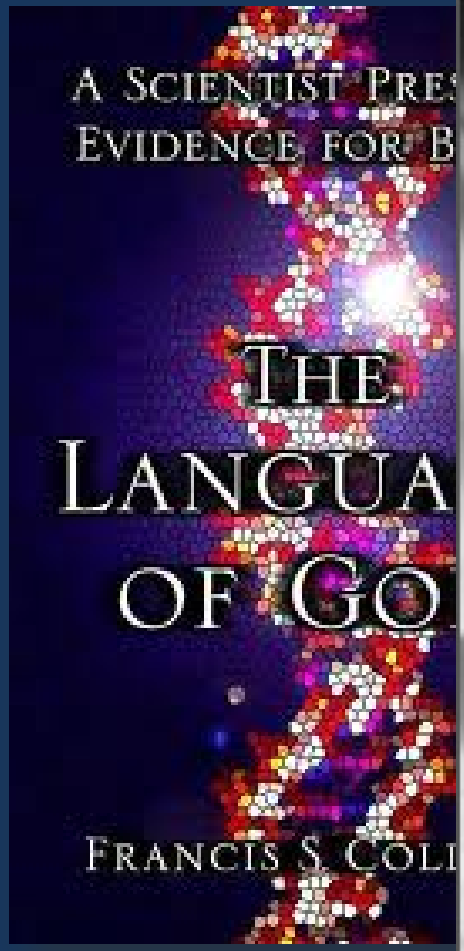
The **$1,000 Genome…**

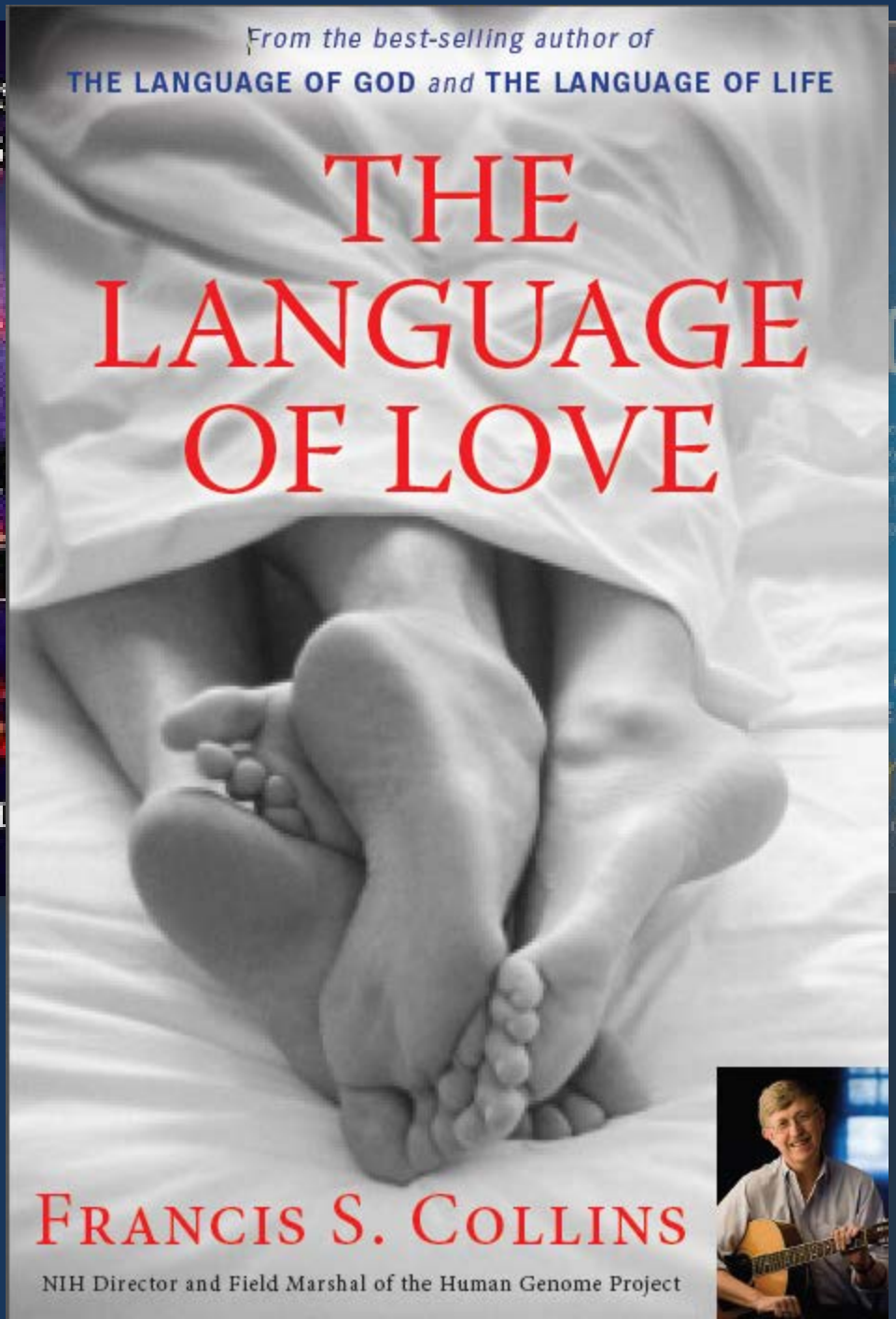
Kevin Davies PhD

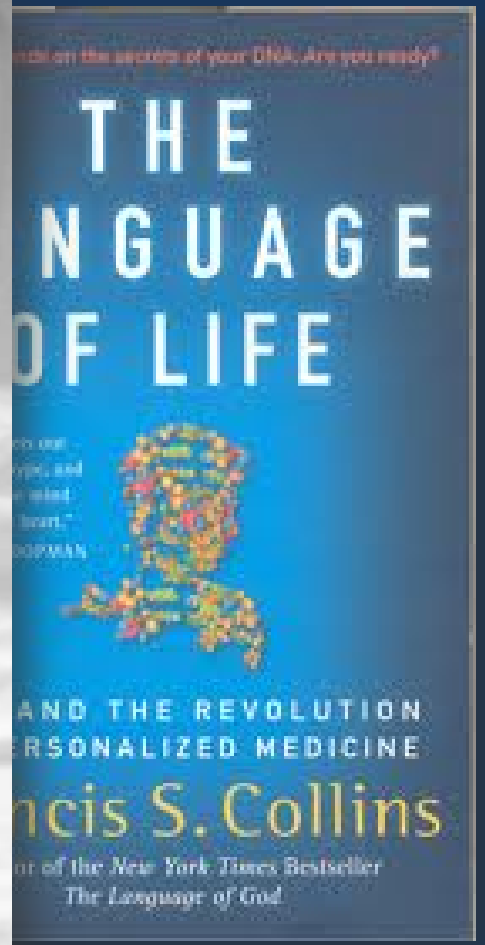
…the **$1 Million Interpretation?**

The Genomics Landscape a Decade After the Human Genome Project – NIH 4/25/13


nature
genetics
Positional cloning: Let's not call it reverse anymore
Positional cloning: Let's not call it reverse anymore
Positional cloning: Let's not call it reverse anymore
Positional cloning: Let's not call it reverse anymore
Positional cloning: Let's not call it reverse anymore







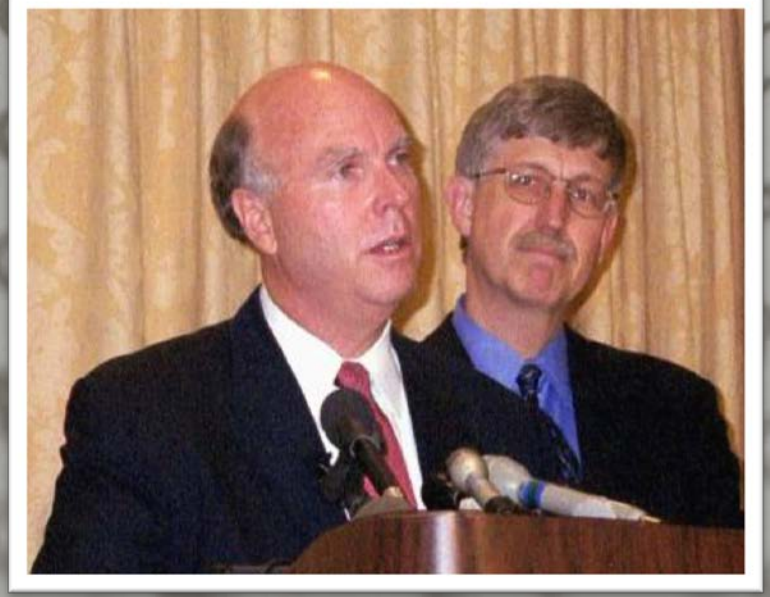
Mark Gabrenya

Helen Hunt

in

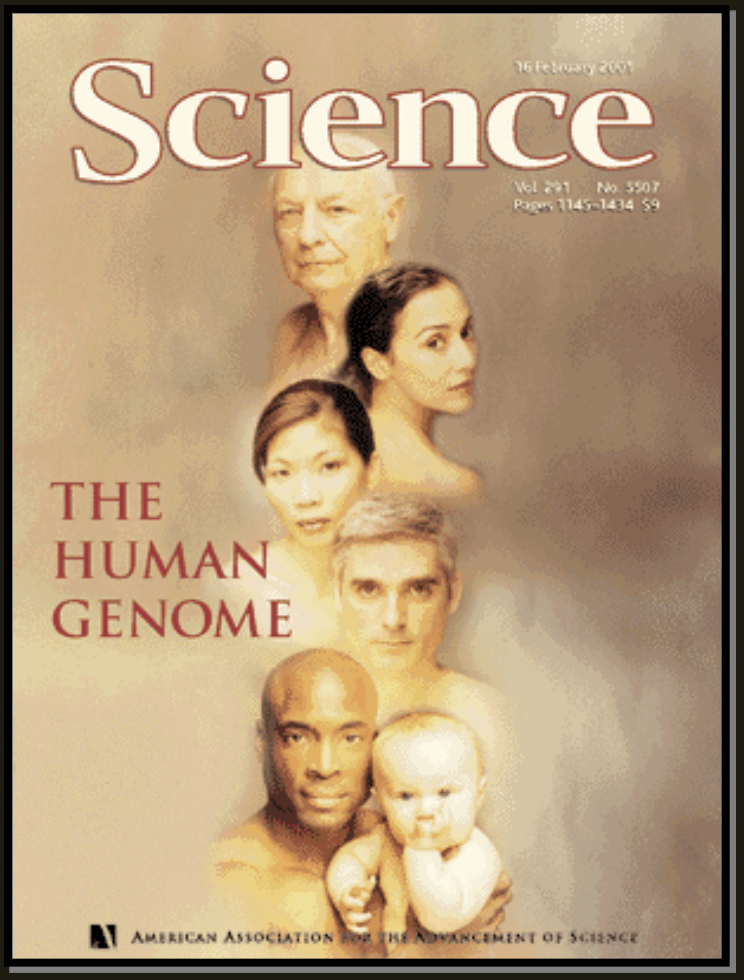
Decoding Annie Parker

“The Language of God”

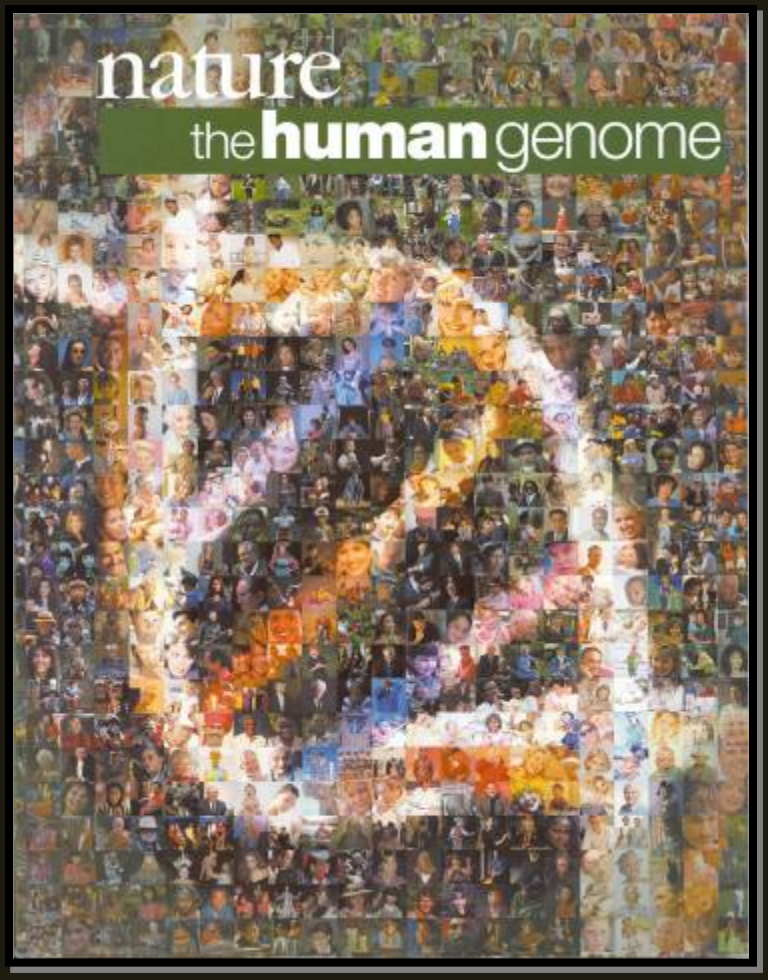


June 26, 2000

February 2001: “The Book of Life”



Celera Genomics



Intl Hum Genome Consortium

WHEN TWO TRIBES…

“This was a race... whatever you read in the media... the public project won, because it's in the public domain! It's actually pretty unusual we win these things. It was a war... but it was a successful war.“

-- TIM HUBBARD (2010)

“The record is pretty clear cut: the first genome in history, the first draft of the human genome, the first complete version of the human genome.“

-- CRAIG VENTER (*2011)*

April 2003

genome.gov
National Human Genome Research Institute

Newsroom

News Releases ▸ International Consortium Completes Human Genome Project

MISSION ACCOMPLISHED !!

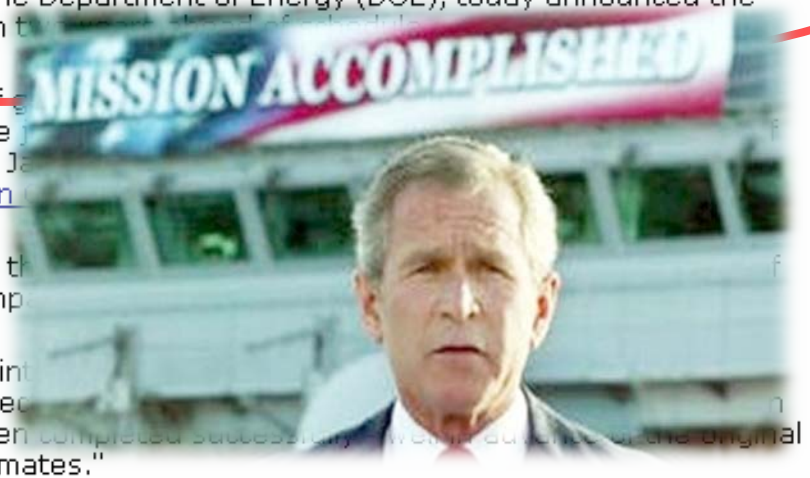
National Human Genome Research Institute
National Institutes of Health
Department of Health and Human Services
and
Office of Science
U.S. Department of Energy

International Consortium Completes Human Genome Project

All Goals Achieved; New Vision for Genome Research Unveiled

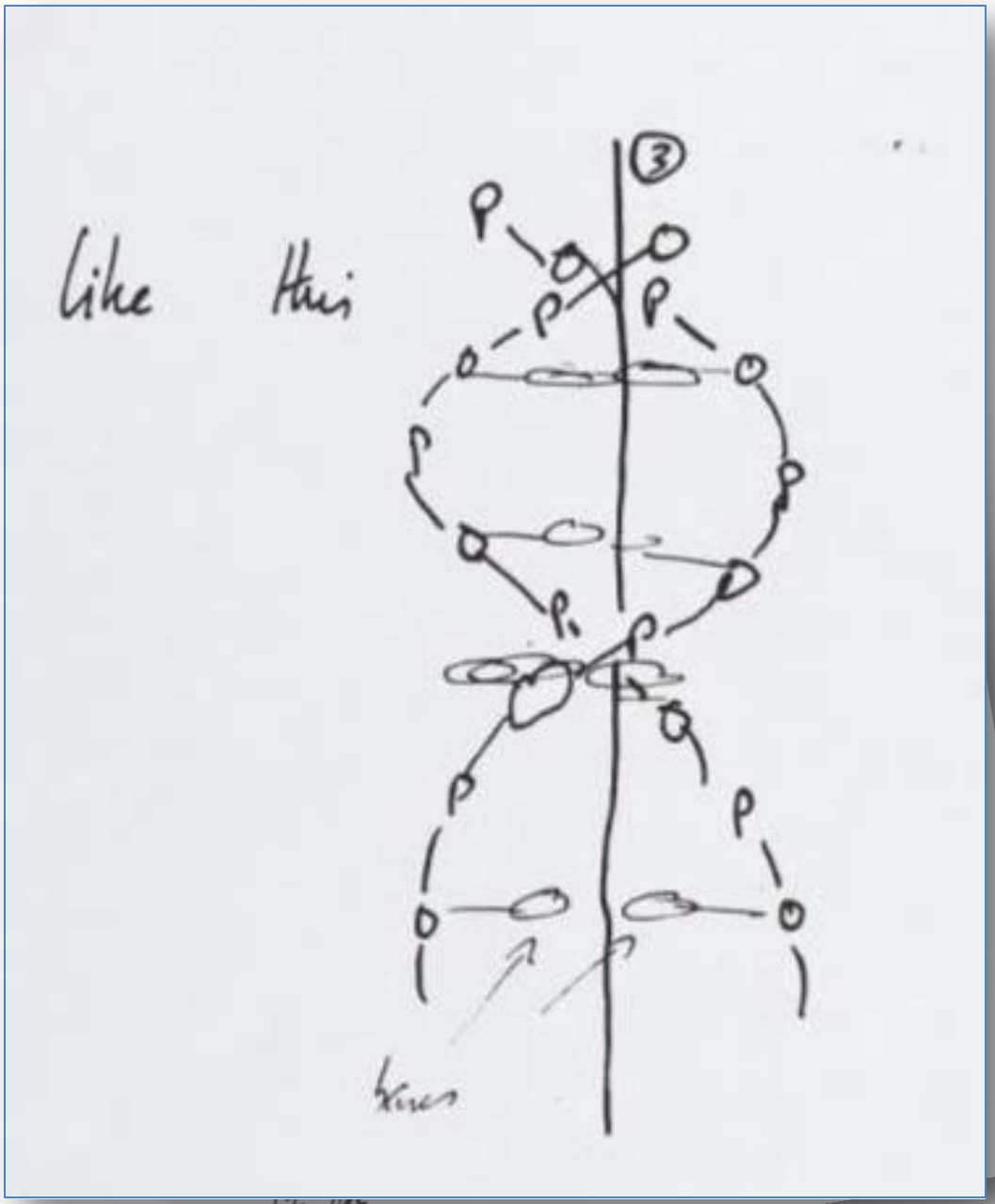
BETHESDA, Md., April 14, 2003 - The International Human Genome Sequencing Consortium, led in the United States by the National Human Genome Research Institute (NHGRI) and the Department of Energy (DOE), today announced the successful completion of the Human Genome Project more than two years ahead of schedule.

Also today, NHGRI unveiled its bold new vision for the future of genome. The vision will be published in the April 24 issue of the *Nature's* publication of the landmark paper by Nobel Laureates J double helix. Dr. Watson also was the first leader of the Human



The international effort to sequence the 3 billion DNA letters in t the most ambitious scientific undertakings of all time, even comp

"The Human Genome Project has been an amazing adventure in book, the shared inheritance of all humankind," said NHGRI Dire Genome Project since 1993. "All of the project's goals have been deadline and for a cost substantially less than the original estimates."



CLUE TO CHEMISTRY OF HEREDITY FOUND

American and Briton Report Solving Molecular Pattern of Vital Nucleic Acid

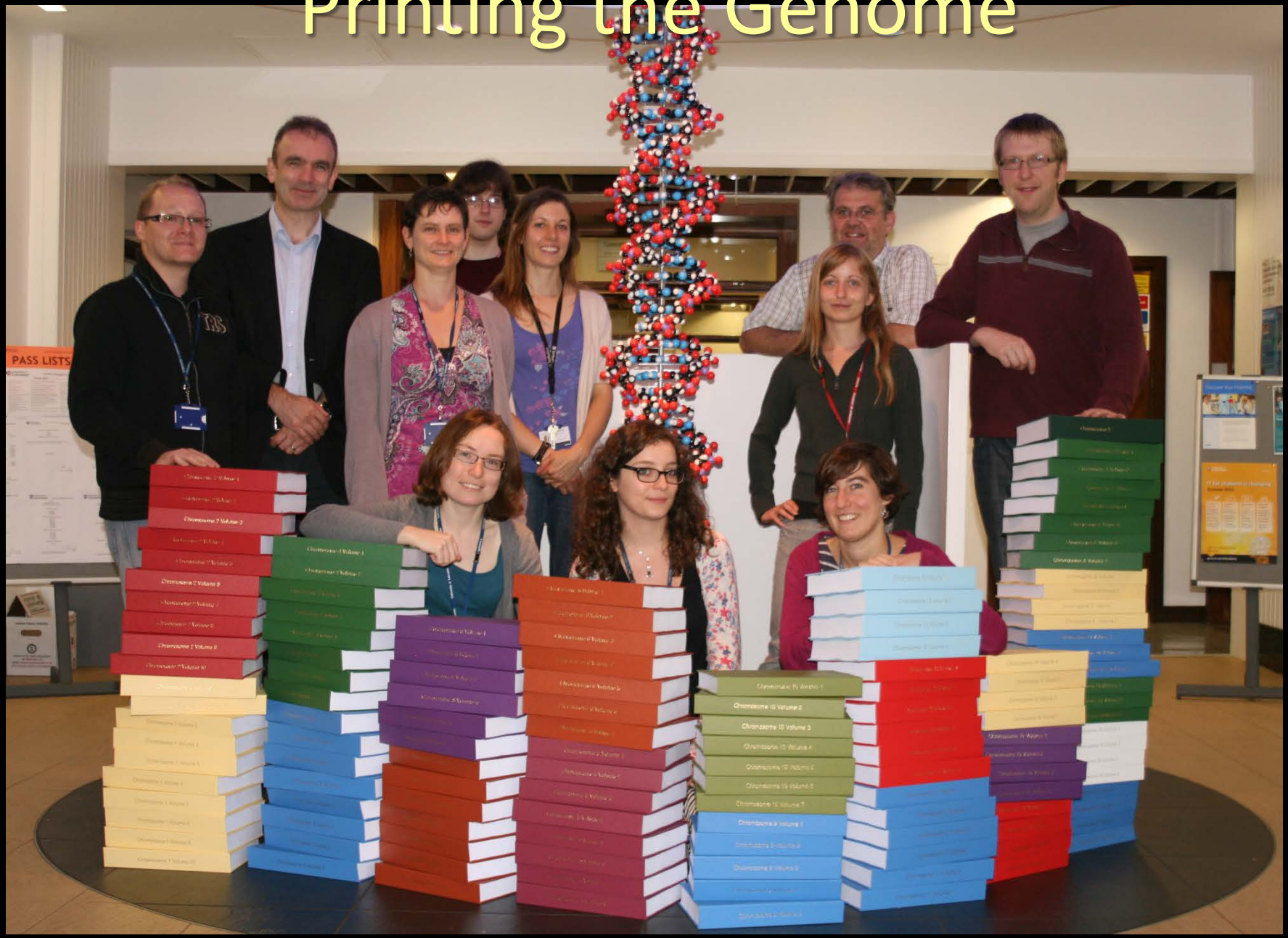
TESTS BY X-RAY PLANNED

Work Done in England, if It Is Confirmed, Should Make Biochemical History

Special to THE NEW YORK TIMES.

LONDON, June 12—A scientific partnership between an American and a British biochemist at the Cavendish Laboratory in Cambridge has led to the unraveling of the structural pattern of a substance as important to biologists as uranium is to nuclear physicists. The substance is nucleic acid, the vital constituent of cells, the car-

Printing the Genome



Cas Kramer (University of Leicester)

WANTED

20 Volunteers

to participate in the

Human Genome Project

a very large international scientific research effort.

The goal is to decode the human hereditary information (*human blueprint*) that determines all individual traits inherited from parents. The outcome of the project will have tremendous impact on future progress of medical science and lead to improved diagnosis and treatment of hereditary diseases.

Volunteers will receive information about the project from the Clinical Genetics Service at Roswell Park, and sign a consent form before participating.

No personal information will be maintained or transferred.

Volunteers will provide a one-time donation of a small blood specimen. A small monetary reimbursement will be provided to the participants for their time and effort.

Individuals must be at least 18 years of age.
Persons who have undergone chemotherapy are not eligible.

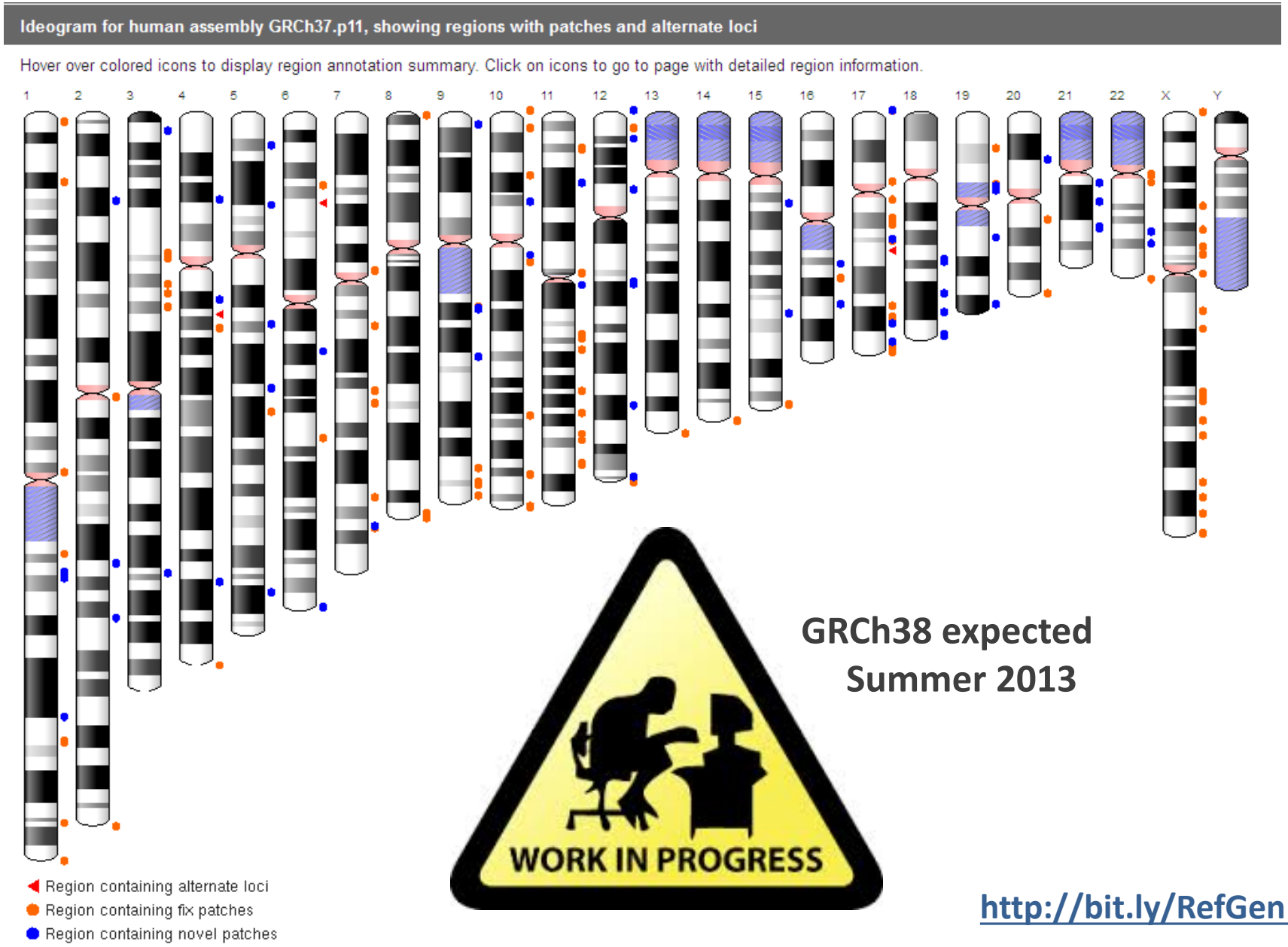
ROSWELL PARK CANCER INSTITUTE

For more information please contact the
Clinical Genetics Service
845-5720 (9:00 am - 3:00 pm)
March 24 - 26, 1997

Courtesy Pieter de Jong


94
51
21

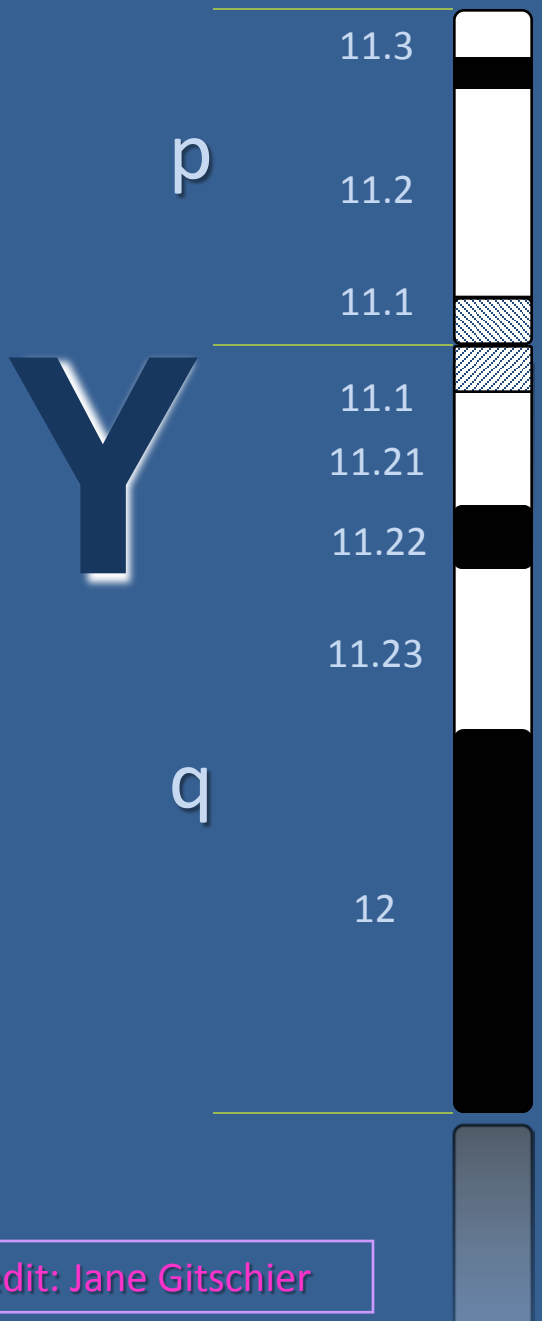
The Reference Genome…



GRCh38 expected Summer 2013

http://bit.ly/RefGen10


KEEP
CALM
AND
carry on the
sequence



Testis determining gene (TDF)*

Gadjetry (IPAD)

Channel flipping (RMT)

Kicking and Scoring (GOAAL!!)

Self-confidence (BLZ-2)

Ability to Remember and Tell Jokes (GOT-1)

Sports Page (BUD-E)

Addiction to death and disaster movies (SAW)

Air Guitar (WAH-WAH)

Ability to identify aircraft (DC10)

Spitting (P2E)

Sitting on the toilet reading (JOHN)

Inability to express affection over the phone (ME-2)

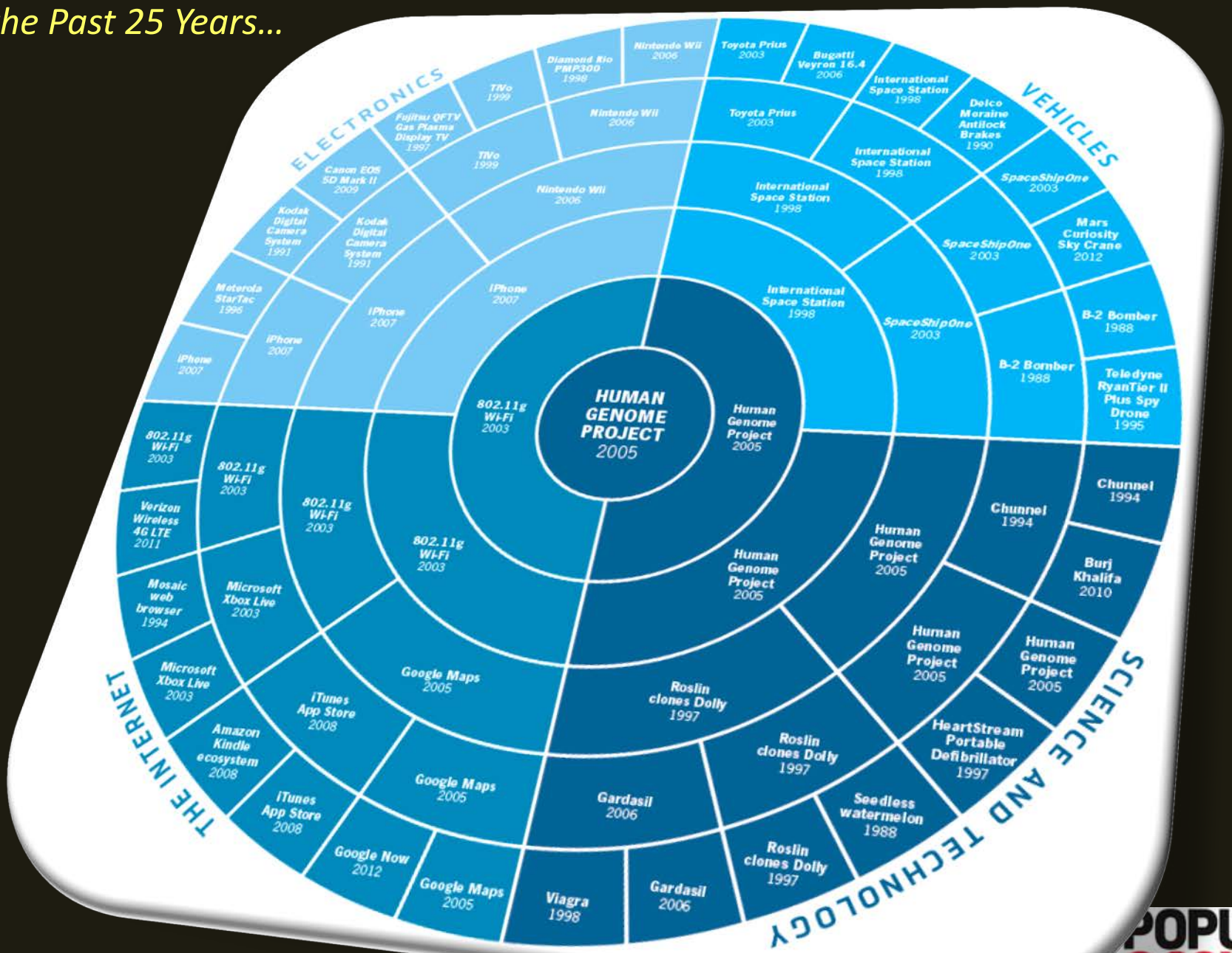
Selective hearing loss (HUH?)*

Total lack of recall for dates (OOPS)

Refusal to ask for directions (LOST)

Credit: Jane Gitschier

The Most Important Invention of the Past 25 Years…

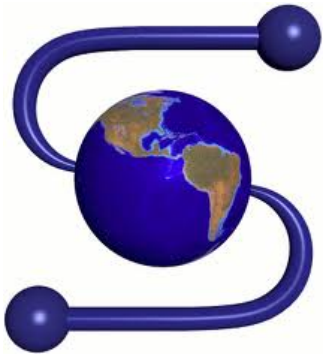


Katie Peek

POPULAR SCIENCE
THE FUTURE NOW


TiVo


TIME
Will There Ever Be Another You?
A SPECIAL REPORT ON CLONING




VGR 50

Economic Impact of the HGP >>

"The federal government invested **$3.8 billion** in the HGP [that] was foundational in generating the economic output of **$796 billion**… Every **$1** of federal HGP investment has contributed to the generation of **$141** in the economy."

-- Battelle report, 2011

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Wanted: The $1,000 Genome

By Mark D. Uehling

November 15, 2002 | It's 2008, and your only daughter is tu
pediatrician, who proudly presents her with a DVD. It's her d
down to the last A, C, T, and G. Maybe it will contain auspicious tidings.
not ...

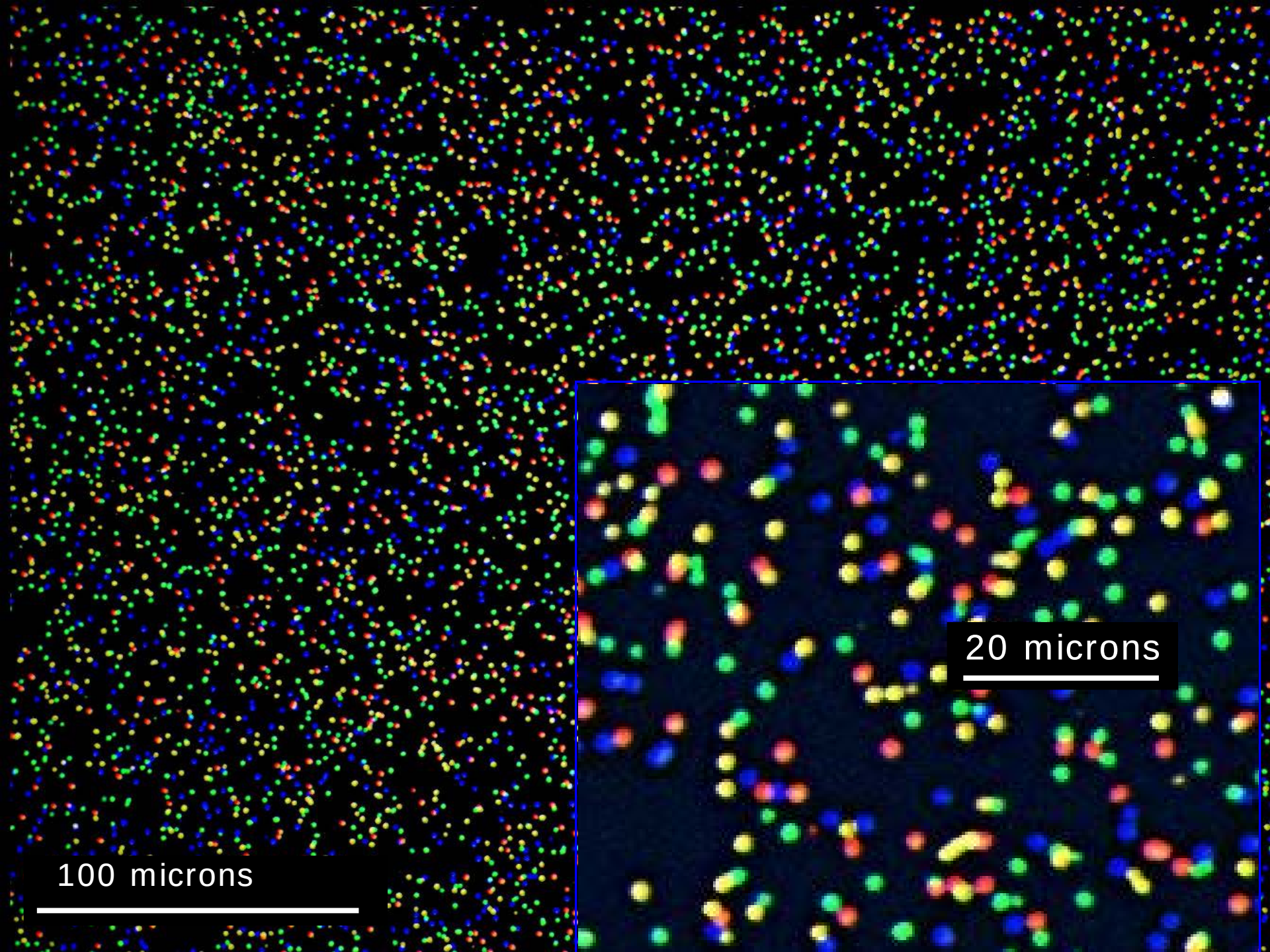
Either way, the news in Boston at The Institute for Genome Research's (TIGR) 14th International Genome Sequencing and Analysis Conference in early October is that the equipment to give everyone a personal genome for the price of a cheap laptop is closer than even conference organizers suspected.

On the opening evening of the meeting, TIGR founder J. Craig Venter hosted presentations from six scientists, each of which poses a potential threat to Venter's former backer and the meeting's sponsor, Applied Biosystems Inc. All but one presenter believed a $1,000 genome -- or more accurately, genotype -- is feasible.

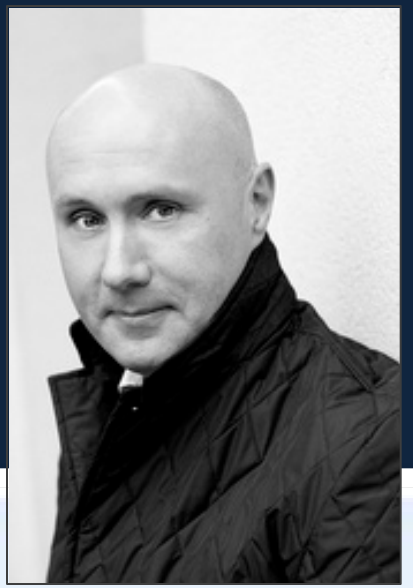
For most of the panelists, the issue is not if but when -- and whether any new concoction of chemistry, optics, fluidics, and software could be profitably combined into a single benchtop instrument that could seriously challenge current sequencing machines costing several hundreds of thousands of dollars.

Shankar Balasubramanian and David Klenerman
(University of Cambridge, UK)

Solexa


100 microns
20 microns

“WE’VE DONE IT !!!!”



From: Clive Brown <clive.Brown@solexa.com>
Date: Sun, 20 Feb 2005 16:34:46 +0100
To: Nick McCooke <Nick.McCooke@solexa.com>, Tony Smith <Tony.Smith@solexa.com>
Swerdlow <Harold.Swerdlow@solexa.com>, John Milton <JM.Milton@solexa.com>, Geo
<Kevin.Hall@solexa.com>, Colin Barnes <Colin.Barnes@solexa.com>, Lisa Davies <
<Vincent.Smith@solexa.com>, Klaus Maisinger <Klaus.Maisinger@solexa.com>
Conversation: WE'VE DONE IT !!!!
Subject: WE'VE DONE IT !!!!

Tony Cox, Peta and I now agree - having looked at all of the PhiX174 data.

We have re-sequenced our first genome !!!!!!!

454's Sequencing by Synthesis

nature Vol 437|15 September 2005|doi:10.1038/nature03959

ARTICLES

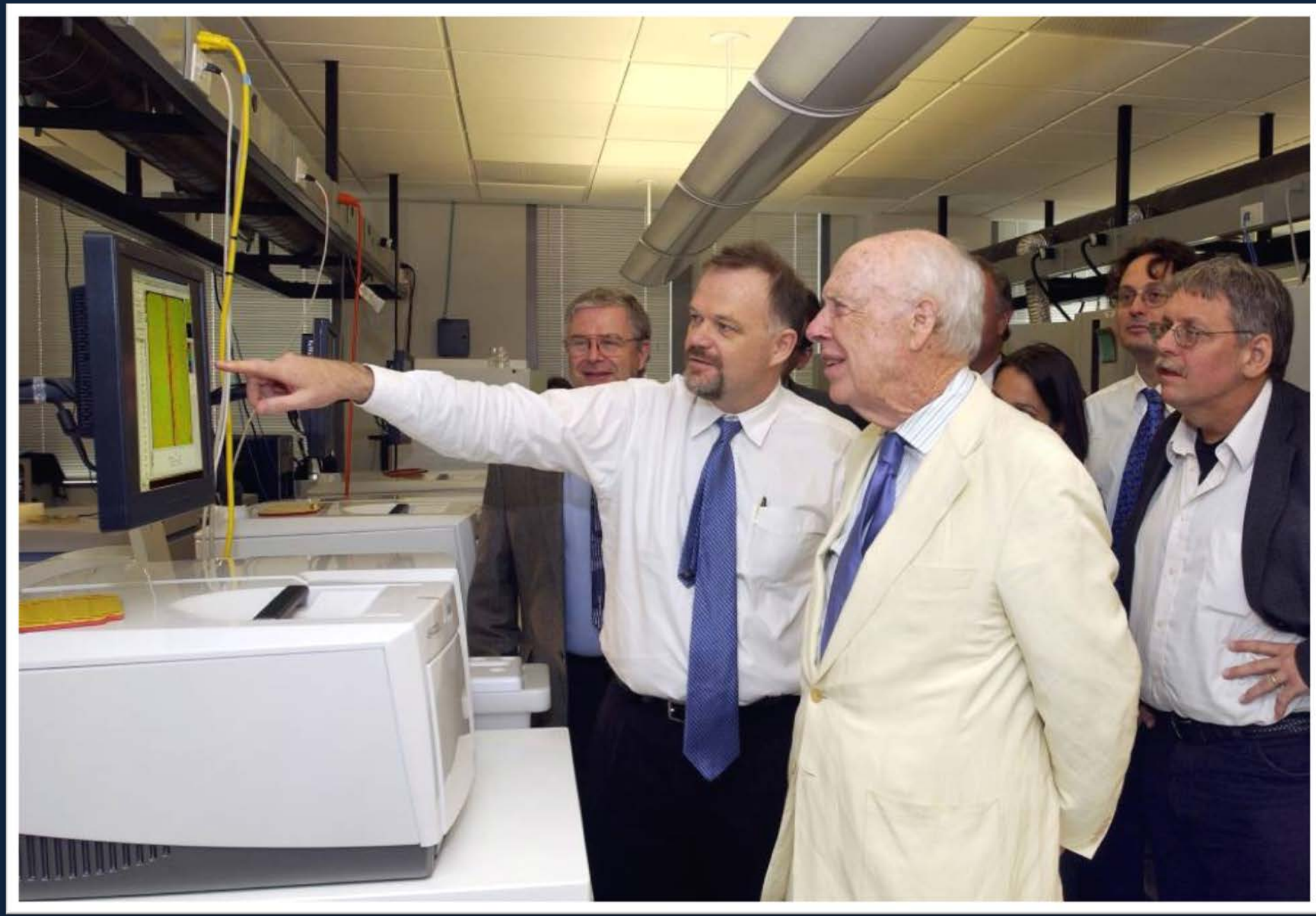
Genome sequencing in microfabricated high-density picolitre reactors

Marcel Margulies[1]*, Michael Egholm[1]*, William E. Altman[1], Said Attiya[1], Joel S. Bader[1], Lisa A. Bemben[1], Jan Berka[1], Michael S. Braverman[1], Yi-Ju Chen[1], Zhoutao Chen[1], Scott B. Dewell[1], Lei Du[1], Joseph M. Fierro[1], Xavier V. Gomes[1], Brian C. Godwin[1], Wen He[1], Scott Helgesen[1], Chun He Ho[1], Gerard P. Irzyk[1], Szilveszter C. Jando[1], Maria L. I. Alenquer[1], Thomas P. Jarvie[1], Kshama B. Jirage[1], Jong-Bum Kim[1], James R. Knight[1], Janna R. Lanza[1], John H. Leamon[1], Steven M. Lefkowitz[1], Ming Lei[1], Jing Li[1], Kenton L. Lohman[1], Hong Lu[1], Vinod B. Makhijani[1], Keith E. McDade[1], Michael P. McKenna[1], Eugene W. Myers[2], Elizabeth Nickerson[1], John R. Nobile[1], Ramona Plant[1], Bernard P. Puc[1], Michael T. Ronan[1], George T. Roth[1], Gary J. Sarkis[1], Jan Fredrik Simons[1], John W. Simpson[1], Maithreyan Srinivasan[1], Karrie R. Tartaro[1], Alexander Tomasz[3], Kari A. Vogt[1], Greg A. Volkmer[1], Shally H. Wang[1], Yong Wang[1], Michael P. Weiner[4], Pengguang Yu[1], Richard F. Begley[1] & Jonathan M. Rothberg[1]

"We won the race. Everyone may not be happy with that, but we are."

-- Jonathan Rothberg (August 2005)

Houston | 31 May 2007



31 May 2007

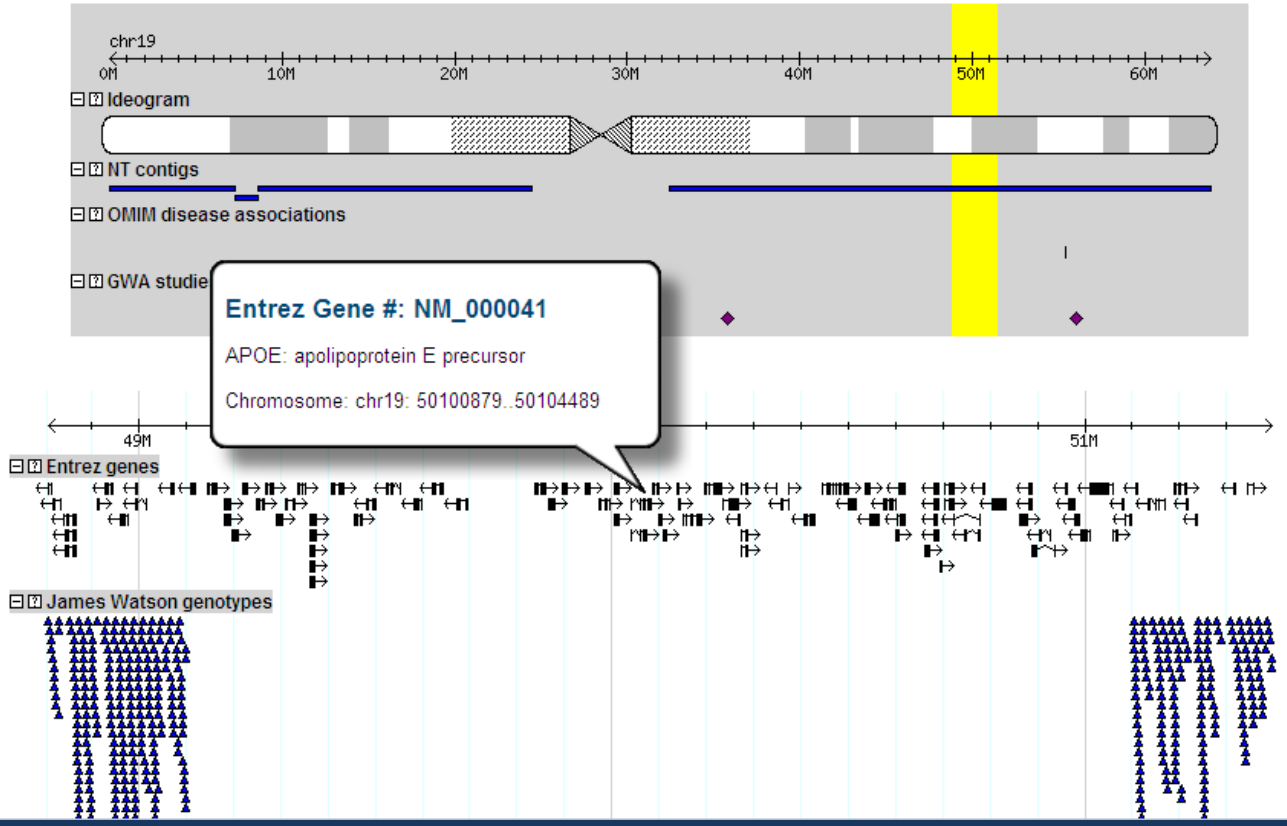
***APOE*: Mind The Gap**

James Watson's Personal Genome Sequence

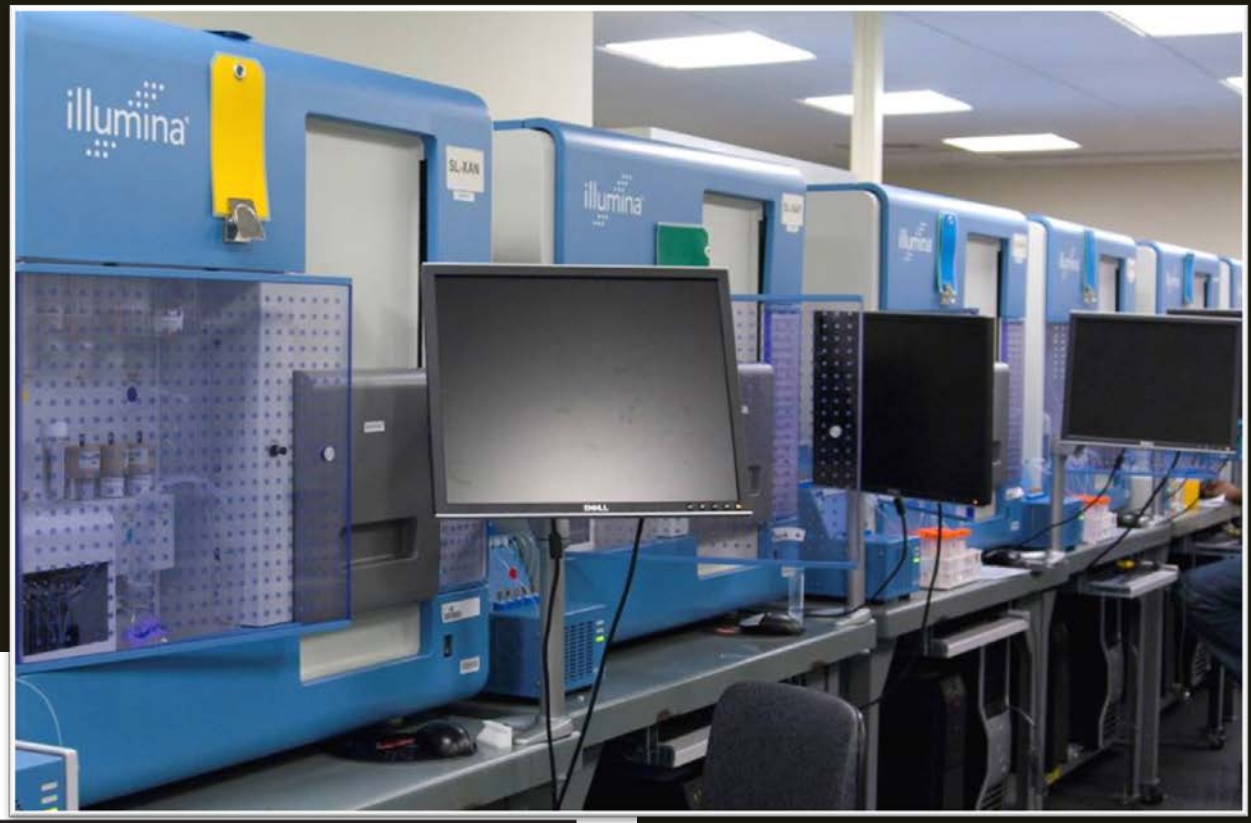
README: How do I use the James Watson Genome Browser?
Downloads: Download bulk JW polymorphisms. For the complete data set, please go to the NCBI Trace Archive and search for *CENTER_NAME = 'CSHL' and CENTER_PROJECT = 'Project Jim'*.

Showing 2.586 Mbp from chr19, positions 48,809,514 to 51,395,851

⊞ Instructions
[Hide banner] [Bookmark this] [Link to Image] [High-res Image] [Help] [Reset]
⊞ Search
⊟ Overview



⊞ Region
⊟ Details



ARTICLES

The diploid genome sequence of an Asian individual

Jun Wang[1,2,3,4]*, Wei Wang[1], Junqing Zhang[1], Jun Li[1], Juan[1], Huiqing Liang[1], Zhenglin Du[1], Ines Hellmann[9], Michael Inou[1], Guoqing Li[1], Zhentao Yang[1], Dawei Li[1], Peixiang Ni[1], Jue Ru[1], Jianguo Zhang[1], Jia Ye[1], Lin [1], Shuang Yang[1], Fang Chen[1,7], Guohua Yang[1,2], Zhuo Li[1], Xiaoli Feng, Karsten Kristiansen, Richard Durbin[8], Lars Bolund[1,11], Xiuqing Zhang[1,6], Songga

Accurate whole human genome sequencing using reversible terminator chemistry

A list of authors and their

DNA sequencing of a cytogenetically normal acute myeloid leukaemia genome

Timothy J. Ley[1,2,3,4]*, Elaine R. Mardis[2,3]*, Li Ding[2,3], Bob Fulton[3], Michael D. McLellan[3], Ken Chen[3], David Dooling[3], Brian H. Dunford-Shore[3], Sean McGrath[3], Matthew Hickenbotham[3], Lisa Cook[3], Rachel Abbott[3], David E. Larson[3],

Nature November 2008

Kriek & Watson

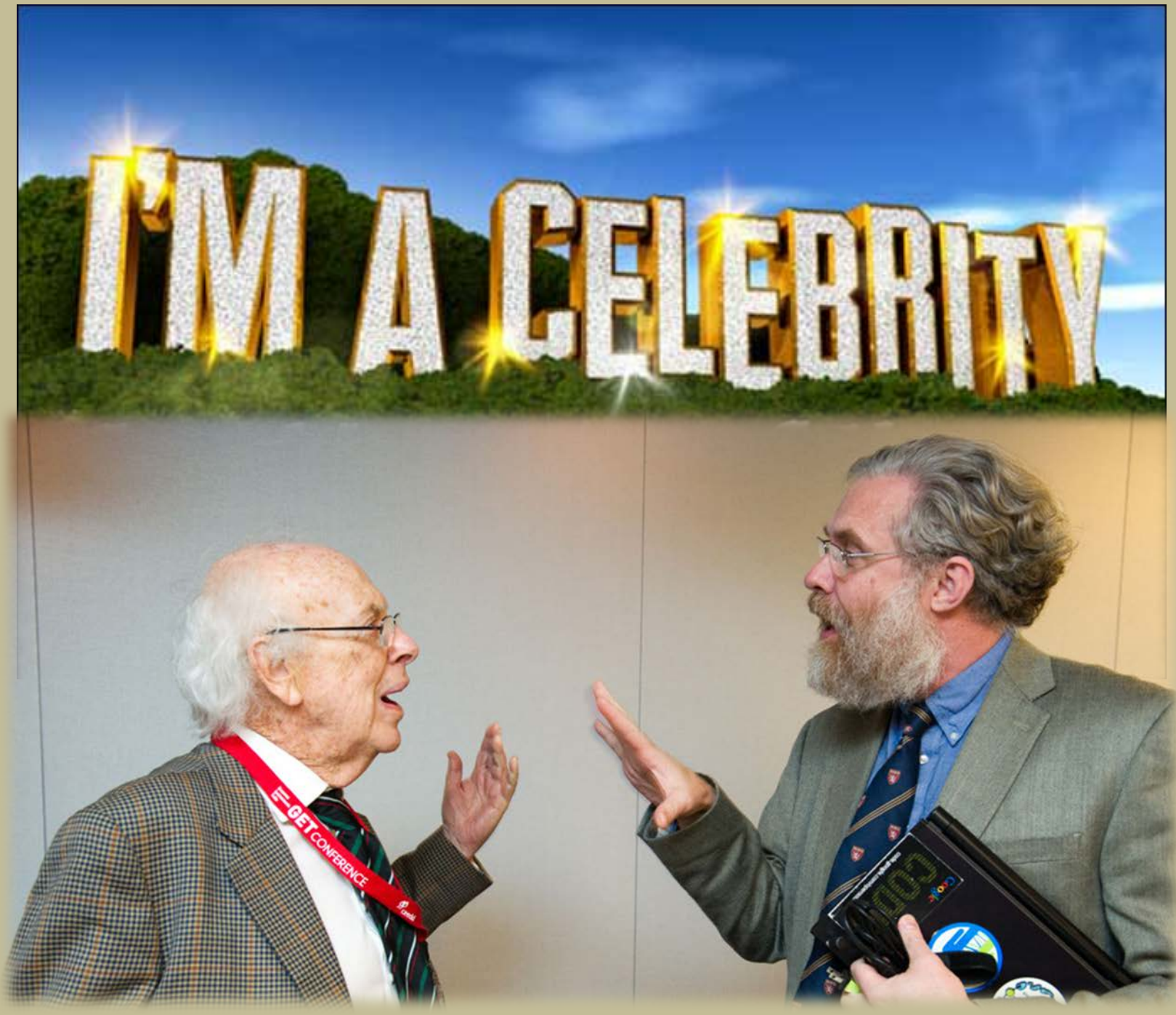
“It's really amazing to be there with Watson and Venter. I am just some girl from the Netherlands!”

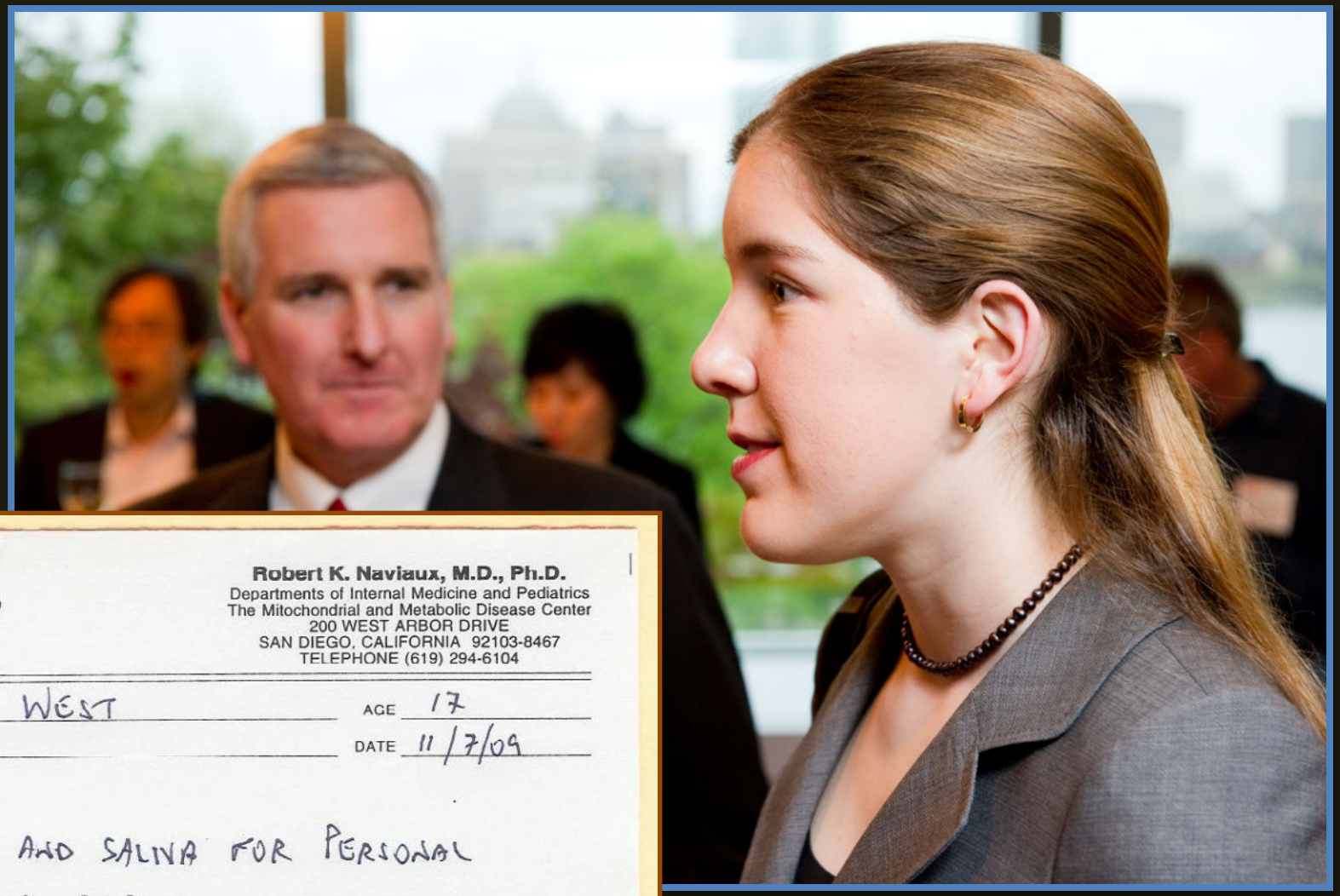
-- **Marjolein Kriek**
University of Leiden
May 2008

"Marjolein Kriek??!"

"Why not sequence the DNA of Scarlett Johansson?!!"

ICHG Montreal; November 2011


I'M A CELEBRITY
GET CONFERENCE



UCSD Medical Group

Robert K. Naviaux, M.D., Ph.D.
Departments of Internal Medicine and Pediatrics
The Mitochondrial and Metabolic Disease Center
200 WEST ARBOR DRIVE
SAN DIEGO, CALIFORNIA 92103-8467
TELEPHONE (619) 294-6104

NAME ANNE WEST AGE 17

ADDRESS _____ DATE 11/7/09

℞

BLOOD AND SALIVA FOR PERSONAL GENOME SEQUENCING BY ILLUMINA

☐ LABEL REFILL ____ TIMES
☐ PRESCRIBE AS WRITTEN

R. K. Naviaux M.D.
CA LIC G61267 • DEA BN1162863

Anne & John West

GET Conference, May 2010

TIME's Best Inventions

Invention of the Year

Next

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

ARTICLE TOOLS

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"1 Rule to Lose Your Gut"

I cut down 36 lbs of


LLANFAIRPWLLGWYNGYLLGOGERYCHWYRNDROBWLLLLANTYSILIOGOGOGOCH
Llan-vire-pooll-guin-gill-go-ger-u-queern-drob-ooll-llandus-ilio-gogo-goch
ARRIVA
Arriva Trains Wales / Trenau Arriva Cymru
Way Out
Holyhe d

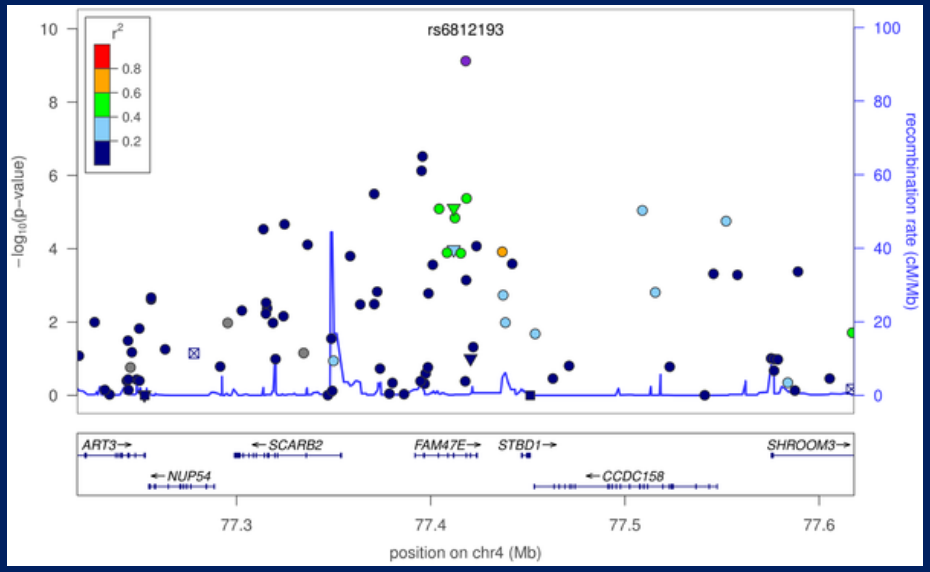
OPEN ACCESS Freely available online

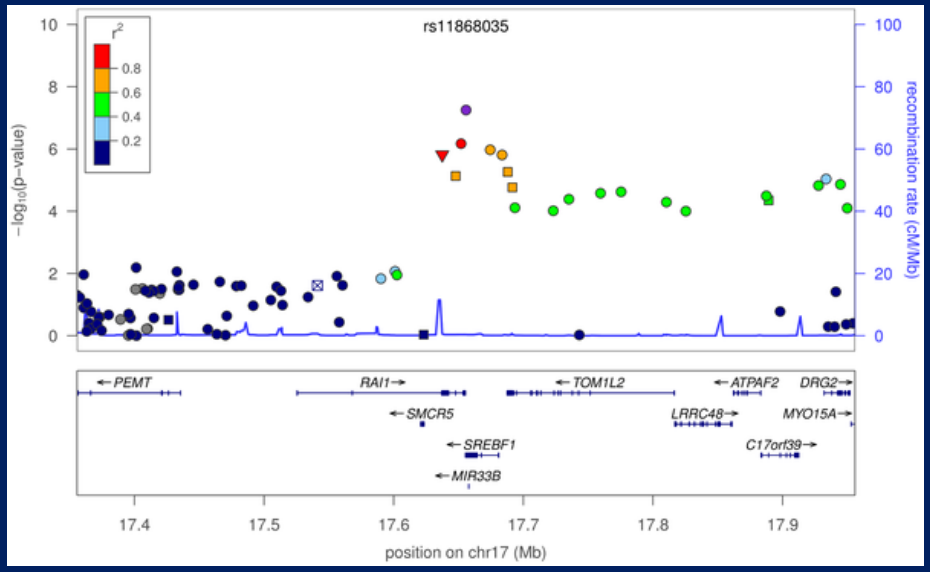
PLoS GENETICS

Web-Based Genome-Wide Association Study Identifies Two Novel Loci and a Substantial Genetic Component for Parkinson's Disease

Chuong B. Do[1]*, Joyce Y. Tung[1], Elizabeth Dorfman[1], Amy K. Kiefer[1], Emily M. Drabant[1], Uta Francke[1], Joanna L. Mountain[1], Samuel M. Goldman[2], Caroline M. Tanner[2], J. William Langston[2], Anne Wojcicki[1], Nicholas Eriksson[1]*

1 23andMe, Mountain View, California, United States of America, **2** Parkinson's Institute, Sunnyvale, California, United States of America





PLoS Genetics 2011

The “Worried Well”…

RITA

Don’t you worry about cholesterol, lung cancer, love handles?

PHIL

I don’t worry about anything anymore.

RITA

What makes you so special? Everybody worries about something.

PHIL

That’s exactly what makes me so special. I don’t even have to floss!

The REVEAL Study

Risk EValuation and Education for ALzheimer's disease

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Disclosure of *APOE* Genotype for Risk of Alzheimer's Disease

Robert C. Green, M.D., M.P.H., J. Scott Roberts, Ph.D., L. Adrienne Cupples, Ph.D., Norman R. Relkin, M.D., Ph.D., Peter J. Whitehouse, M.D., Ph.D., Tamsen Brown, M.S., Susan LaRusse Eckert, M.S., Melissa Butson, Sc.M., A. Dessa Sadovnick, Ph.D., Kimberly A. Quaid, Ph.D., Clara Chen, M.H.S., Robert Cook-Deegan, M.D., and Lindsay A. Farrer, Ph.D., for the REVEAL Study Group*

- 111 subjects with a parent with Alzheimer's disease tested for *APOE* gene
- 53 carried at least one copy of the E4 gene
- **NO significant differences between the groups in terms of anxiety, depression or test-related distress**

Scripps Genomic Health Initiative (2013)

ORIGINAL ARTICLE

Impact of direct-to-consumer genomic testing at long term follow-up

Cinnamon S Bloss,[1] Nathan E Wineinger,[1] Burcu F Darst,[1] Nicholas J Schork,[1,2] Eric J Topol[1,2,3]

ABSTRACT

Background There are few empirical data to inform the debate surrounding the use and regulation of direct-to-consumer (DTC) genome-wide disease risk tests. This study aimed to determine the long term psychological, behavioural, and clinical impacts of genomic risk testing for common disease.

Methods The Scripps Genomic Health Initiative is a prospective longitudinal cohort study of adults who purchased the Navigenics Health Compass, a commercially available genomic test. Web based assessments were administered at baseline, short (3 months), and long term (1 year) follow-up.

Results 2240 participants completed either or both follow-ups and a subset of ´325 completed long term follow-up. There were no significant differences from baseline in anxiety (p=0.50), fat intake (p=0.34), or exercise (p=0.39) at long term follow-up, and 96.8% of the sample had no test related distress. Longitudinal linear mixed model analyses were consistent with results of cross-sectional analyses. Screening test completion was associated with sharing genomic test results with a physician (36.0% shared; p<0.00´) and perceived utility of the test (6´.5% high perceived utility; p=0.002), but was not associated with the genomic risk estimate values themselves.

- 2,200 subjects took Navigenics genotype test
- No long-term psychological risks or differences in anxiety
- 1/3 recipients shared results with personal physician
- Most participants “perceived the test to be of high personal utility.”
- AD risk tends to be “most impactful from a psychological standpoint” but still negligible from a clinical standpoint
- Several positive anecdotes, including potentially life-saving colonoscopy scheduled after testing

Cinnamon Bloss *et al. J. Med Genet*. April 4, 2013

www.jsonline.com/dna

One In A Billion: A boy's life, a medical mystery

Nicholas Volker, born October 2004

- Severe (autoimmune?) inflammatory intestinal disease
- Colostomy, >100 surgeries, >$1M
- Exome seq ~$75,000 (454)
- 16,000 DNA variants
- Cys203Tyr mutation in ***XIAP***
- Dx of hemophagocytic lymphohistiocytosis >> bone marrow transplant

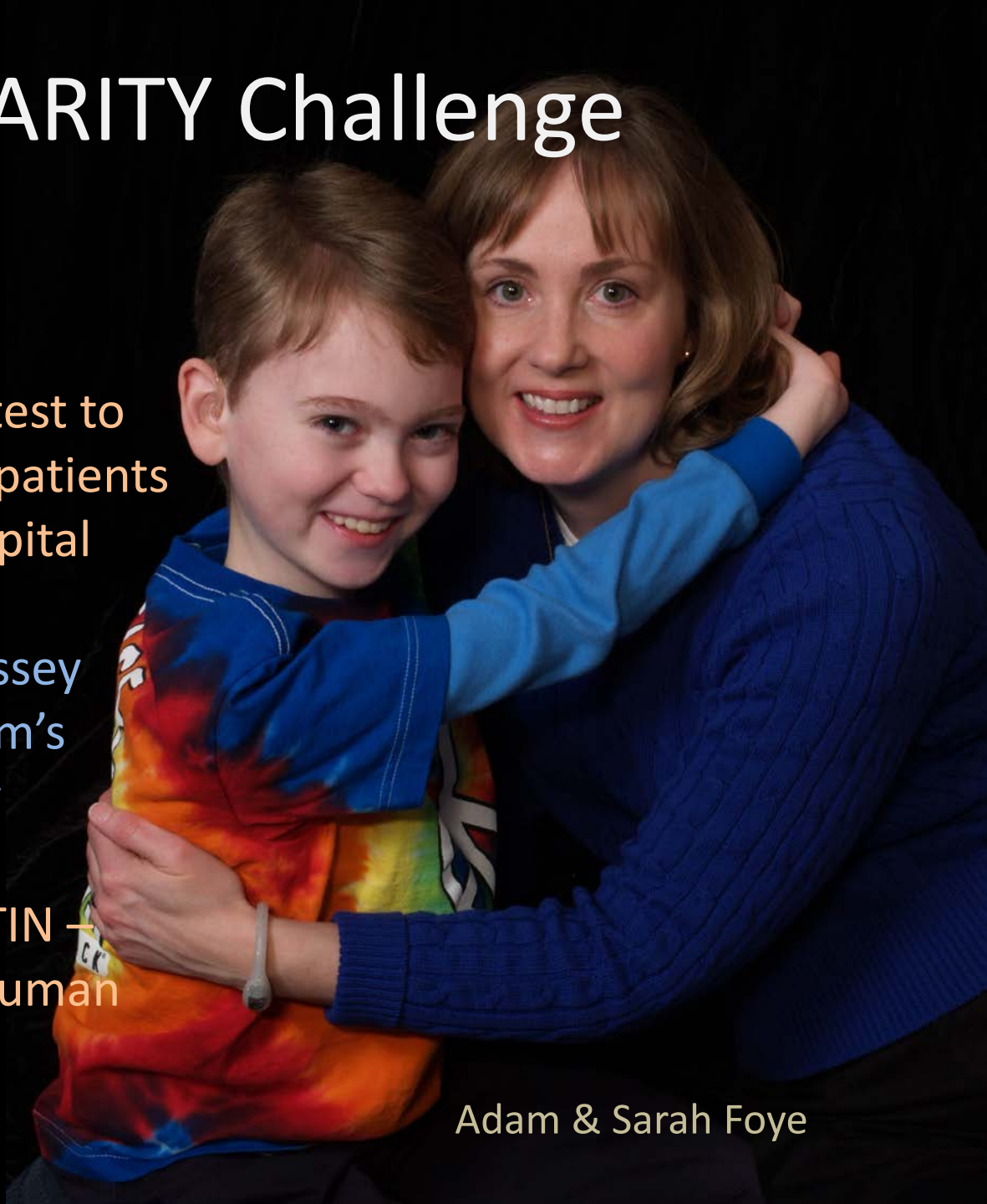
E. Worthey *et al. Genetics in Medicine* (2010)

www.jsonline.com/dna

JS Online 2012

The CLARITY Challenge

- 30 teams entered contest to interpret genomes of 3 patients at Boston Children's Hospital
- End of 11-year Dx odyssey to uncover cause of Adam's centronuclear myopathy
- Mutations found in TITIN – the largest gene in the human genome



Adam & Sarah Foye

Ending a Dx Odyssey: Batten Disease

(Late Infantile Neuronal Ceroid Lipofuscinosis, *TPP1*)

John & Lisa Allingham, with Jacob and Dylan

http://bit.ly/15NJibw

Shelby Valint

- TGen (Trent, Craig et al.)
- Dopa Decarboxylase (*DDC*)
- Dopa treatment

Youtube video:
http://bit.ly/ShelbyV

2013: The "Here's My Number" Genome

"… The 15-minute genome…"

– PacBio CEO **Hugh Martin**

"… The $30 genome…"

– **Dave Weitz** (Harvard/GnuBio)

"… The $1,000 genome…"

– **Jonathan Rothberg** (Ion Torrent CEO)

– Oxford Nanopore CTO **Clive Brown**

– Complete Genomics CEO **Clifford Reid**

– **Daniel Franklin** *The Economist*

The $2,500 Genome?

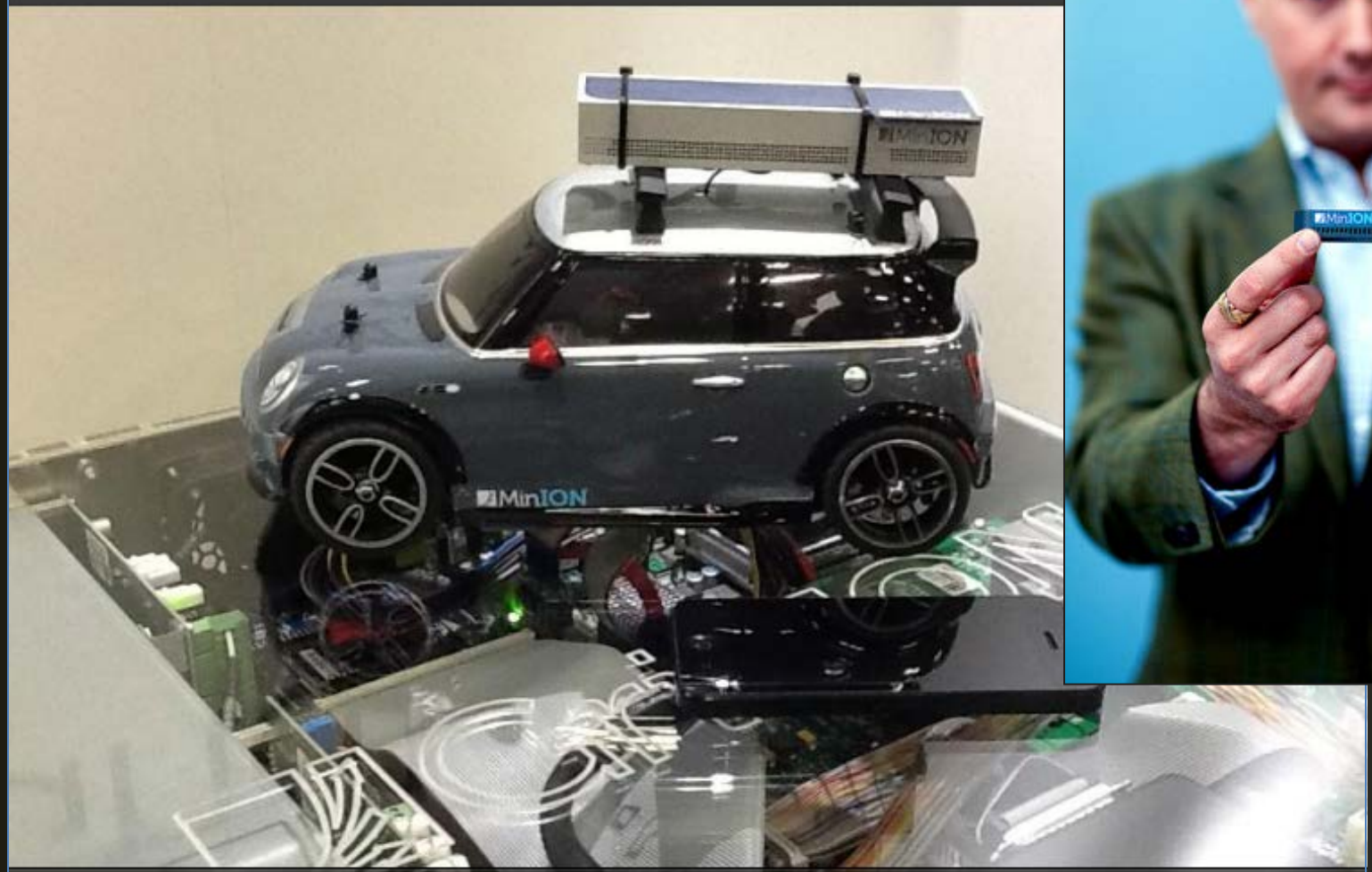
5 genomes/run = $25,000

$5,000 genome*

10,000 human genomes shipped to date…

*list price
(HiSeq 2500/BATCH mode)

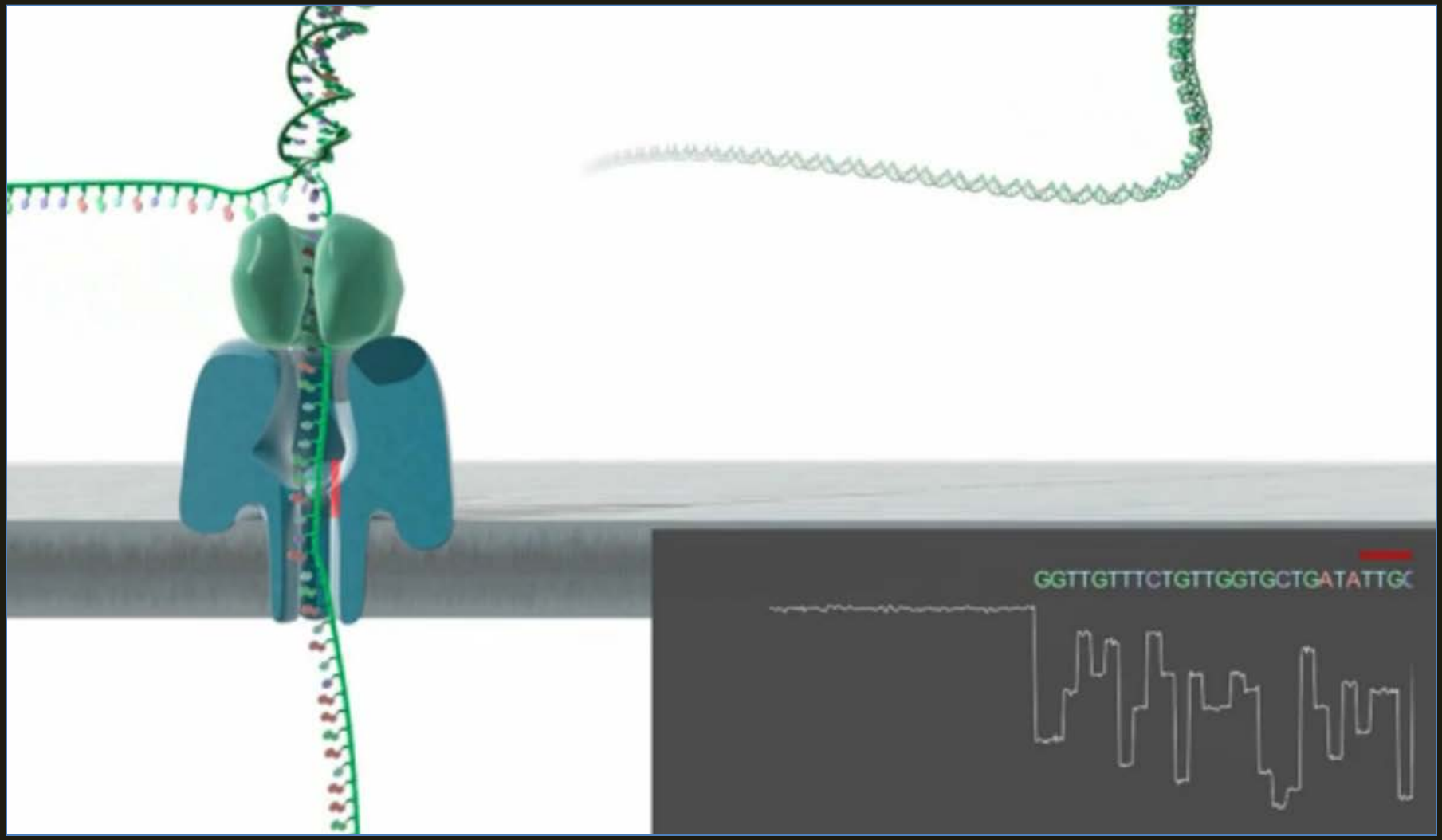
Photo



Bio-IT World @bioitworld 9 Nov

Exclusive: Oxford @nanopore debuts its version of the @iontorrent bus! #ashg2012 pic.twitter.com/KvaYtm2U

Reply Delete Favorite Flag media



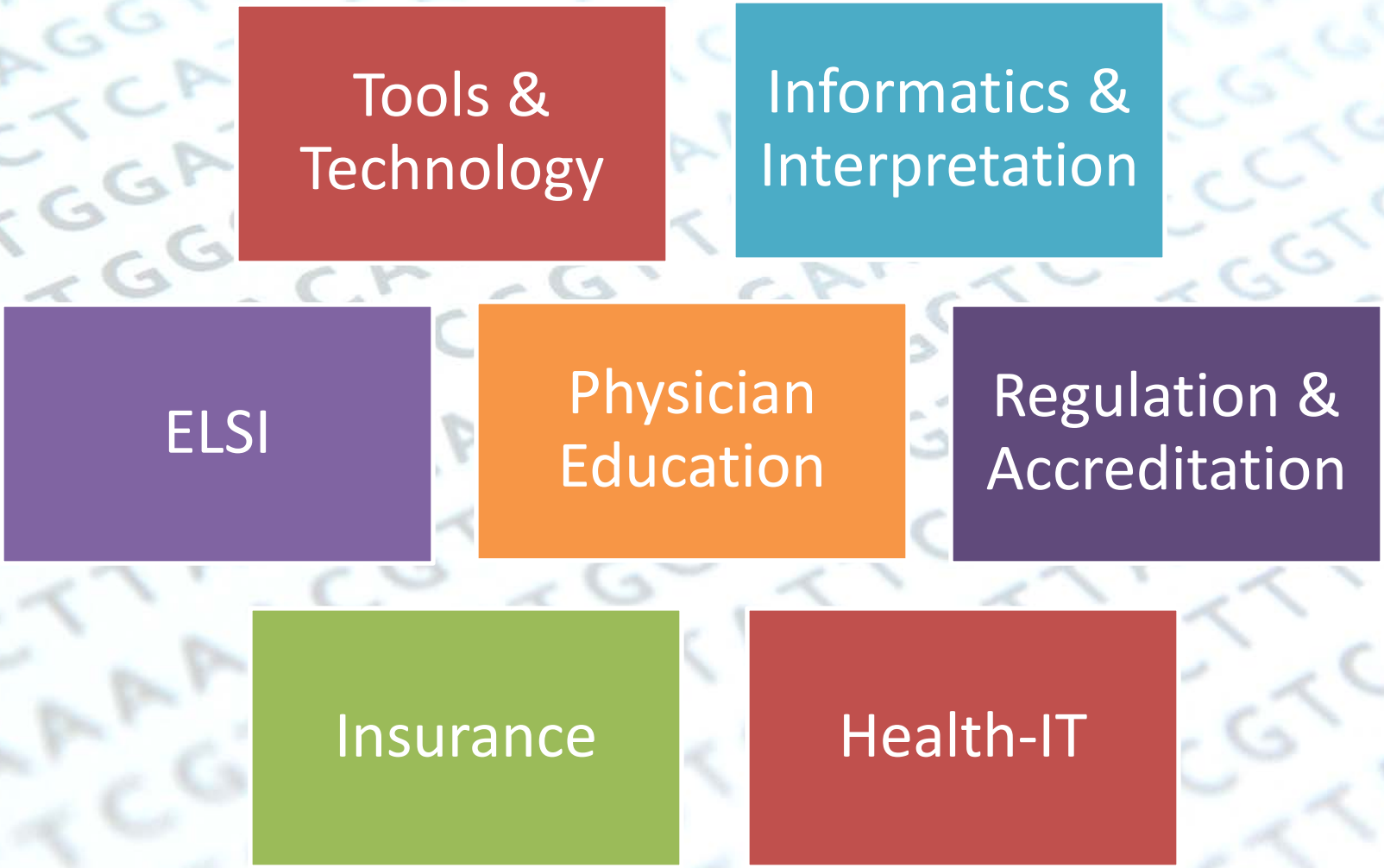
Oxford NANOPORE Technologies

The $1,000,000 Interpretation?

"We are close to having a **$1,000 genome** sequence, but this may be accompanied by a **$1 million interpretation**."

-- Bruce Korf M.D.
Past President, ACMG

Clinical Genome Sequencing Ecosystem



Mark Boguski

Enlis Genomics

iPad 9:41 AM

(PRODUCT LOGO)

Patient: **Jane Smith**
DOB: 6/1/1960 Gender: Female
SSN: 123-45-6789
FMI Case #: 1234567
Medical Record #: 56789
Requisition #: 98765

Client:
New England Oncologic Associates
FMI Client #: 1234567
Treating Physician:
Dr. Davy Jones
Submitting Pathologist:
Dr. John Smith
Additional Recipient:
Dr. David Gilman

FOUNDATION MEDICINE

Patient Information

Primary Tumor Site: Non Small Cell Lung Cancer
Specimen Site: Non Small Cell Lung Cancer
Specimen Collected: 1/1/2011
Collection Method: Surgical Resection
Specimen Type(s): Slides, Block
Specimen Received: 6/1/2011
Date Reported 6/15/2011

Pathology & Lab Results




PATHOLOGY DIAGNOSIS:
Although on primary examination at frozen section this tumor show solid core of cells with distinct intercellular bridges and individual keratinization which favoured squamous cell…

CBC
Normal for all 20 values, including white blood cell count

Vitamin D
Total vitamin D: 22 ng/mL

FMI Molecular Test Results

GENE	ALTERATION(S) IDENTIFIED
EGFR	L858R
KRAS	No alterations found
BRAF	No alterations found
PIK3CA	E542K
TP53	G157T

Therapeutic Agents

ON NCCN COMPENDIUM™
Carboplatin, Cisplatin, Erlotinib

OFF NCCN COMPENDIUM™
Gefitinib

Clinical Trials

Phase 2	
Molecular Profiling and Targeted Therapy for Advanced…	TN, NY
A Study of Tarceva (Erlotinib) as First Line Therapy in Patie…	TN
A Phase II Multi Center Study Investigating Translational Science in Chemothe…	TN
Phase 1	
A Phase IA, Multicenter, Open-Label Dose Escalation Stu…	TN, TX

Client Services

Foundation Medicine Customer Service

Ask a Foundation Medicine physician

Consult an expert

Courtesy of

FOUNDATION MEDICINE

“Whole-genome sequencing will become the standard of care. SEQUENCE ONCE. READ OFTEN.”

-- **DAVID VALLE M.D.** (Johns Hopkins)
CSHL 10.01.11

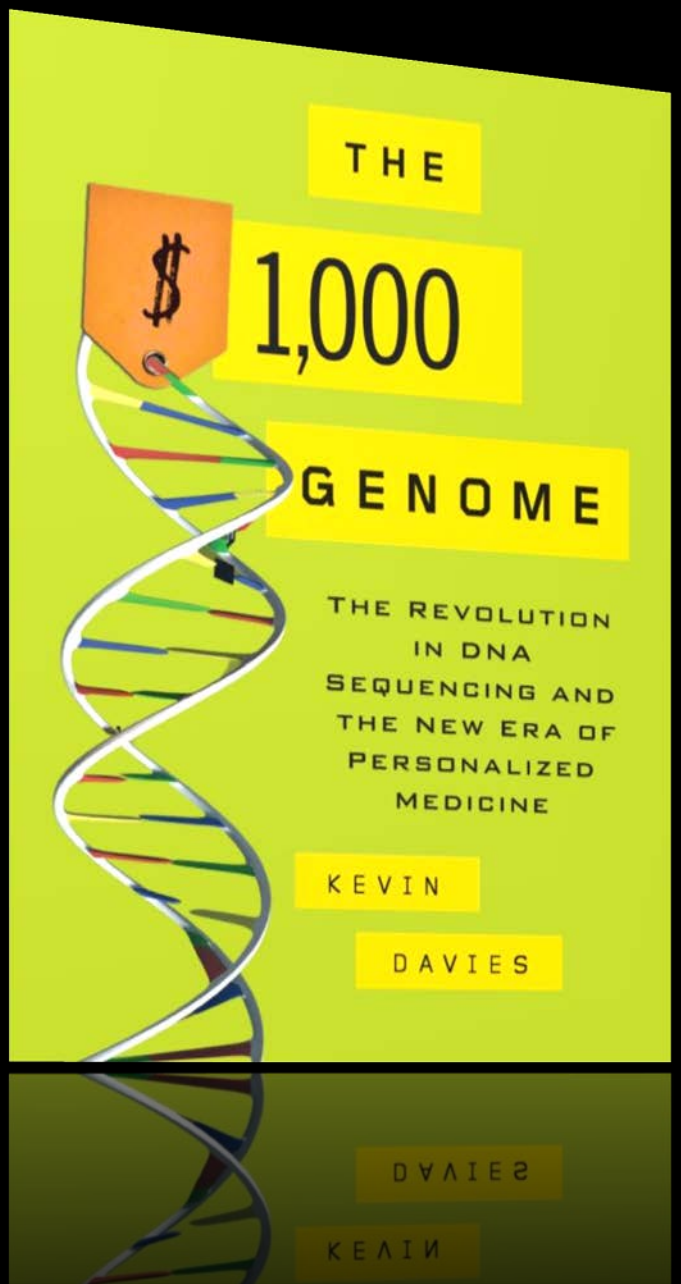
“Living By the Code”
Annie Newman

The INDEPENDENT

Fresh twist to the DNA story signals major cancer breakthrough

Crucial discovery at Cambridge, 60 years after Crick and Watson's double helix


JAMES D WATSON
The Double Helix
MOLECULAR BIOLOGY
OF THE GENE



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@KevinADavies

http://amzn.to/KD1kgen