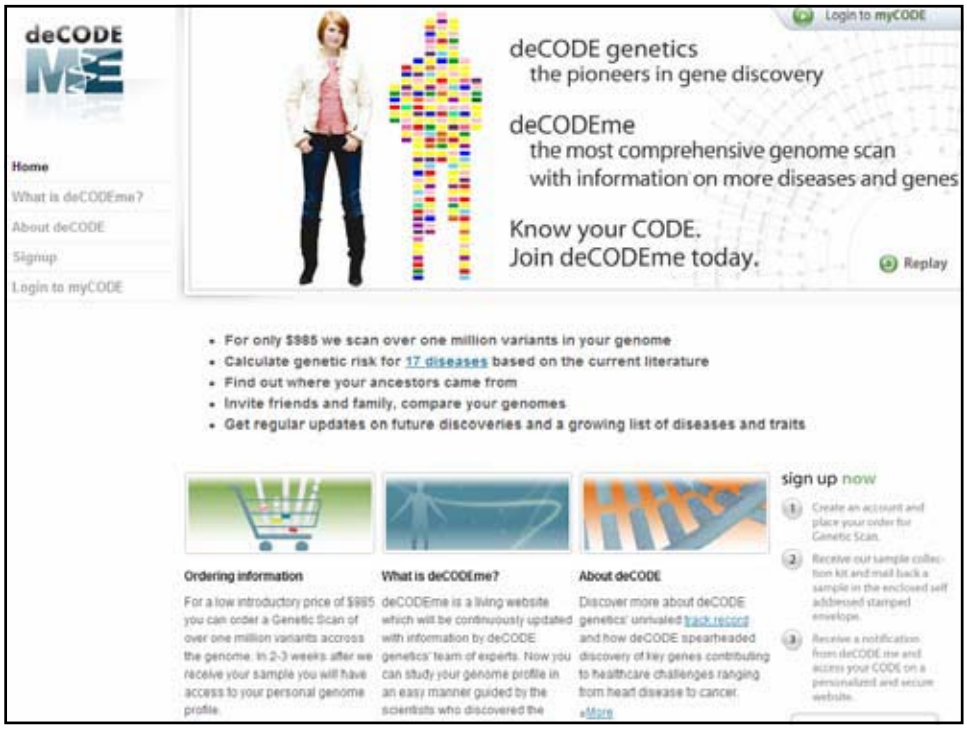
1. Heart disease (28.5% of deaths in '02) *
2. Cancer (22.8%) *
3. Stroke (6.7%) *
4. Emphysema (5.1%) *
5. Injury (4.4%)
6. Diabetes (3.0%) *
7. Pneumonia/Influenza (2.7%)*
8. Alzheimer disease (2.4%) *
9. Kidney disease (1.7%) *
10. Blood infection (1.4%)*

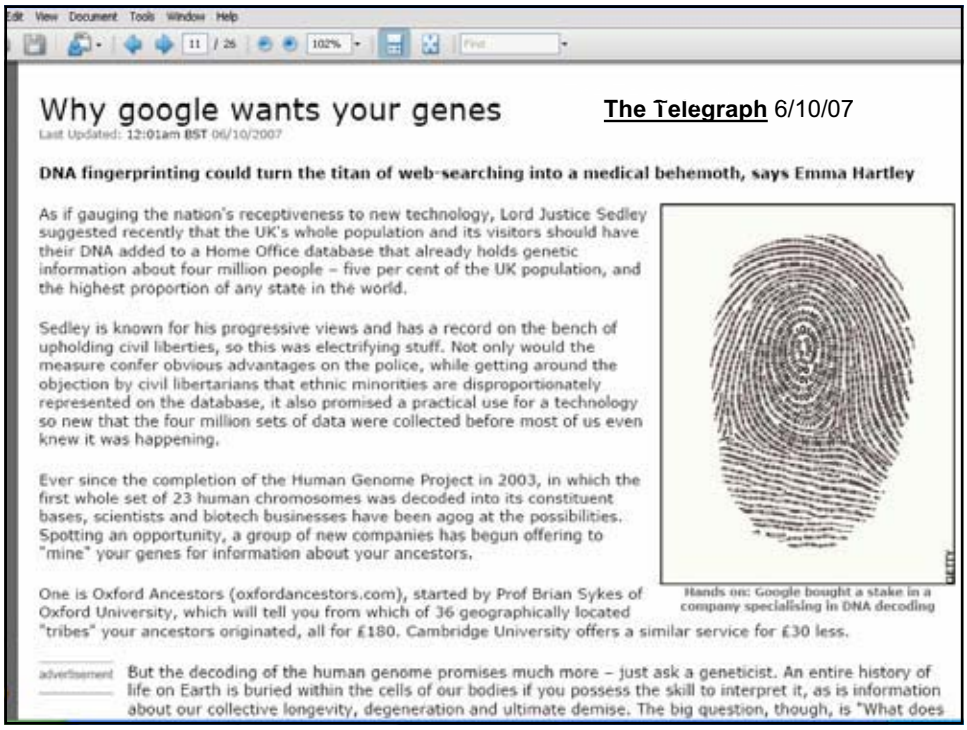
Chronic disease!

- All have at least some genetic component
- Occur over a long time, and can usually be treated, but not cured
- Might be **avoided** (or at least held off) in many cases if we could effectively
  - **Assess risk**
  - Effectively intervene (individualized prevention, environmental modification, medication)

Can genomics be used to get a handle on chronic disease?







Why google wants your genes

The Telegraph 6/10/07

Last Updated: 12:01am BST 06/10/2007

DNA fingerprinting could turn the titan of web-searching into a medical behemoth, says Emma Hartley

As if gauging the nation's receptiveness to new technology, Lord Justice Sedley suggested recently that the UK's whole population and its visitors should have their DNA added to a Home Office database that already holds genetic information about four million people – five per cent of the UK population, and the highest proportion of any state in the world.

Sedley is known for his progressive views and has a record on the bench of upholding civil liberties, so this was electrifying stuff. Not only would the measure confer obvious advantages on the police, while getting around the objection by civil libertarians that ethnic minorities are disproportionately represented on the database, it also promised a practical use for a technology so new that the four million sets of data were collected before most of us even knew it was happening.

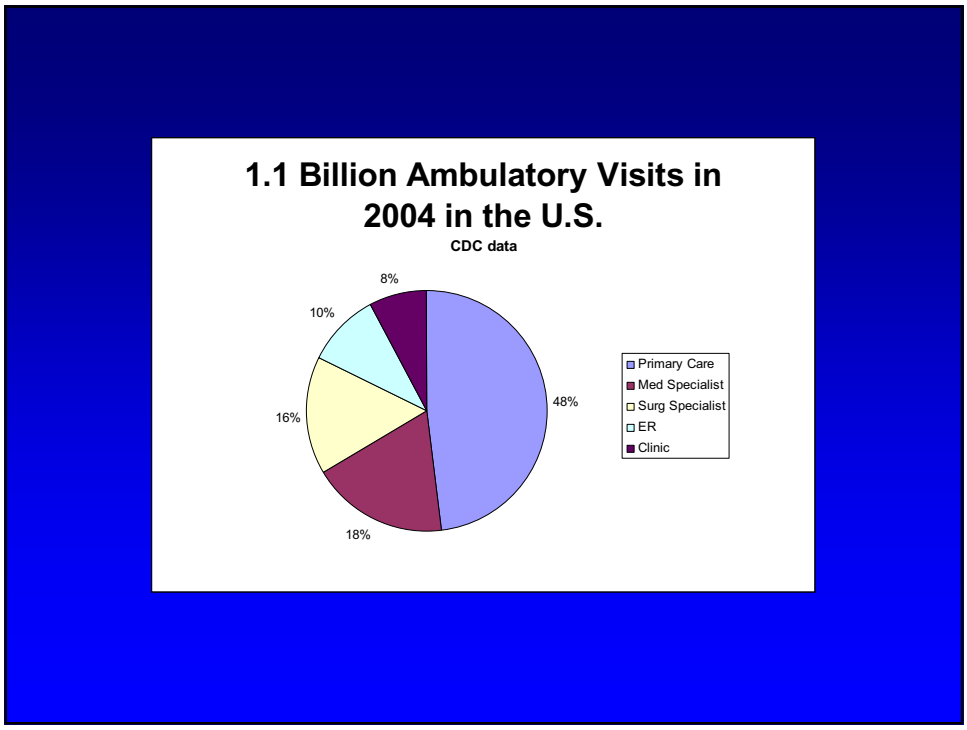
Ever since the completion of the Human Genome Project in 2003, in which the first whole set of 23 human chromosomes was decoded into its constituent bases, scientists and biotech businesses have been agog at the possibilities. Spotting an opportunity, a group of new companies has begun offering to "mine" your genes for information about your ancestors.

Hands on: Google bought a stake in a company specialising in DNA decoding

One is Oxford Ancestors (oxfordancestors.com), started by Prof Brian Sykes of Oxford University, which will tell you from which of 36 geographically located "tribes" your ancestors originated, all for £180. Cambridge University offers a similar service for £30 less.

But the decoding of the human genome promises much more – just ask a geneticist. An entire history of life on Earth is buried within the cells of our bodies if you possess the skill to interpret it, as is information about our collective longevity, degeneration and ultimate demise. The big question, though, is "What does


23andMe genetics just got personal.
our service
genetics 101
for the experts
store
about us
2007: 23andMe introduces the first Personal Genome Service.
Unlock the secrets of your own DNA. Today.
Gene Journal
What do your genes say about you?
Ancestry
Who were your ancient ancestors?
Family Inheritance
Do you have your mother's sense of taste?
Genome Labs
Would you like to search your genome?


1.1 Billion Ambulatory Visits in 2004 in the U.S.
CDC data
8%
10%
16%
18%
48%
Primary Care
Med Specialist
Surg Specialist
ER
Clinic

Primary Care

"If you knew there was a genetic disorder already present in your immediate family, with what or whom would you be most likely to consult to learn about the possibility of inheriting it?"

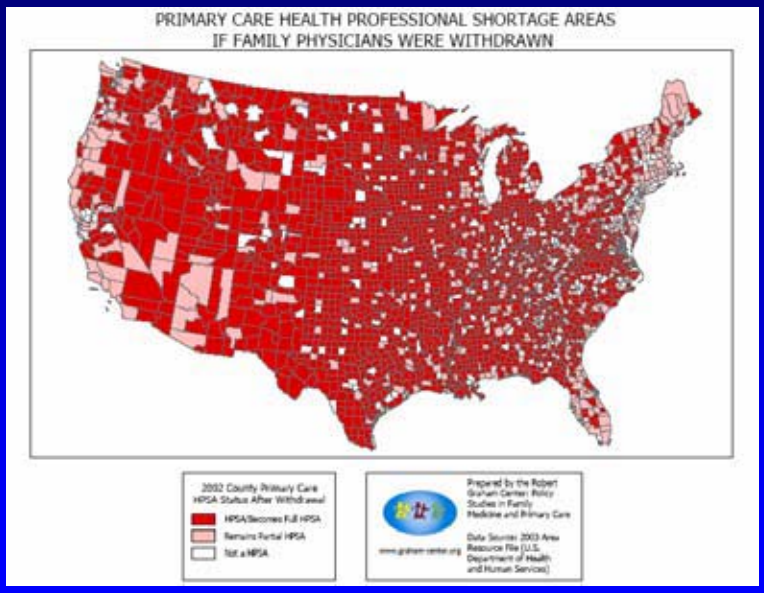
- 71% chose their PCP

1998 AMA survey of 1000 U.S. Adults

Access to genetic services

NSGC web site and places I've lived + 50 miles:

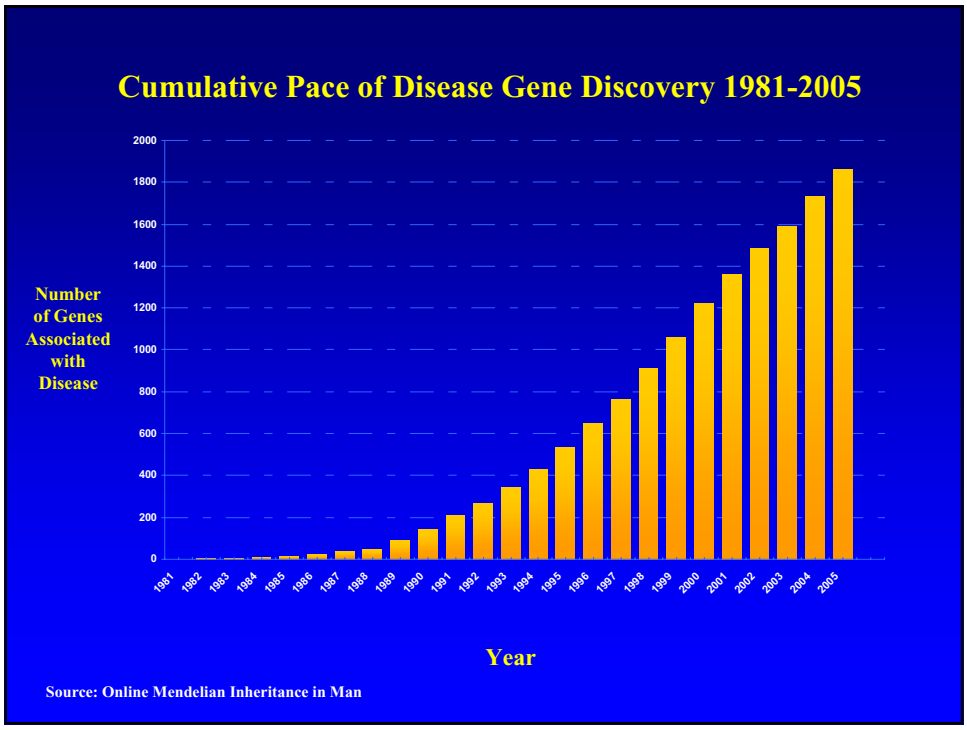
	2006	2007
Pittsburgh, PA –	8	14
Vienna, VA –	40	60
State College, PA –	0	0
Durham, NC –	18	28
Waterville, ME –	0	0



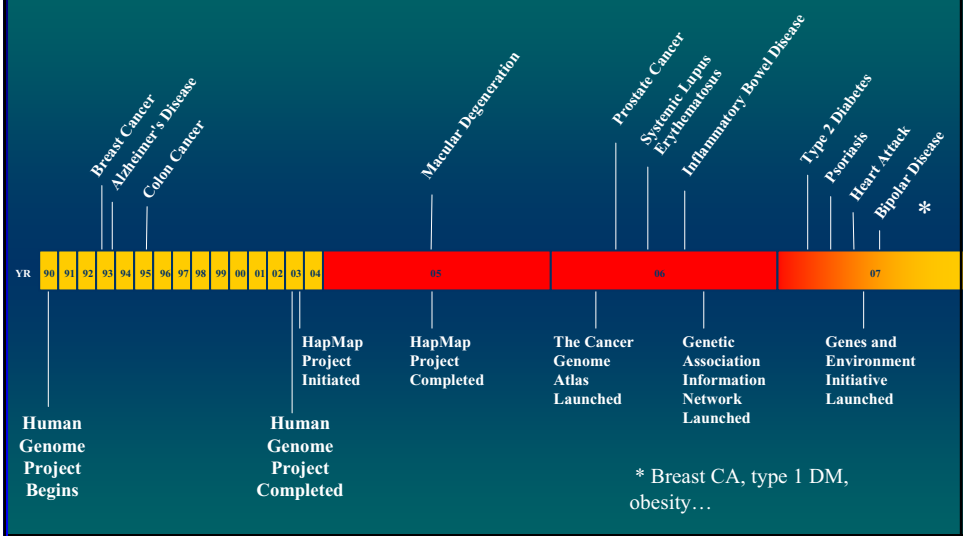
Jim receiving his own personal genome sequence on a DVD

May 31, 2007

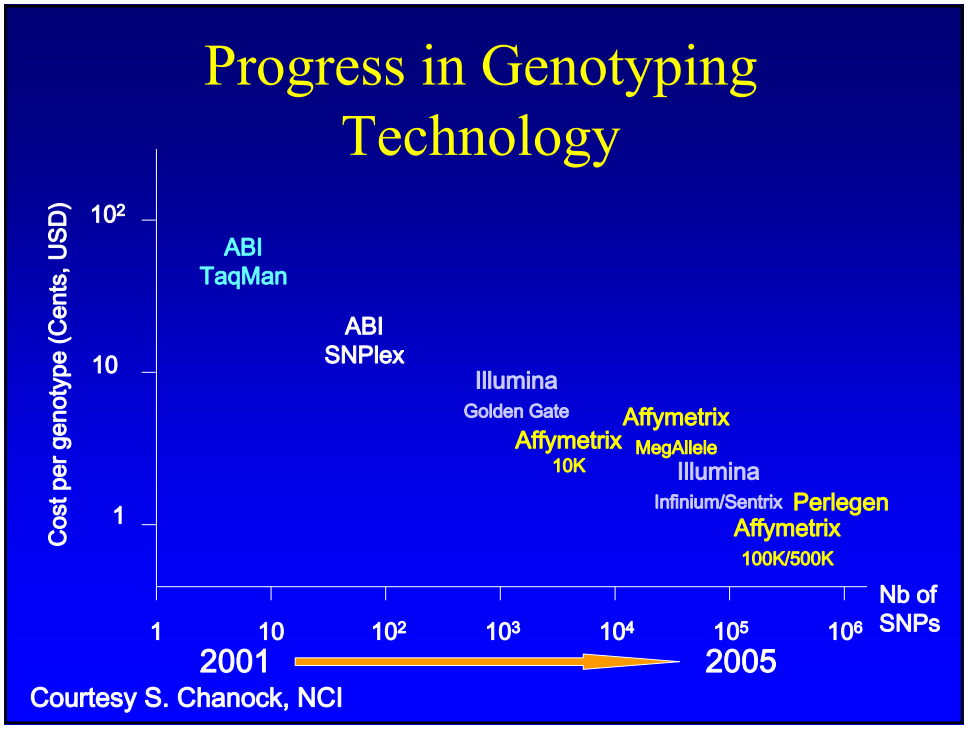

Resources
Technology Development
Computational Biology
Training
ELSI
Education
Genomics to Society
Genomics to Health
Genomics to Biology
Human Genome Project

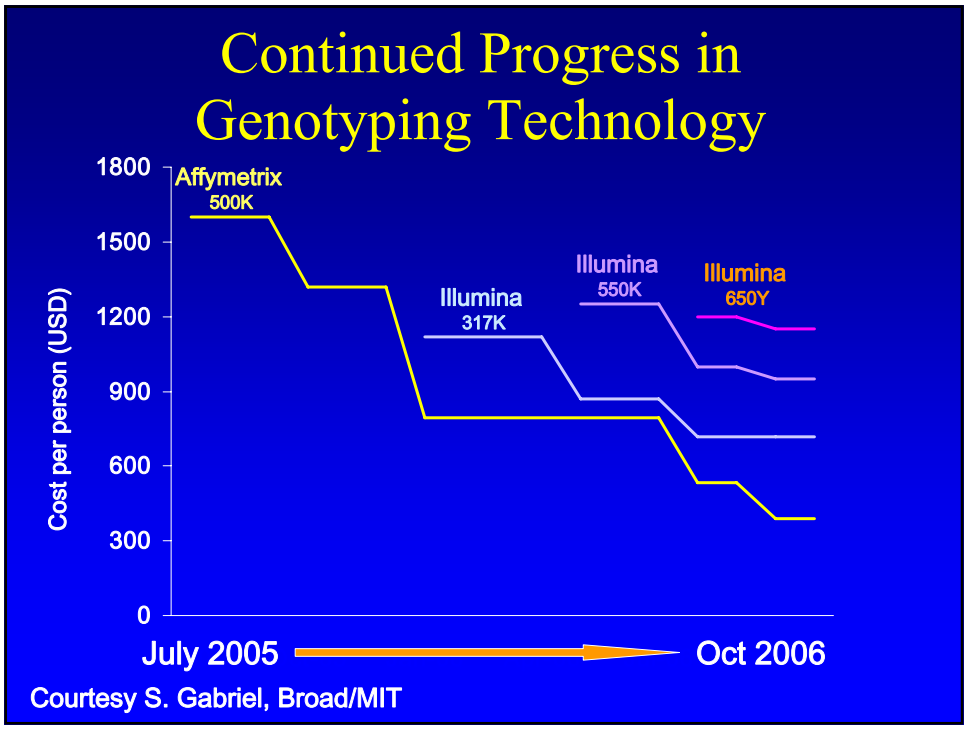

Cumulative Pace of Disease Gene Discovery 1981-2005
Number of Genes Associated with Disease
2000
1800
1600
1400
1200
1000
800
600
400
200
0
1981
1982
1983
1984
1985
1986
1987
1988
1989
1990
1991
1992
1993
1994
1995
1996
1997
1998
1999
2000
2001
2002
2003
2004
2005
Year
Source: Online Mendelian Inheritance in Man

Gene Discoveries for Common Complex Diseases



NIH Research Initiatives


Progress in Genotyping Technology
Cost per genotype (Cents, USD)
10²
10
1
ABI TaqMan
ABI SNPlex
Illumina Golden Gate
Affymetrix 10K
Affymetrix MegAllele
Illumina Infinium/Sentrix
Perlegen
Affymetrix 100K/500K
1
10
10²
10³
10⁴
10⁵
10⁶
Nb of SNPs
2001
2005
Courtesy S. Chanock, NCI


Continued Progress in Genotyping Technology
Cost per person (USD)
1800
1500
1200
900
600
300
0
Affymetrix 500K
Illumina 317K
Illumina 550K
Illumina 650Y
July 2005
Oct 2006
Courtesy S. Gabriel, Broad/MIT

Cost of a Genome-Wide Association Study in 2,000 People

Year	Number of SNPs	Cost/SNP	Cost/Study
2001	10,000,000	$1.00	$20 billion
2007	500,000	0.1¢	$1 million

A common variant associated with prostate cancer in European and African populations

Laufey T Amundadottir[1,12], Patrick Sulem[1,12], Julius Gudmundsson[1,12], Agnar Helgason[1], Adam Baker[1],

Genome-wide association study identifies a second prostate cancer susceptibility variant at 8q24

Multiple regions within 8q24 independently affect risk for prostate cancer

Prostate Cancer

Christopher A Haiman[1], Nick Patterson[2], Matthew L Freedman[2,3], Simon R Myers[2], Malcolm C Pike[1],

Genome-wide association study of prostate cancer identifies a second risk locus at 8q24

Meredith Yeager[1,2], Nick Orr[3], Richard B Hayes[2], Kevin B Jacobs[4], Peter Kraft[5], Sholom Wacholder[2], Mark J Minichiello[6], Paul Fearnhead[7], Kai Yu[2], Nilanjan Chatterjee[2], Zhaoming Wang[1,2], Robert Welch[1,2], Brian J Staats[1,2], Eugenia E Calle[8], Heather Spencer Feigelson[8], Michael J Thun[8], Carmen Rodriguez[8], Demetrius Albanes[2], Jarmo Virtamo[9], Stephanie Weinstein[2], Fredrick R Schumacher[5], Edward Giovannucci[10], Walter C Willett[10], Geraldine Cancel-Tassin[11], Olivier Cussenot[11], Antoine Valeri[11], Gerald L Andriole[12], Edward P Gelmann[13], Margaret Tucker[2], Daniela S Gerhard[14], Joseph F Fraumeni Jr[2], Robert Hoover[2], David J Hunter[2,5], Stephen J Chanock[2,3] & Gilles Thomas[2]

Sequence variants in the autophagy gene *IRGM* and multiple other replicating loci contribute to Crohn's disease susceptibility

Miles Parkes[1,13], Jeffrey C Barrett[2,13], Natalie J Prescott[1,13], Mark Tremelling[1], Carl A Anderson[2], Sheila A Fisher[3],

We followed up on 37 SNPs from 31 distinct loci, associated at $P < 10^{-5}$ on initial analysis of the WTCCC data set. Support for some of these markers diminished in the final WTCCC analysis after extensive data filtering[5]. We selected two markers for each locus where low linkage disequilibrium (LD) between associated SNPs in areas of unbroken LD suggested distinct causal variants. We genotyped SNPs in a new panel of 1,182 individuals of European descent with Crohn's disease using TaqMan assays (**Supplementary Table 1** and **Supplementary Methods** online). Concordance with Affymetrix data was 99.7%, based on genotyping 96 WTCCC cases on both platforms. To target SNPs for replication testing and limit unnecessary genotyping, we made a preliminary comparison between allele frequencies in

Sciencexpress Report

A Genome-Wide Association Study Identifies *IL23R* as an Inflammatory Bowel Disease Gene

Richard H. Duerr,[1,2] Kent D. Taylor,[3,4] Steven R. Brant,[5,6] John D. Rioux,[7,8] Mark S. Silverberg,[9] Mark J. Daly,[8,10] A. Hillary Steinhart,[9] Clara Abraham,[11] Miguel Regueiro,[1] Anne Griffiths,[12] Themos Dassopoulos,[5] Alain Bitton,[13] Huiying Yang,[3,4] Stephan Targan,[4,14] Lisa W. Datta,[5] Emily O. Kistner,[15] L. Philip Schumm,[15] Annette Lee,[16] Peter K. Gregersen,[16] M. Michael Barmada,[2] Jerome I. Rotter,[3,4] Dan L. Nicolae,[11,17] Judy H. Cho[18]*

Crohn's Disease

Sciencexpress Report

A Common Variant in the *FTO* Gene Is Associated with Body Mass Index and Predisposes to Childhood and Adult Obesity

Timothy M. Frayling,[1,2*] Nicholas J. Timpson,[3,4*] Michael N. Weedon,[1,2*] Eleftheria Zeggini,[3,5*] Rachel M. Freathy,[1,2] Cecilia M. Lindgren,[3,5] John R. B. Perry,[1,2] Katherine S. Elliott,[3] Hana Lango,[1,2] Nigel W. Rayner,[3,5] Beverley Shields,[2] Lorna W. Harries,[2] Jeffrey C. Barrett,[3] Sian Ellard,[2,6] Christopher J. Groves,[5] Bridget Knight,[2] Ann-Marie Patch,[2,6] Andrew R. Ness,[7] Shah Ebrahim,[8] Debbie A. Lawlor,[9] Susan M. Ring,[9] Yoav Ben-Shlomo,[9] Marjo-Riitta Jarvelin,[10,11] Ulla Sovio,[10,11] Amanda J. Bennett,[5] David Melzer,[1,12] Luigi Ferrucci,[13] Ruth J. F. Loos,[14] Inês Barroso,[15] Nicholas J. Wareham,[14] Fredrik Karpe,[5] Katharine R. Owen,[5] Lon R. Cardon,[3] Mark Walker,[16] Graham A. Hitman,[17] Colin N. A. Palmer,[18] Alex S. F. Doney,[19] Andrew D. Morris,[19] George Davey-Smith,[4] The Wellcome Trust Case Control Consortium,[20] Andrew T. Hattersley,[1,2†‡] Mark I. McCarthy[3,5†]

Obesity

Sciencexpress / www.sciencexpress.org / 12 April 2007 / Page 1 / 10.1126/science.1141634

Type 2 Diabetes

A Genome-Wide Association Study of Type 2 Diabetes in Finns Detects Multiple Susceptibility Variants

Laura J. Scott,[1] Karen L. Mohlke,[2] Lori L. Bonnycastle,[3] Cristen J. Willer,[3] Yun Li,[3]
William L. Duren,[1] Michae
Anne U. Jackson,[3] Ludmila
Tianle Hu,[1] Randall Pruim
Andrew G. Sprau,[1] Maurin
Craig W. Bark,[5] Janet L. G
Thomas A. Buchanan,[7] Ric
Gonçalo R. Abecasis,[1] Eliz
Jaakko Tuomilehto,[10,11,12]

Identifying the genetic vari
been a formidable challeng
Finnish T2D cases and 117
single-nucleotide polymorp
autosomal SNPs. We carrie
that predispose to T2D, com
and genotyped 80 SNPs in
We identify T2D-associated
to the identification of T2D
region of *CDKN2A* and *CDK*
PPARG, and *KCNJ11* are ass
identified to at least 10.

Genome-Wide Association Analysis Identifies Loci for Type 2 Diabetes and Triglyceride Levels

Diabetes Genetics Initi
and Novartis Institutes

New strategies for preve
disease etiology. We an
patients with T2D and 1
metabolism, lipids, obes
we identified and confir
and *CDKN2B*, in an intro
HHEX and in *SLC30A8* f
confirmed association of
triglycerides. The discov
illustrates the ability of
the pathogenesis of com

Replication of Genome-Wide Association Signals in UK Samples Reveals Risk Loci for Type 2 Diabetes

Eleftheria Zeggini,[1,2*] Michael N. Weedon,[3,4*] Cecilia M. Lindgren,[1,2*] Timothy M. Frayling,[3,4*] Katherine S. Elliott,[2] Hana Lango,[3,4] Nicholas J. Timpson,[2,3] John R. B. Perry,[3,4] Nigel W. Rayner,[1,2] Rachel M. Freathy,[3,4] Jeffrey C. Barrett,[2] Beverley Shields,[4] Andrew P. Morris,[2] Sian Ellard,[4,6] Christopher J. Groves,[5] Lorna W. Harries,[4] Jonathan L. Marchini,[7] Katharine R. Owen,[8] Beatrice Knight,[4] Lon R. Cardon,[2] Mark Walker,[9] Graham A. Hitman,[9] Andrew D. Morris,[10] Alex S. F. Doney,[10] The Wellcome Trust Case Control Consortium (WTCCC),† Mark I. McCarthy,[1,2]‡§ Andrew T. Hattersley[3,4]‡

The molecular mechanisms involved in the development of type 2 diabetes are poorly understood. Starting from genome-wide genotype data for 1924 diabetic cases and 2938 population controls generated by the Wellcome Trust Case Control Consortium, we set out to detect replicated diabetes association signals through analysis of 3757 additional cases and 5346 controls and by integration of our findings with equivalent data from other international consortia. We detected diabetes susceptibility loci in and around the genes *CDKAL1*, *CDKN2A/CDKN2B*, and *IGF2BP2* and confirmed the recently described associations at *HHEX/IDE* and *SLC30A8*. Our findings provide insight into the genetic architecture of type 2 diabetes, emphasizing the contribution of multiple variants of modest effect. The regions identified underscore the importance of pathways influencing pancreatic beta cell development and function in the etiology of type 2 diabetes.

SCIENCE VOL 316 1 JUNE 2007

Sciencexpress Report

A Common Allele on Chromosome 9 Associated with Coronary Heart Disease

Ruth McPherson,[1*†] Alexander Pertsemlidis,[2*] Nihan Kavaslar,[1] Alexandre Stewart,[1] Robert Roberts,[1] David R. Cox,[3] David A. Hinds,[3] Len A. Pennacchio,[4] Anne Tybjaerg-Hansen,[5] Aaron R. Folsom,[6] Eric Boerwinkle,[7] Helen H. Hobbs,[2,3] Jonathan C. Cohen[2,8†]

[1]Division of Cardiology, University of Ottawa Heart Institute, Ottawa K1Y4W7, Canada. [2]Donald W. Reynolds Cardiovascular Clinical Research Center and the Eugene McDermott Center for Human Growth and Development, University of Texas Southwestern Medical Center, Dallas, TX 75390, USA. [3]Perlegen Sciences, Mountain View, CA 94043, USA. [4]Genomics

Sciencexpress Report

A Common Variant on Chromosome 9p21 Affects the Risk of Myocardial Infarction

Anna Helgadottir,[1*] Gudmar Thorleifsson,[1*] Andrei Manolescu,[1*] Solveig Gretarsdottir,[1] Thorarinn Blondal,[1] Aslaug Jonasdottir,[1] Adalbjorg Jonasdottir,[1] Asgeir Sigurdsson,[1] Adam Baker,[1] Arnar Palsson,[1] Gisli Masson,[1] Daniel Gudbjartsson,[1] Kristinn P. Magnusson,[1] Karl Andersen,[2] Allan I. Levey,[3] Valgerdur M. Backman,[1] Sigurborg Matthiasdottir,[1] Thorbjorg Jonsdottir,[1] Stefan Palsson,[1] Helga Einarsdottir,[1] Steinunn Gunnarsdottir,[1] Arnaldur Gylfason,[1] Viola Vaccarino,[3] W. Craig Hooper,[3] Muredach P. Reilly,[4] Christopher B. Granger,[5] Harland Austin,[3] Daniel J Rader,[4] Svati H. Shah,[5] Arshed A. Quyyumi,[3] Jeffrey R. Gulcher,[1] Gudmundur Thorgeirsson,[3] Unnur Thorsteinsdottir,[1] Augustine Kong,[1†] Kari Stefansson[1†]

Heart Disease

Sciencexpress / www.sciencexpress.org / 3 May 2007

Genome-wide association study identifies novel breast cancer susceptibility loci

Douglas F. Easton[1], Karen A. Pooley[2], Alison M. Dunning[2], Paul D. P. Pharoah[2], Deborah Thompson[1], Dennis G. Ballinger[1], Jeffery P. Struewing[1], Jonathan Morrison[2], Helen Field[2], Robert Luben[3], Nicholas Wareham[3],

A genome-wide association study identifies alleles in *FGFR2* associated with risk of sporadic postmenopausal breast cancer

Breast Cancer

David J Hunt
Sholom Wach
Nilanjan Chat
Saundra S Bu
Richard B Ha
Gilles Thoma
Margaret McCredie
Hiltrud Brauch[54], U
kConFab[57*], AOCS
Jaana Hartikainen[51]

Common variants on chromosomes 2q35 and 16q12 confer susceptibility to estrogen receptor–positive breast cancer

Simon N Stacey[1], Andrei Manolescu[1], Patrick Sulem[1], Thorunn Rafnar[1], Julius Gudmundsson[1], Sigurjon A Gudjonsson[1], Gisli Masson[1], Margret Jakobsdottir[1], Steinunn Thorlacius[1], Agnar Helgason[1], Katja K Aben[2,3], Luc J Strobbe[4], Marjo T Albers-Akkers[5], Dorine W Swinkels[5], Brian E Henderson[6], Laurence N Kolonel[7], Loic Le Marchand[7], Esther Millastre[8], Raquel Andres[8], Javier Godino[9], Maria Dolores Garcia-Prats[10], Eduardo Polo[11], Alejandro Tres[8], Magali Mouy[1], Jona Saemundsdottir[1], Valgerdur M Backman[1], Larus Gudmundsson[1], Kristleifur Kristjansson[1], Jon T Bergthorsson[1], Jelena Kostic[1], Michael L Frigge[1], Frank Geller[1], Daniel Gudbjartsson[1], Helgi Sigurdsson[12], Thora Jonsdottir[12], Jon Hrafnkelsson[12], Jakob Johannsson[12], Thorarinn Sveinsson[12], Gardar Myrdal[12], Hlynur Niels Grimsson[12], Thorvaldur Jonsson[12], Susanna von Holst[13], Barbro Werelius[13], Sara Margolin[14], Annika Lindblom[13], Jose I Mayordomo[8], Christopher A Haiman[6], Lambertus A Kiemeney[3], Oskar Th Johannsson[12], Jeffrey R Gulcher[1], Unnur Thorsteinsdottir[1], Augustine Kong[1] & Kari Stefansson[1]

Robust associations of four new chromosome regions from genome-wide analyses of type 1 diabetes

John A Todd[1], Neil M Walker[1,9], Jason D Cooper[1,9], Deborah J Smyth[1,9], Kate Downes[1], Vincent Plagnol[1], Rebecca Bailey[1], Sergey Nejentsev[1], Sarah F Field[1], Felicity Payne[1], Christopher E Lowe[1], Jeffrey S Szeszko[1], Jason P Hafler[1], Lauren Zeitels[1], Jennie H M Yang[1], Adrian Vella[1,8], Sarah Nutland[1], Helen E Stevens[1], Helen Schuilenburg[1], Gillian Coleman[1], Meeta Maisuria[1], William Meadows[1], Luc J Smink[1], Barry Healy[1], Oliver S Burren[1], Alex A C Lam[1], Nigel R Ovington[1], James Allen[1], Ellen Adlem[1], Hin-Tak Leung[1], Chris Wallace[2], Joanna M M Howson[1], Cristian Guja[3], Constantin Ionescu-Tîrgovişte[3], Genetics of Type 1 Diabetes in Finland[4], Matthew J Simmonds[5], Joanne M Heward[5], Stephen C L Gough[5], The Wellcome Trust Case Control Consortium[6], David B Dunger[7], Linda S Wicker[1] & David G Clayton[1]

Type 1 Diabetes

Neuron
Report

Alzheimer's Disease

Cell PRESS

GAB2 Alleles Modify Alzheimer's Risk in *APOE* ε4 Carriers

Eric M. Reiman,[1,2,3,17,18,*] Jennifer A. Webster,[1,17,18] Amanda J. Myers,[4,5,18] John Hardy,[5,6] Travis Dunckley,[1,17] Victoria L. Zismann,[1,17] Keta D. Joshipura,[1,17] John V. Pearson,[1,17] Diane Hu-Lince,[1,17] Matthew J. Huentelman,[1,17] David W. Craig,[1,17] Keith D. Coon,[1,7,17] Winnie S. Liang,[1,17] RiLee H. Herbert,[1,17] Thomas Beach,[8,17] Kristen C. Rohrer,[5] Alice S. Zhao,[5] Doris Leung,[5] Leslie Bryden,[5] Lauren Marlowe,[5] Mona Kaleem,[5] Diego Mastroeni,[8] Andrew Grover,[8,17] Christopher B. Heward,[9] Rivka Ravid,[10] Joseph Rogers,[8,17] Michael L. Hutton,[11] Stacey Melquist,[11] Ron C. Petersen,[12] Gene E. Alexander,[13,17] Richard J. Caselli,[14,17] Walter Kukull,[16] Andreas Papassotiropoulos,[1,15] and Dietrich A. Stephan[1,2,17,*]

Neuron 54, 713-720, June 7, 2007

Genetic variants regulating *ORMDL3* expression contribute to the risk of childhood asthma

Miriam F. Moffatt[1*], Michael Kabesch[2*], Liming Liang[3*], Anna L. Dixon[4], David Strachan[5], Simon Heath[6], Martin Depner[2], Andrea von Berg[7], Albrecht Bufe[8], Ernst Rietschel[9], Andrea Heinzmann[10], Burkard Simma[11], Thomas Frischer[12], Saffron A. G. Willis-Owen[1], Kenny C. C. Wong[1], Thomas Illig[13], Christian Vogelberg[14], Stephan K. Weiland[15], Erika von Mutius[2], Gonçalo R. Abecasis[3], Martin Farrall[4], Ivo G. Gut[6], G. Mark Lathrop[6] & William O. C. Cookson[1]

Asthma

Variants conferring risk of atrial fibrillation on chromosome 4q25

Daniel F. Gudbjartsson[1], David O. Arnar[2], Anna Helgadottir[1], Solveig Gretarsdottir[1], Hilma Holm[2], Asgeir Sigurdsson[1], Adalbjorg Jonasdottir[1], Adam Baker[1], Gudmar Thorleifsson[1], Kristleifur Kristjansson[1], Arnar Palsson[1], Thorarinn Blondal[1], Patrick Sulem[1], Valgerdur M. Backman[1], Gudmundur A. Hardarson[1], Ebba Palsdottir[1], Agnar Helgason[1], Runa Sigurjonsdottir[2], Jon T. Sverrisson[3], Konstantinos Kostulas[4], Maggie C. Y. Ng[5], Larry Baum[5], Wing Yee So[5], Ka Sing Wong[5], Juliana C. N. Chan[5], Karen L. Furie[6], Steven M. Greenberg[6], Michelle Sale[6], Peter Kelly[6], Calum A. MacRae[7], Eric E. Smith[6], Jonathan Rosand[6], Jan Hillert[4], Ronald C. W. Ma[5], Patrick T. Ellinor[7], Gudmundur Thorgeirsson[2], Jeffrey R. Gulcher[1], Augustine Kong[1], Unnur Thorsteinsdottir[1] & Kari Stefansson[1]

Atrial fibrillation

2007: The Year of GWA Studies?

Consistently replicated associations found for:

- 10 Jun 2007: Celiac disease
- 1 Jul 2007: Atrial fibrillation
- 8 Jul 2007 : Colorectal cancer
- 15 Jul 2007: Gallstones
- 18 Jul 2007: Periodic limb movements in sleep
- 19 Jul 2007: HIV viral setpoint
- 26 Jul 2007: Childhood asthma
- 29 Jul 2007: Multiple sclerosis
- 1 Aug 2007: Amyotrophic Lateral Sclerosis
- 9 Aug 2007: Exfoliation glaucoma
- 2 Sep 2007: Height
- 5 Sep 2007: Rheumatoid arthritis

Following from GWAS

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

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!

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!

"The bulk of this {healthcare} spending growth, however, appears to result not from increasing disease prevalence but from the development and diffusion of new medical technologies and therapies."

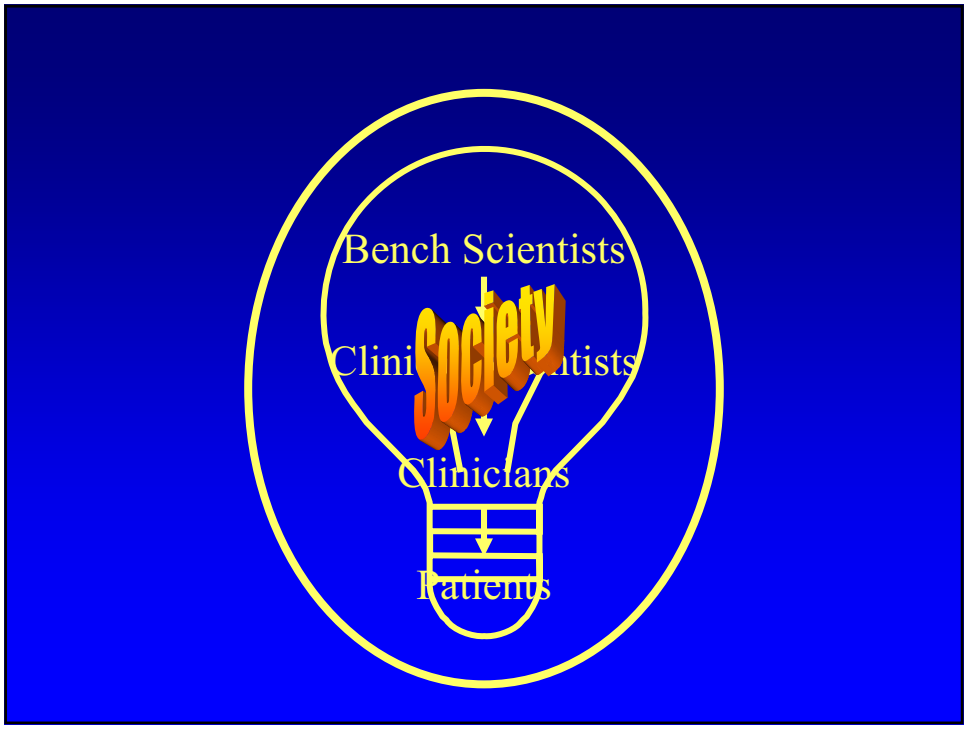
Orszag PR, Ellis P. NEJM Nov. 1 2007

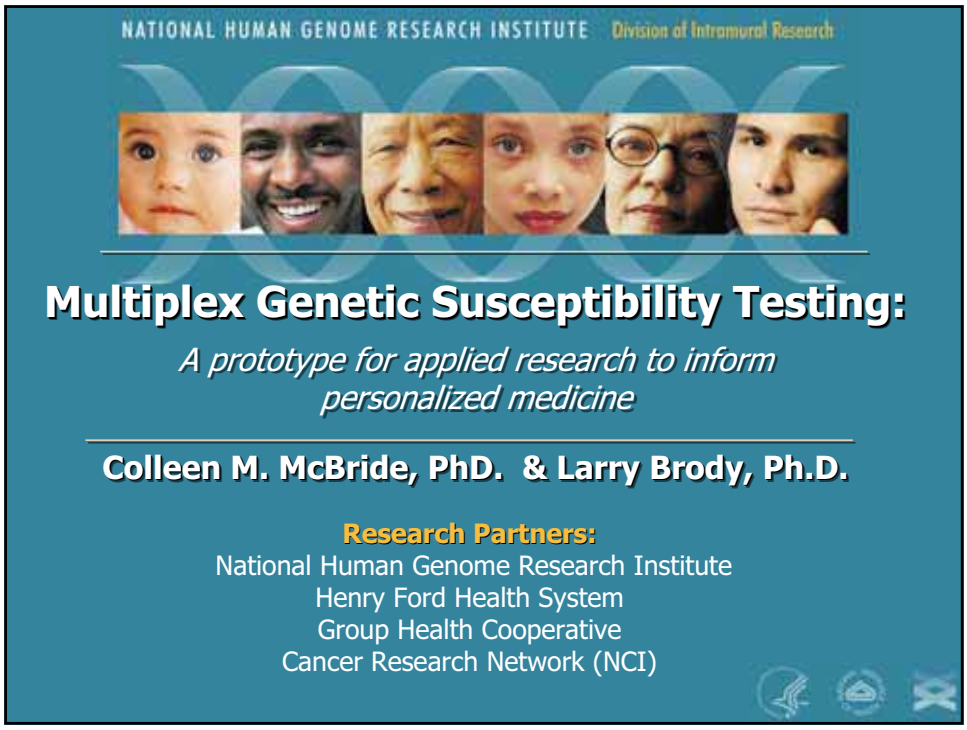
Translating Genomics…

Filling the gap

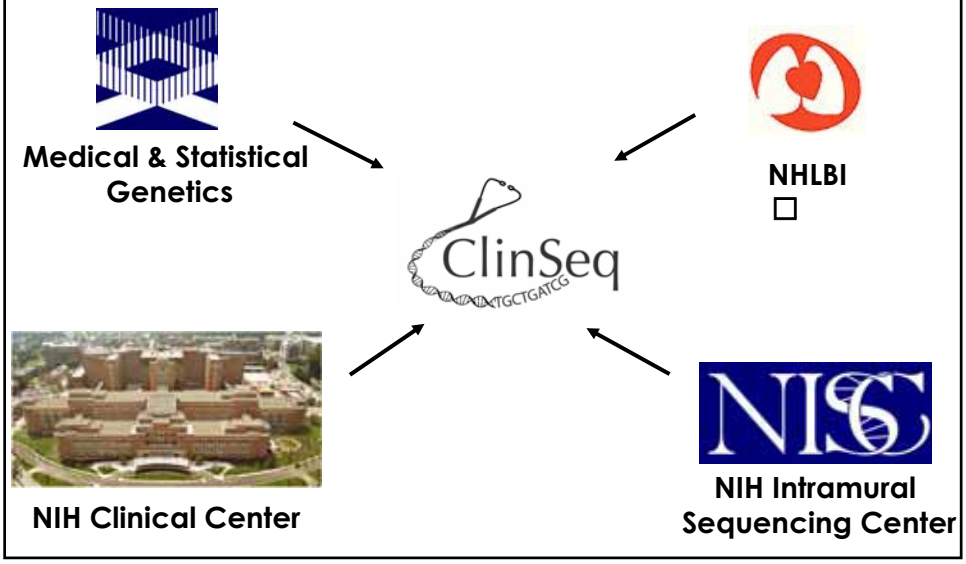
- » Does the application address a clinical need?
- » Does the application meet a clinical need?
- » Is the application acceptable to patients?
- » Is the application acceptable to health care providers?
- » Is the application acceptable to insurers?
- » Is the application acceptable to society?
- » How are patients best educated about the application?
- » How are providers best educated about the application?

Who will (pay to) fill the gap?


Bench Scientists
Clinical Scientists
Society
Clinicians
Patients


NATIONAL HUMAN GENOME RESEARCH INSTITUTE
Division of Intramural Research
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)

ClinSeq: A translational research project in clinical genomics



Health Professionals' Understanding of Human Genetic Variation Study

Vence Bonham, JD
Associate Investigator
Social and Behavioral Research Branch
Principal Investigator

Can health care providers become genetically literate in time?

Key Obstacles to Genetic Literacy in Primary Care

Climate
Time
Money

Climate

"Unless there are changes in the broader health care system and within the specialty, the position of family medicine in the United States will be untenable in a 10- to 20-year time frame."

– Task Force 1 FFM, Ann Fam Med 2004; 2:S33-S50.

Time:

Patient priorities

Physician priorities

Insurer priorities

Other priorities

Time:

Yarnall KS, et al. Primary Care: is there enough time for screening? Am J Public Health 93(4):635-641, 2003.

- 1996 USPSTF Guidelines
- 2500 patients
- **1773 hours or 7.4 hours every working day for a year!**
- **Average pt is due for 25 guidelines!**
- **Getting worse not better!**

Money:

Lack of adequate value/reimbursement for E/M codes is a major barrier to primary care taking on the management of genetic topics.

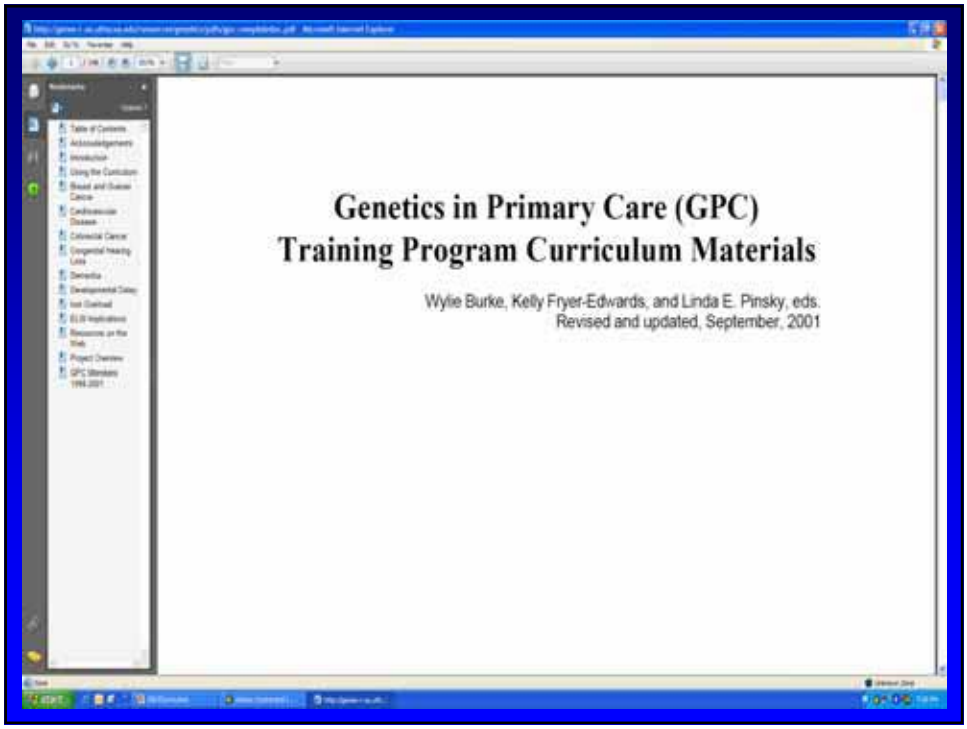
alcohol abuse vs. colonoscopy

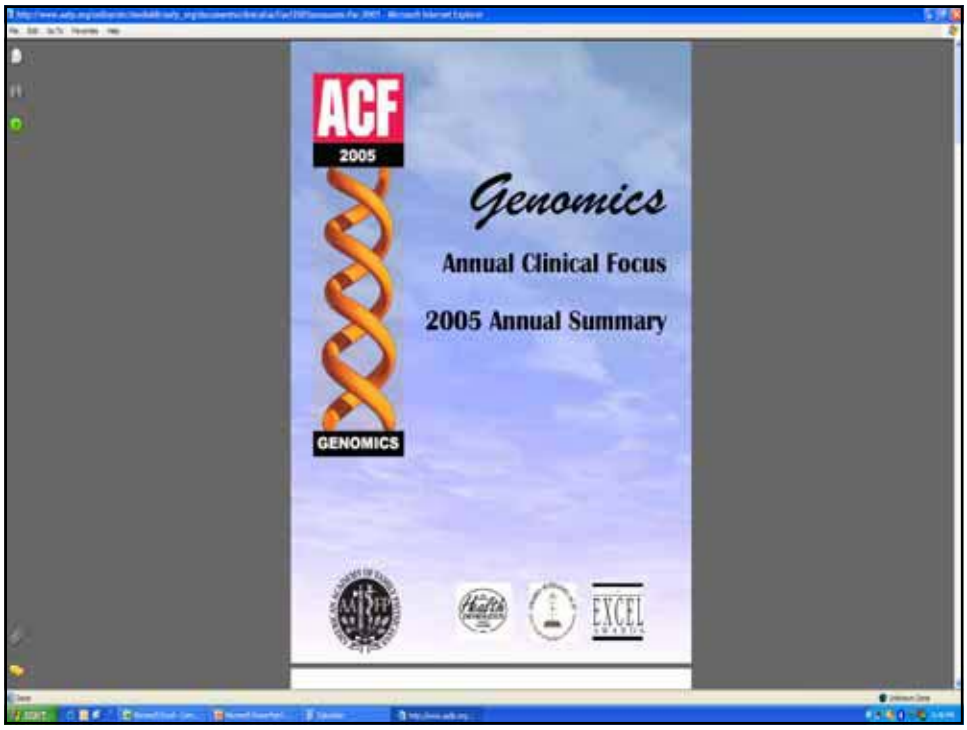
Money:

Aside from infrastructure development, should much be spent on moving genetics up in the agenda of current primary care, given competing priorities? May 3, 2006 JAMA

Education:

- Genetics community has been reaching out for years with varying degrees of success
  - Genetests/Geneclinics
  - March of Dimes education modules
  - NEJM genetics articles
  - NCHPEG
  - Meeting presentations

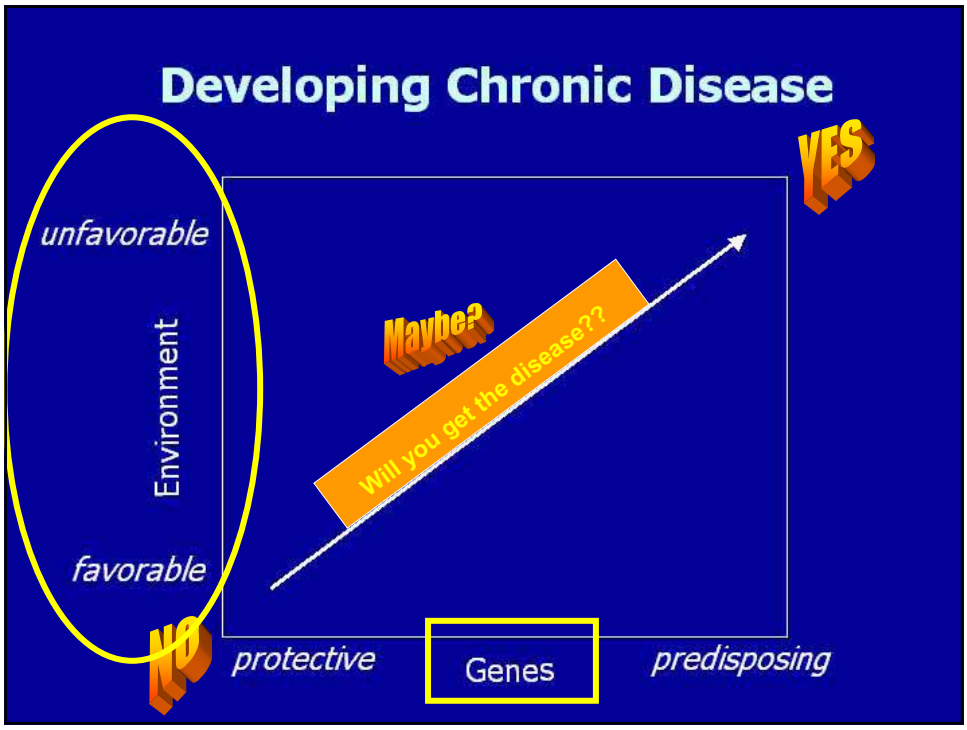

Genetics in Primary Care (GPC)
Training Program Curriculum Materials
Wylie Burke, Kelly Fryer-Edwards, and Linda E. Pinsky, eds.
Revised and updated, September, 2001


ACF
2005
GENOMICS
Genomics
Annual Clinical Focus
2005 Annual Summary
EXCEL

Education:

- Why might efforts have failed?
  - Top down approach
  - Not very eviden
  - Mechanism/theo driven
  - Subject fatigue
  - Lack of maturity of genetics in areas of interest to primary care
  - Preaching to the converted

Climate!



Family history is still the cheapest, most accessible, most time-tested way to get a rough estimate of the genetic component of disease risk.

Family History may change how your doctor may screen or treat you for:

- Breast Cancer
- Cardiomyopathy
- Colon Cancer
- Coronary Artery Disease
- Developmental Delay
- Diabetes
- Dyslipidemia
- Emphysema
- Gastric cancer
- Hearing Impairment
- Heart failure
- Hip Dysplasia
- Kidney Cancer
- Hypertension
- Iron Def Anemia
- Liver Cancer
- Osteoporosis
- Pancreatitis
- Prostate Cancer
- Syncope
- Thromboembolism
- Thyroid Cancer
- Thyroid Disease
- Urticaria
- Visual Impairment

From Alan Guttmacher, MD address 10/11/04

Family History

Mother, father, brother, sister, child affected:

- Type 2 diabetes – 2-6X risk increase
- Hypertension – 2-3X risk increase
- Coronary heart disease – 2X risk increase

Web-Based Family History Tool Available in English and Spanish

www.surgeongeneral.gov/familyhistory/

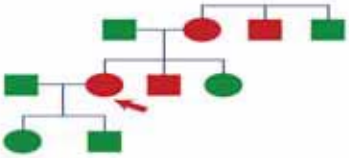
Do YOU know Vanessa?

Vanessa, 35, just finished walking with her daughter and feels great. These walks are now part of their daily routine, and her health care provider tells her she won't need medication for her diabetes in the foreseeable future.

But for a thorough primary care provider, Vanessa's outlook may not have been so good. All too often, diabetes goes undiagnosed for years while high blood sugars silently attack vulnerable organs like the eyes, kidneys and heart. By the time symptoms appear, organ damage has already occurred.

Luckily for Vanessa, her health care provider asked about her family history at her last physical and found that her mother, uncle and brother all developed diabetes in their mid-40s. Vanessa's fasting blood sugars were in the diabetic range.

One year later, thanks to changes in diet and exercise, Vanessa's sugars are nearly normal and she is helping the rest of her family adopt a healthy lifestyle.



The next time you see a "Vanessa," take the time to obtain a complete family history. She—and her family—will thank you.

The U.S. Surgeon General's My Family Health Portrait Tool can help your clients gather and organize their family history before visiting your office.
Direct them to it at www.surgeongeneral.gov/familyhistory/

http://www.cdc.gov/genomics/activities/famhx.htm

Genomics|Activities|Family History

CDC Home | Search | Health Topics A-Z

CDC

National Office of
Public Health Genomics

SITE SEARCH

home > activities > family history

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CDC Activities

Evaluating Family History for Preventive Medicine and Public Health

Family history is known to be a risk factor for many chronic diseases—including coronary heart disease, cancer, and diabetes—but its use in preventive medicine has been de-emphasized compared with modifiable risk factors such as smoking and diet. Although clinicians are trained to collect family histories, they often fail to do so because of lack of time, inadequate reimbursement, and a lack of skill in interpreting family history information. According to the Healthstyles 2004 survey, 96% of Americans believe that knowing their family history is important to their health, yet only 33% have ever tried to gather and organize their family health history.

Most common diseases result from the interactions of multiple genes with multiple environmental factors in complex patterns that, despite progress in sequencing the human genome, are unlikely to be understood fully in the near future. In the meantime, a person's family health history can be used as a low-cost, low-tech "genomic tool" with which to capture the interactions of genetic, environmental, and behavioral factors in determining that person's disease risk. Recognizing the importance of family history for disease prevention and health promotion, the National Office of Public Health Genomics (NOPHG) at the Centers for Disease Control and Prevention (CDC) began CDC's Family History Public Health Initiative in 2002.

Internet | 100%

http://www.ahrq.gov/downloads/pub/evidence/pdf/famhistory/famhist.pdf

Genomics|Activities|Family Hi... | http://www.ahrq.gov/do...

1 / 201 | 102%

Evidence Report/Technology Assessment
Number 159

Collection and Use of Cancer Family History in Primary Care

Prepared for:
Agency for Healthcare Research and Quality
U.S. Department of Health and Human Services
540 Gaither Road
Rockville, MD 20850
www.ahrq.gov

Contract No. 290-02-0020

Prepared by:
McMaster University Evidence-based Practice Center, Hamilton, ON

Unknown Zone

http://consensus.nih.gov/ABOUTCDP.htm

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NIH Consensus Development Program

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Introduction

The Consensus Development Program (CDP) is an unbiased, independent, evidence-based assessment of complex medical issues and is conducted by the National Institutes of Health (NIH). The program has operated since 1977. Each conference is jointly sponsored and administered by one or more Institutes or Centers (ICs) of NIH and by the Office of Medical Applications of Research (OMAR) in the Office of the Director of NIH. Depending on the topic, other Federal agencies with biomedical components may join in sponsoring a CDP conference. In conjunction with each conference, the Agency for Healthcare Research and Quality (AHRQ) provides a systematic review of literature on the conference topic through one of its Evidence-Based Practice Centers.

The purpose of a CDP conference is to evaluate the available scientific information on a biomedical issue and develop a statement that advances understanding of the issue under consideration and will be useful to health professionals and the public. The panel is an independent, broad-based, non-Department of Health and Human Services (DHHS), nonadvocacy group with appropriate expertise. The panel listens to the scientific data presented by invited experts and comments from the general public. The panel weighs the information and then composes a statement that addresses a set of predetermined questions. This statement is an independent report of the panel and is not a policy statement of NIH or the Federal Government and is not an advisory body to NIH.

Conference statements and recommendations focus on medical safety and efficacy, although they may refer to related issues (e.g. economic, sociologic, legal and ethical) that help to provide a context for the issue. CDP conferences are particularly useful for providing guidance when a controversy exists over preventive, therapeutic, or diagnostic options, or when the issue is of public as well as professional interest.

A consensus statement is based on publicly available data and information. It is not intended as a legal document, practice guideline, or primary source of detailed technical information. Rather, the statement reflects the views of a panel of thoughtful people who understand the issue before them and who carefully examine and discuss the scientific data available on the issue. The creative work

EMR and Genomics

- Risk stratification by expert systems

- Point of care patient/physician education

- Tracking and integration with other health care

American Health Information Community

Personalized Health Care Workgroup Recommendations

Douglas E. Henley
American Academy of Family Physicians

John Glaser
Partners HealthCare

July 31, 2007

Family Health History

Recommendation 3.0:

A multi-stakeholder workgroup, including the private sector, federal health care providers, and federal Public Health Service agencies, should be formed to develop a core minimum data set and common data definition available for primary care collection of family health history information.

☐ Accept ☐ Table ☐ Reject

A Report of the Family Health History

Multi-Stakeholder Workgroup

Presented to the Personalized Health Care Workgroup of

The American Health Information Community

October 25, 2007

Workgroup Co-chairs:

Mary Beth Bigley, DrPH, MSN, ANP
Senior Health Fellow
Office of the U.S. Surgeon General
Department of Health and Human Services

W. Gregory Feero, M.D., Ph.D.
Chief, Genomic Healthcare Branch
National Human Genome Research Institute
National Institutes of Health
Department of Health and Human Services

Genomics and Healthcare

Pitfall

- Poorly educated providers
- Over- or under interprets genetic and environmental risks
- Gets tests and fails to act, or acts on unproven interventions
- Minimally effective therapeutics developed and effectively marketed for "pseudo-disease"

Promise

- Well educated providers
- Understands genetic and environmental risk
- Tests appropriately, proactively takes proven steps to mitigate risk
- New, effective, cost-saving therapies are developed based on genomic insights

Multiple Marker Testing: A Disruptive Technology?

- What will the business model be ultimately?
- What position will the FDA take on this type of testing?
- What will be the fate of the data?
  - In the company's domain?
  - In the patient's domain?
  - In the doctors domain?
- Where will the costs and benefits accrue?

Multiple Marker Testing: A Disruptive Technology?

Should medical societies (especially primary care societies) review and or take a position on this type of testing?

THANKS!

Slides courtesy of:

- Leslie Biesecker, NHGRI
- Francis Collins, NHGRI
- Alan Guttmacher, NHGRI
- Teri Manolio, NHGRI
- Colleen McBride, NHGRI