

Personalized Medicine: From Promise To Practice

Francis S. Collins, M.D., Ph.D.
National Human Genome Research Institute

Research!America Forum
September 19, 2006



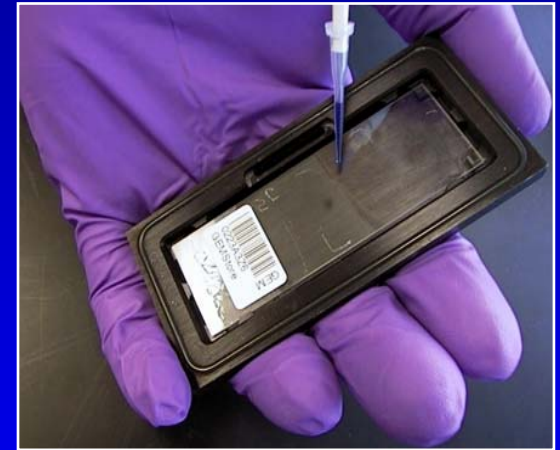
We wouldn't think of buying shoes in a single size



So why should we be satisfied with one-size-fits-all medicine?

Personalized Medicine

Genomics today is where the computer industry was in the 1970s -- at the beginning of a technology revolution...



Biotechnology + Bioinformatics + Genomics

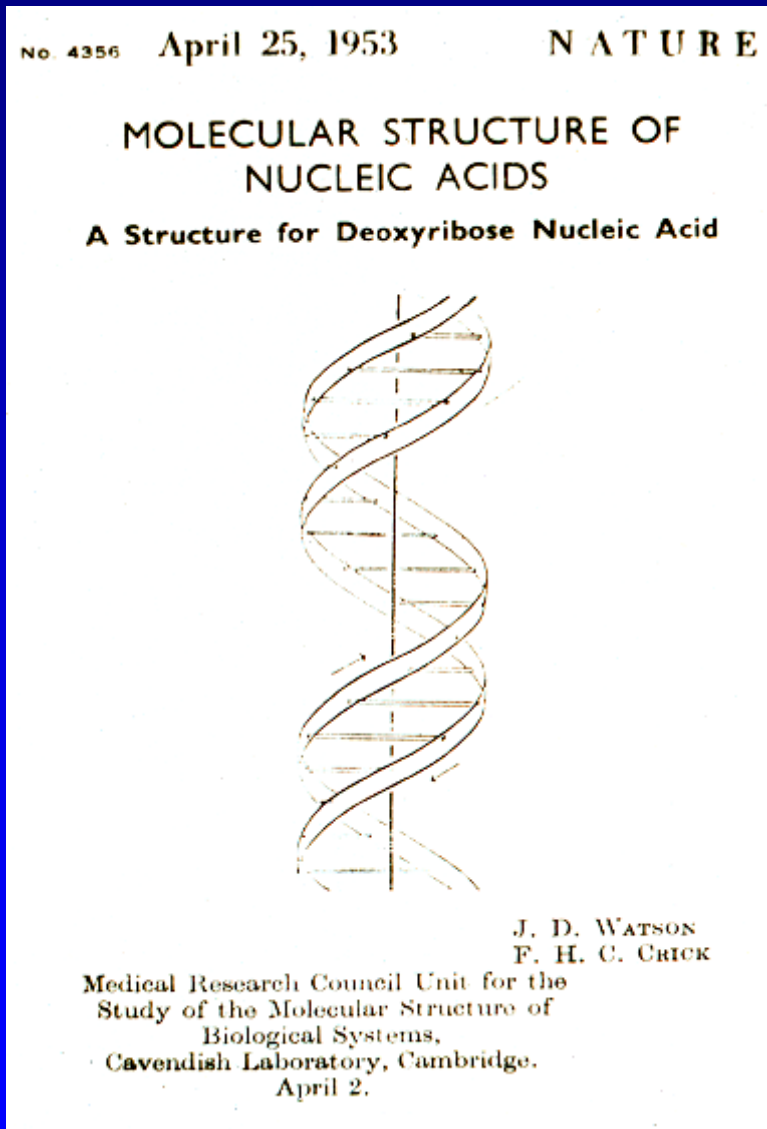
+ Proteomics + Imaging + Public Health +

= Revolution in Healthcare

April, 1953



April, 2003



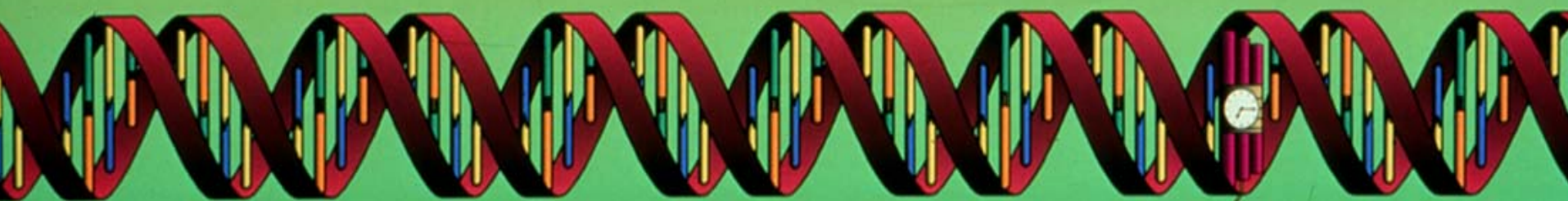
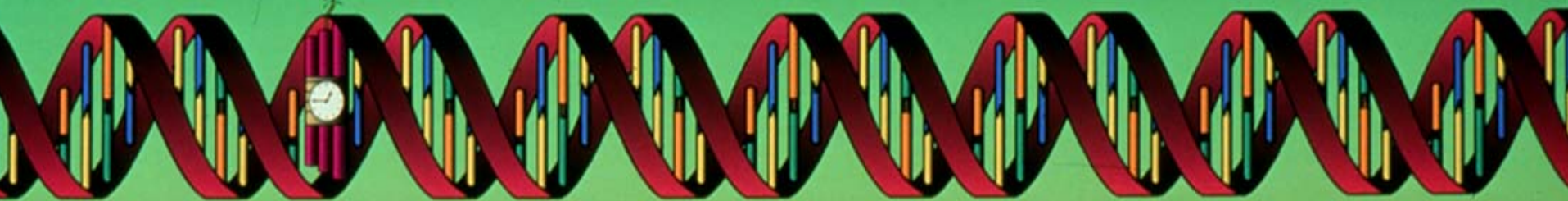
Disease with Genetic Component



Identify Genetic Defect(s)



Time



International HapMap Project

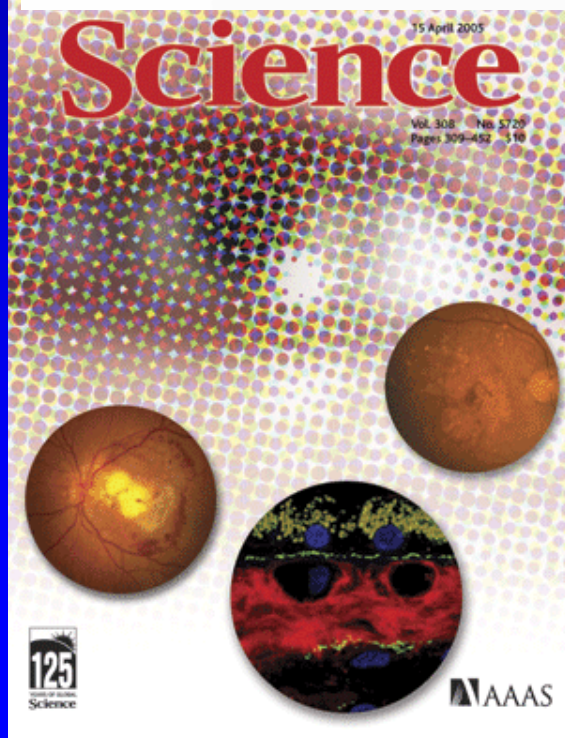
The image features a world map in shades of yellow and green, overlaid with a white DNA double helix. The DNA helix is positioned across the map, with one strand following the outline of the continents and the other strand following the gaps between them. The text 'International HapMap Project' is written in a bold, black, serif font, with 'HapMap' being the largest and most prominent word. The background is a solid blue gradient.

www.hapmap.org

The First HapMap Success Story: Age-Related Macular Degeneration

Complement Factor H Polymorphism in Age-Related Macular Degeneration

Robert J. Klein,¹ Caroline Zeiss,^{2*} Emily Y. Chew,^{3*} Jen-Yue Tsai,^{4*} Richard S. Sackler,¹ Chad Haynes,¹ Alice K. Henning,⁵ John Paul SanGiovanni,³ Shrikant M. Mane,⁶ Susan T. Mayne,⁷ Michael B. Bracken,⁷ Frederick L. Ferris,³ Jurg Ott,¹ Colin Barnstable,² Josephine Hoh^{7†}



Two other risk variants have now been identified.

Together these account for 74% of risk, and point to powerful new approaches to prevention and treatment.

The Genetic Association Information Network (GAIN)

- **A public-private partnership between**
 - **NIH**
 - **The Foundation for NIH**
 - **The private sector: Pfizer, Perlegen, Affymetrix, Abbott, ...**
- **Goal is to encourage whole genome association studies of common disease**
- **Will provide genotyping for approximately seven studies, each with 1000 cases and 1000 controls**
- **Final decisions expected later this month**

The Genes and Environment Initiative (GEI)

- **Proposed in the President's budget for FY07**
- **Aims to accelerate understanding of genetic and environmental contributions to health and disease**
- **Two components:**
 - **Genotyping of case-control studies of common disease: with emphasis on health disparities**
 - **Development of innovative technologies to measure environmental exposures, diet, and physical activity**

**Public input is earnestly solicited
on a new NIH policy proposal for
genome wide association studies**

Genome-Wide Association Studies (GWAS)

- OER Home
- Funding Opportunities
- Applications & Forms
- Awarded Grants
- Grants Policy
- eRA
- About OER

The NIH is interested in advancing Genome-Wide Association Studies (GWAS) to identify common genetic factors that influence health and disease. GWAS are currently defined as any study of genetic variation across the entire human genome that is designed to identify genetic associations with observable traits (such as blood pressure or weight), or the presence or absence of a disease or condition of the public through the creation of a centralized NIH GWAS data repository. The purpose of this Website is to support the public use the information derived from such studies will be proposed policy is to advance science for the benefit of the public through policy development activities.

The "Overview" section of this site presents the essential background and responses to frequently asked questions on GWAS. This page focus on the notices released to date which will result in a request for information through which the National Institutes of Health (NIH) will solicit advice and comments.

Overview

- [Background](#)

Notices and Announcements

- [Submit a Comment](#) - Comments may be submitted through this link.
- [NIH Press Release \(08/30/2006\)](#) - NIH Seeks Public Input on Proposed Policy for Sharing of Genetic Information
- [Federal Register Notice \(08/30/2006\)](#) - Proposed Policy for Sharing of Data Obtained in NIH Supported or Conducted Genome-Wide Association Studies (GWAS)
- [NIH Guide Notice NOT-OD-06-L](#) - Request for Information (RFI): Proposed Policy for Sharing of Data obtained in NIH supported or conducted Genome-Wide Association Studies (GWAS)
- [NIH Guide Notice NOT-OD-06-071](#) - Request for Information (RFI): Proposed Policy for Sharing of Data obtained in NIH supported or conducted Genome-Wide Association Studies (GWAS)
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Comments or Questions?

- Please send email to GWAS@nih.gov.

Google: "GWAS policy"

The major genetic risk factors for common diseases like diabetes, cancer, heart disease, autism, hypertension, bipolar illness, asthma, Alzheimer's disease, osteoporosis, and many other diseases will be identified in the next 2 – 3 years

Case-control studies are powerful in discovering risk factors

But lousy at quantifying them

And even worse at discovering G x E contributions

To derive those crucial data, we need prospective studies

The U.S. does not currently have an adequate plan for this

insight commentary

The case for a US prospective cohort study of genes and environment

Francis S. Collins

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NATURE | VOL 429 | 27 MAY 2004 |

Disease with Genetic Component



Identify Genetic Defect(s)



Diagnostics



**Preventive
Medicine**

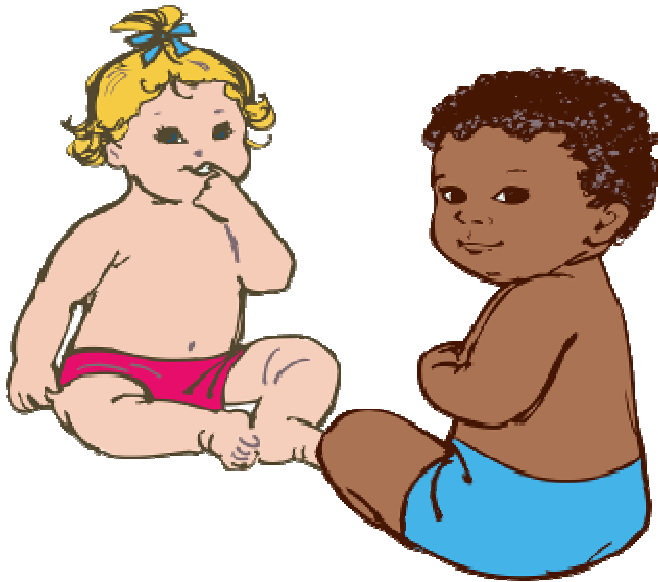
**Accelerated
by Human
Genome Project
and HapMap**

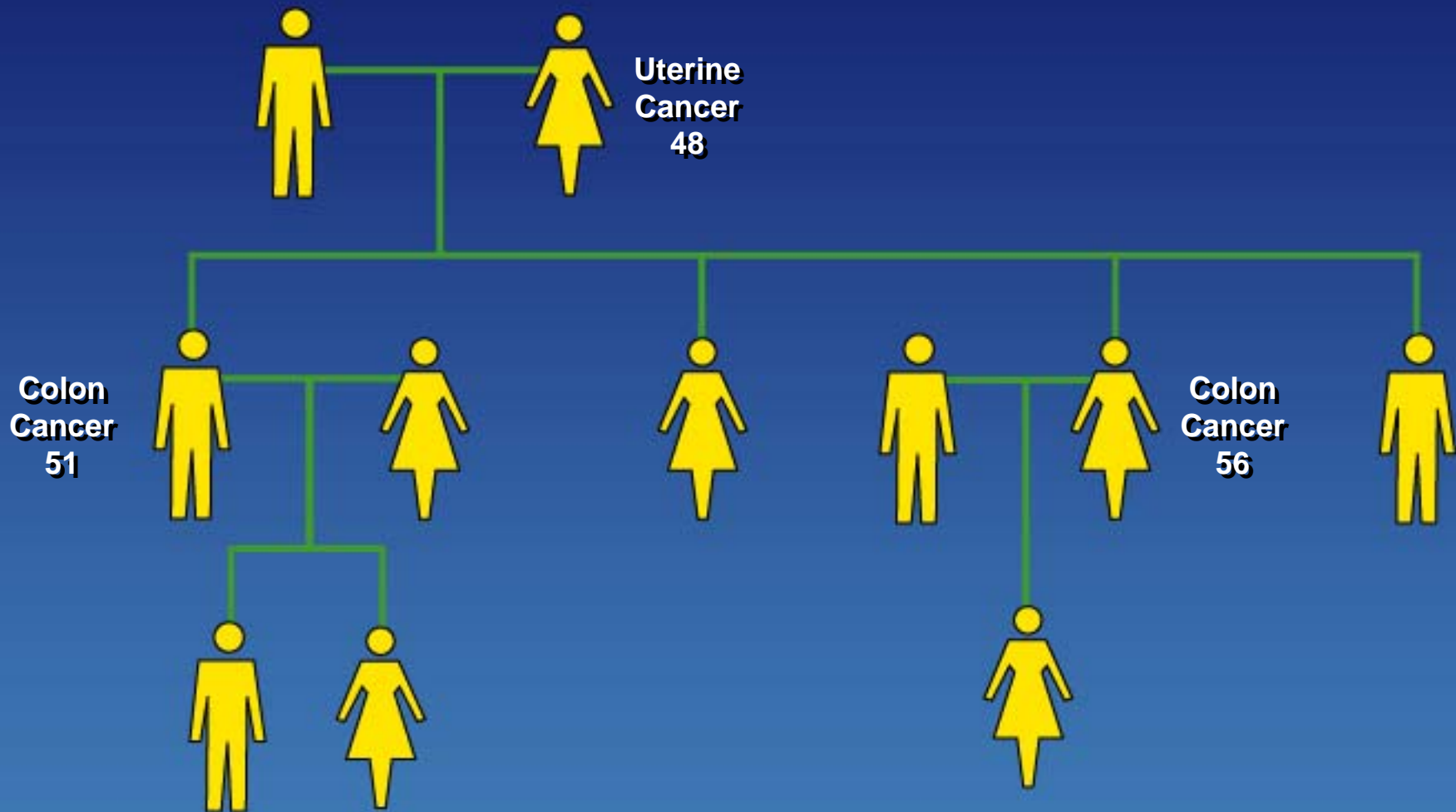


Time

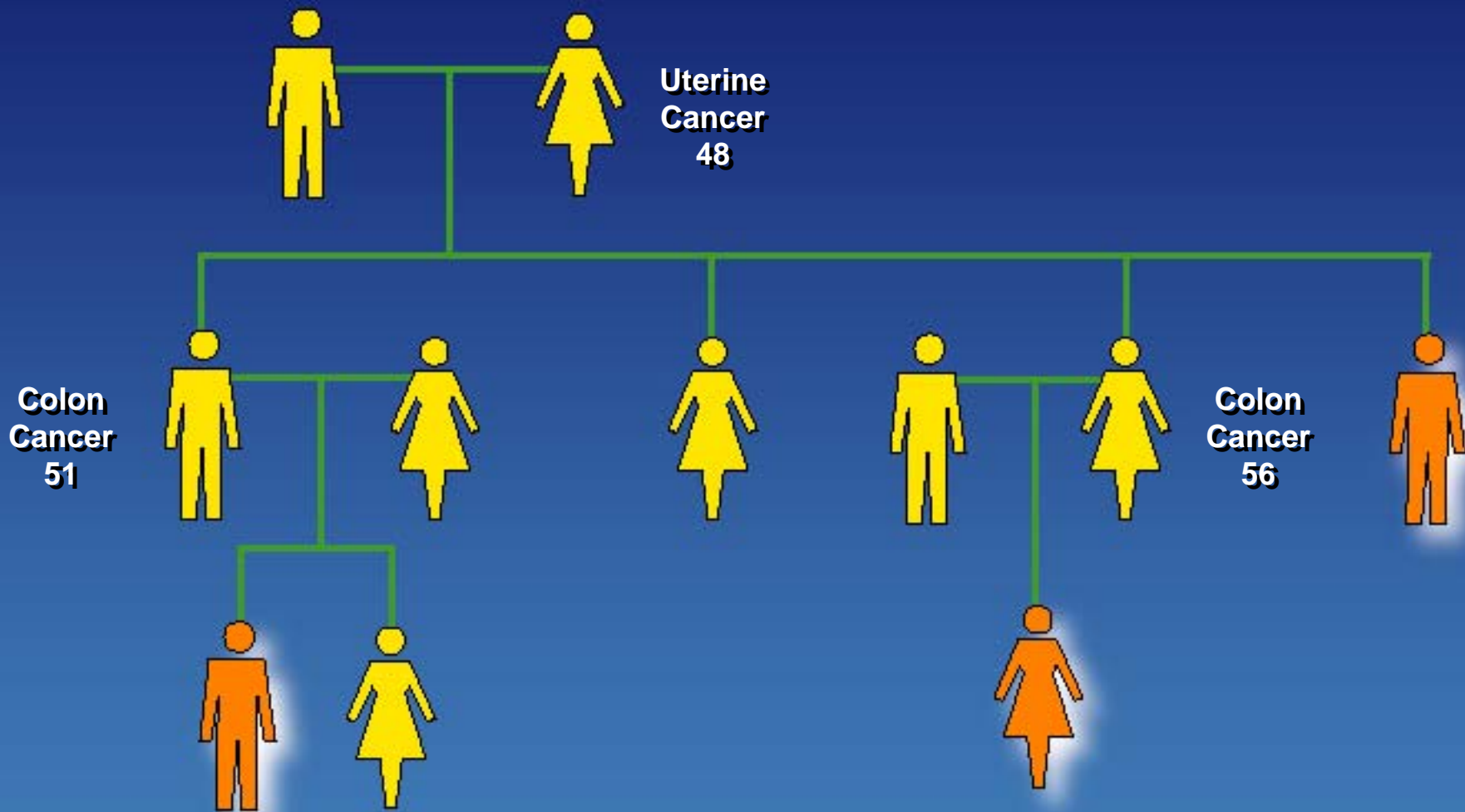
PKU Screening

- **All published studies show that PKU screening and treatment represent a net direct cost savings to society**





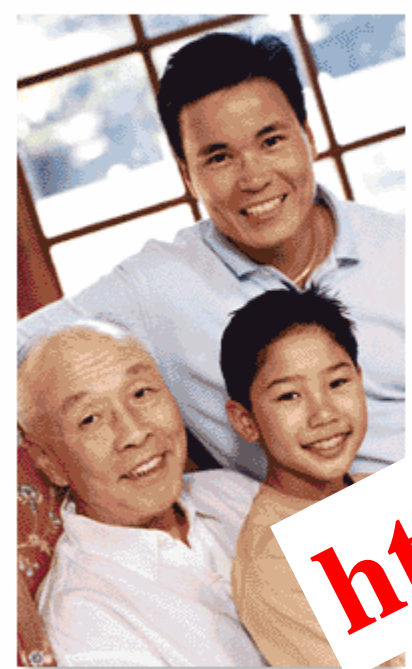
Hereditary NonPolyposis Colon Cancer (HNPCC)



Identifying Those At Risk



Help with this page



Welcome to My Family Health Portrait

My Family Health Portrait allows you to create a personalized family health history report from any computer with an Internet connection and an up-to-date Web browser. The report includes a drawing of your family tree and a chart of your family health history. Both the chart and drawing can be shared with your family members or your healthcare professional. Used in consultation with your healthcare professional, your family health history can help you review your family's health history and develop a plan of care that is right for you.

New users can click on **Load a New Family History** to begin creating a personalized family health history. Returning users can click on **Load a Saved Family History** to update an existing personalized family health history.

[Load a New Family History](#)

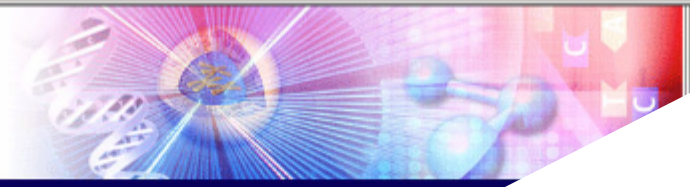
[Load a Saved Family History](#)

My Family Health Portrait has been tested on following browsers on Windows: Internet Explorer 5.0+, Netscape 7.0+ and Mozilla Firefox 1.0+. It has also been tested on the following browsers on Mac: Safari 1.3+, Netscape 7.0+ and Mozilla Firefox 1.0+. Internet Explorer 5.2 or lower on Mac is not a supported browser. To update your browser, visit the [Browser Update](#) page.

Additional Information

Since **My Family Health Portrait** is Web-based, no additional software needs to be downloaded or installed. The health information you provide is stored only on your computer and not on a U.S. government server. You own the file and can choose what to do with it at any time.

With My Family Health Portrait, you can:



PREPARING HEALTH PROFESSIONALS FOR THE GENOMICS REVOLUTION

- ABOUT NCHPEG**
- MISSION AND BACKGROUND
- MEMBERSHIP
- NCHPEG IN THE LITERATURE
- CONTRACTS AND GRANTS
- ANNUAL MEETING
- DIVERSITY INITIATIVES
- TECHNICAL ASSISTANCE

NCHPEG/GROW 10th Annual Meeting
February 1,2 2007
Click the image below for more information



...discipline
...ured
...proposals for 2008
...ber 1, 2006.

www.nchpeg.org

Try our Genetics Search Engine
GROW
(Genetics Resources on the Web)

GlaxoSmithKline

GlaxoSmithKline scientists are using the study of genetics to understand the basis of disease and to gain insight into why people respond differently to medicines. By understanding how genetic factors influence health and disease, GSK is leading the way to the development of safer, more effective treatments for patients.

All Health Professionals

Select an option below

Selected Health Disciplines

Select an option below

Core Principles of Genetics for Health Professionals

The principles focus on basic biology related to genetics. This document is a companion piece to the Core Competencies that provides additional guidance about the content that should constitute basic instruction in genetics for those in health care.

Race, Genetics, and Healthcare

Available On-Line

Watch the NCHPEG CME Broadcast "Race, Genetics, and Health Care: What we know and what it means for your patients". This broadcast is phase one of a project supported by grants from the Robert Wood Johnson Foundation and the Josiah Macy, Jr. Foundation. NCHPEG will develop additional web-based materials during the second phase of the project.

[Click here to watch the broadcast online](#)

[Click here to request a DVD](#)

In Practice Newsletter

The In Practice Newsletter has been revamped! Take a look at the [newest issue](#).

~~109th~~
108th CONGRESS
1ST SESSION

~~S. 1053~~

S.306

HR.1227

AN ACT

To prohibit discrimination on the basis of genetic information
with respect to health insurance and employment.

1 *Be it enacted by the Senate and House of Representa-*
2 *tives of the United States of America in Congress assembled,*

3 **SECTION 1. SHORT TITLE; TABLE OF CONTENTS.**

4 (a) SHORT TITLE.—This Act may be cited as the
5 “Genetic Information Nondiscrimination Act of 2003”.

Disease with Genetic Component



Identify Genetic Defect(s)



Diagnostics



Pharmacogenomics



**Preventive
Medicine**

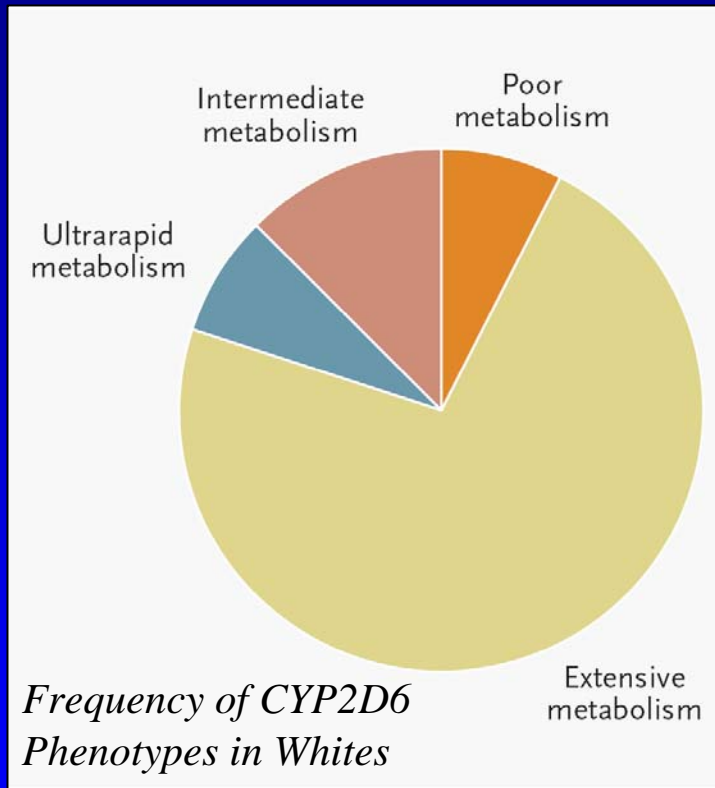
**Accelerated
by Human
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Time



Using Genetic Information to Predict Drug Metabolism: The AmpliChip CYP450



Depending on your own spelling of the CYP450 genes, you may need much higher or much lower doses of a many different drugs to get the benefit.

Predicted economic benefit of CYP2C9 testing for warfarin dosing

- **Predict 1 major bleed prevented for every 44 patients screened (\$135/assay)**
- **\$6,000 testing costs ~ cost of 1 major bleed**
- **Neutral economic result, but significant improvement in patient outcome**
- **Prospective trial needed**

Higashi and Veenstra, Am J Manag Care 2003; 9: 493-500

ORIGINAL ARTICLE

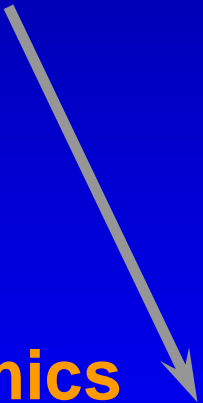
Effect of *VKORC1* Haplotypes on Transcriptional Regulation and Warfarin Dose

Mark J. Rieder, Ph.D., Alexander P. Reiner, M.D., M.P.H.,
Brian F. Gage, M.D., M.Sc., Deborah A. Nickerson, Ph.D., Charles S. Eby, M.D.,
Howard L. McLeod, Pharm.D., David K. Blough, Ph.D.,
Kenneth E. Thummel, Ph.D., David L. Veenstra, Pharm.D., Ph.D.,
and Allan E. Rettie, Ph.D.

Disease with Genetic Component



Identify Genetic Defect(s)



Diagnostics

Pharmacogenomics

Therapeutic Developments

**Preventive
Medicine**



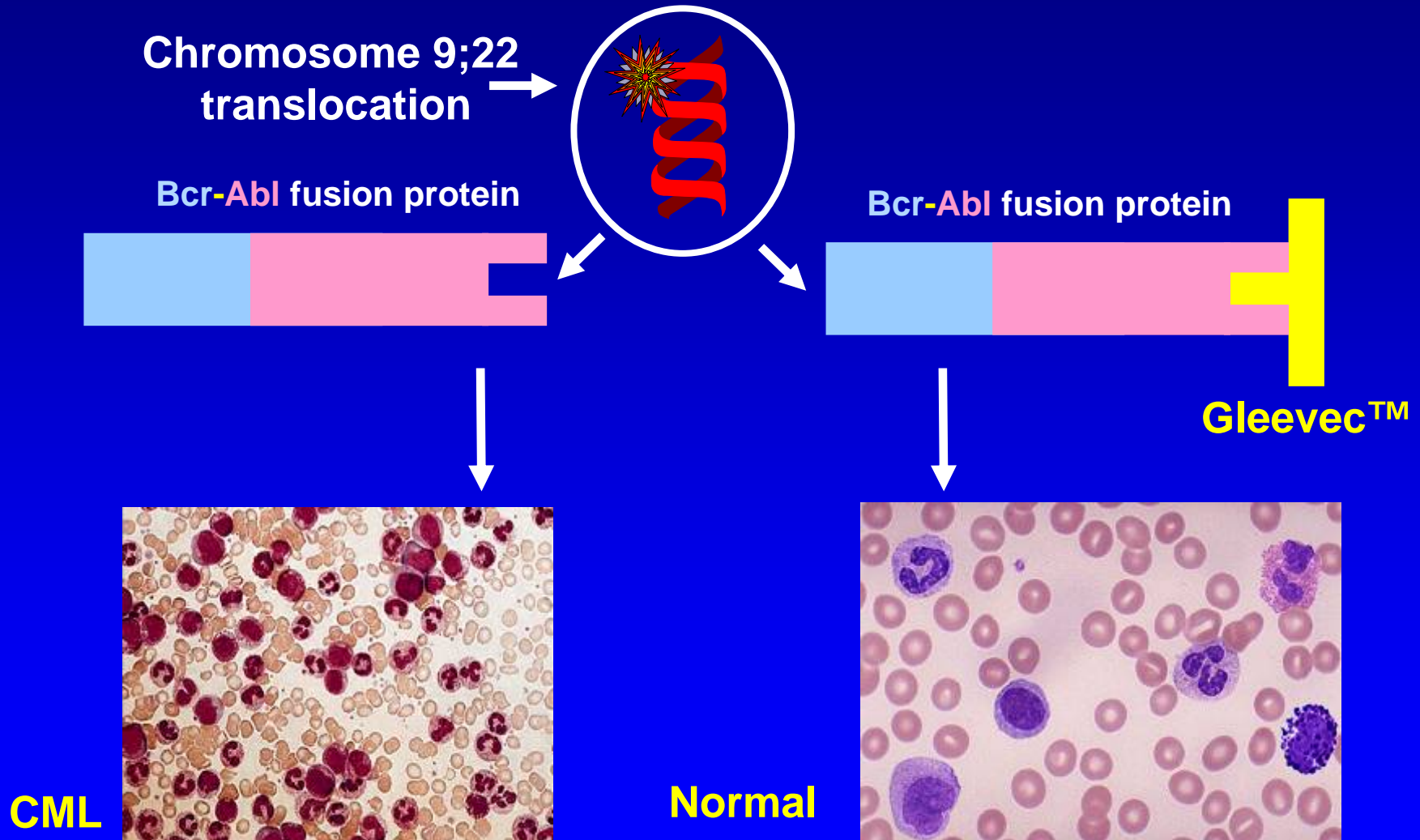
**Accelerated
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Time



Gleevec™ – Specifically Targets An Abnormal Protein, Blocking Its Ability To Cause Chronic Myeloid Leukemia



The Cancer Genome Atlas (TCGA):

**A Bold New Project To Achieve
Comprehensive Understanding of
the Genetic and Epigenetic
Causes of Cancer**



Personalized Medicine: A future dream



Betty's story in 2015

- Betty completes the Surgeon General's family history tool at age 25, learns of uncles with early heart disease.
- She consults her health care provider, who has made an effort to stay informed about genomic medicine. The provider suggests complete genome sequencing for \$1000.
- Betty inquires about the risk of genetic discrimination, but effective legislation has outlawed this.
- She is found to have three gene variants that have been shown conclusively in well validated studies to increase her risk of early heart attack 4-fold.
- She and her provider design a program of prevention based on diet, exercise, and medication precisely targeted to her genetic situation.

Betty's story continues

- Betty does well until age 75.
- She develops left arm pain that she assumes is due to gardening, but her provider knows her higher risk and diagnoses an acute MI.
- Referring to her genome sequence, the provider chooses the drugs that will work best to treat her.
- She survives and is alive and well in the 22nd century.

Personalized Medicine: Could the dream become a nightmare?



Betty's story gone wrong

- Betty never learns about her family history, educational efforts for the public and health care providers were defunded, and Betty's provider thought genetics was irrelevant to practice.
- Betty hears about genome sequencing, but after seeing her brother lose his health insurance from this information, she decides not to.
- Betty eats an unhealthy diet, gains weight, and develops high blood pressure.
- While tests to predict which drug would be most effective for Betty have been proposed, they have never been validated, and are not reimbursed.

Betty's story gone wrong, continued

- Betty's hypertension is treated with a drug that causes a hypersensitivity reaction, so she stops treatment.
- After 10 years of uncontrolled hypertension, Betty develops left arm pain at age 50.
- Unaware of her high risk, her provider assumes this is musculoskeletal and prescribes rest.
- Betty returns to the ER a few hours later in cardiogenic shock.
- The absence of her genome sequence information prevents immediate optimum choice of therapy.
- Betty dies in the ER.

Charge to all of us:

SAVE BETTY!!!