

Research Targeted by “Race” in Translational Genomics

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U. of California, San Francisco

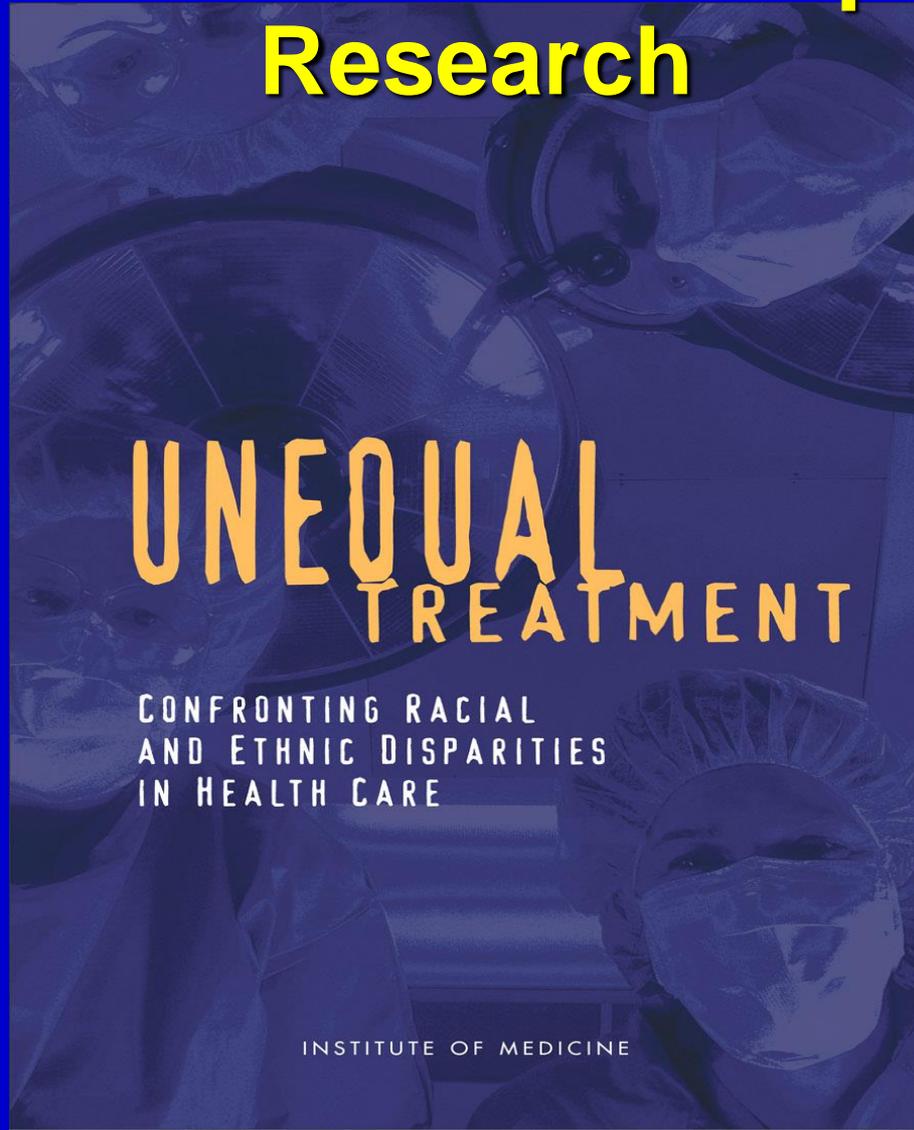
U. of No. Texas Ctr. for Health Disparities

May 30, 2014

Main Points

- **Categories (of difference) are hard!**
- **How we use them in genomics matters!**
- **A short story to illustrate**

What's at Stake? Genomics & Health Disparities Research



UNEQUAL TREATMENT

CONFRONTING RACIAL
AND ETHNIC DISPARITIES
IN HEALTH CARE

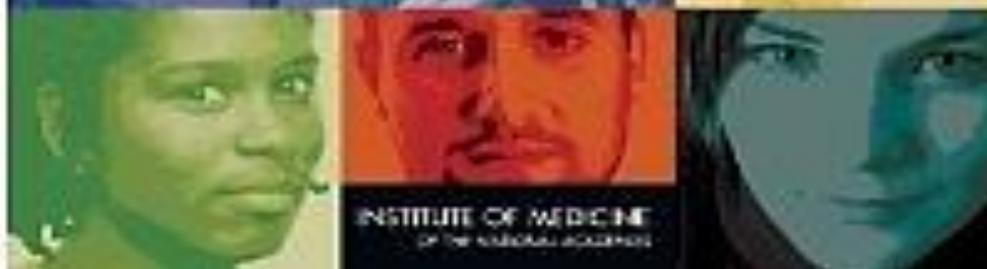
INSTITUTE OF MEDICINE



HOW FAR HAVE WE COME IN REDUCING HEALTH DISPARITIES?

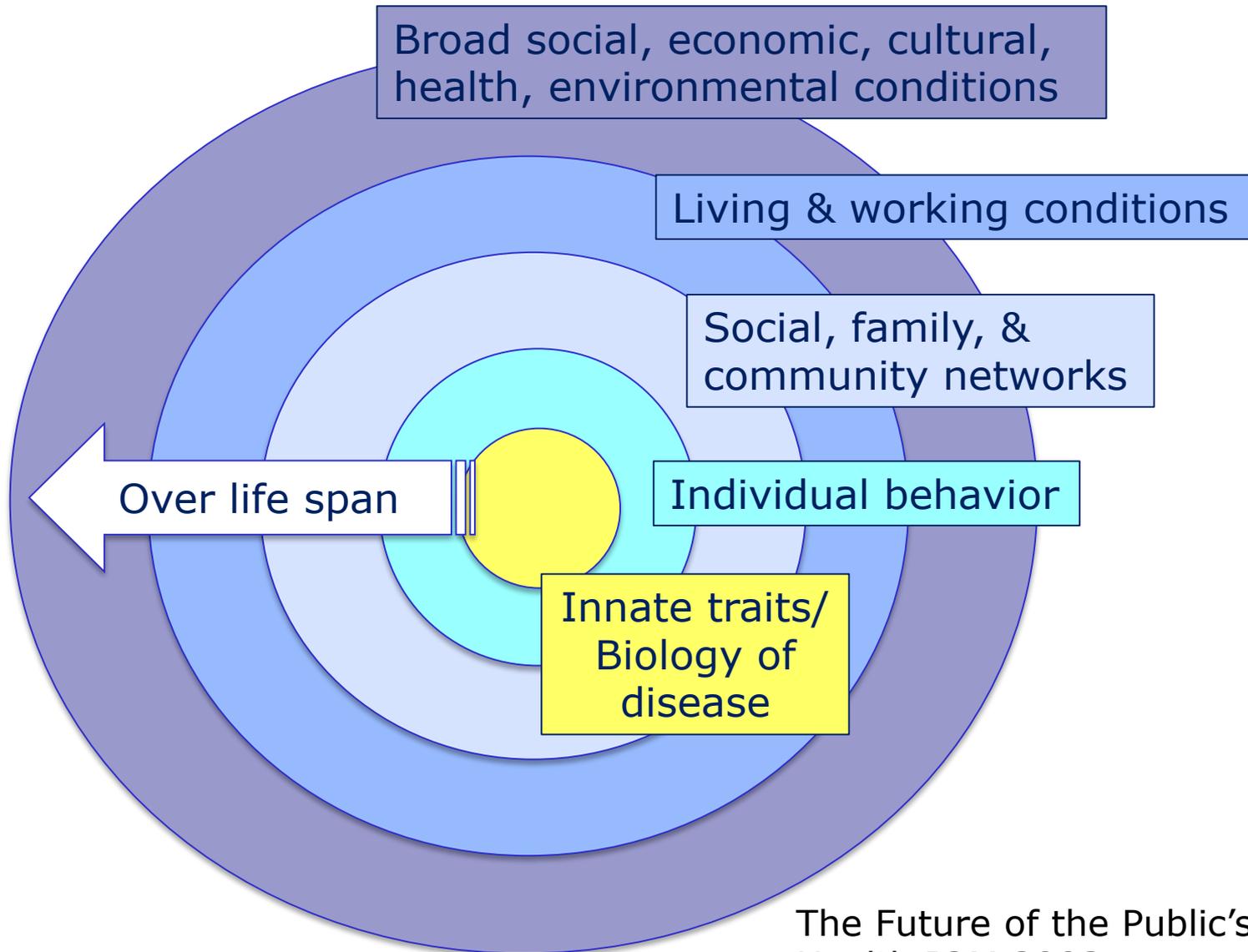
Progress Since 2000

Workshop Summary



INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES

IOM ecological model of health



Anthropology in the Clinic



- **Ethnographic approach to understanding the culture of contemporary biomedicine**

A close-up portrait of an elderly woman with short, wavy brown hair, looking directly at the camera with a neutral expression. She is wearing a white turtleneck sweater. The background is a light blue, slightly textured surface.

**CANCER. WHERE YOU'RE TREATED FIRST
CAN MAKE ALL THE DIFFERENCE.**

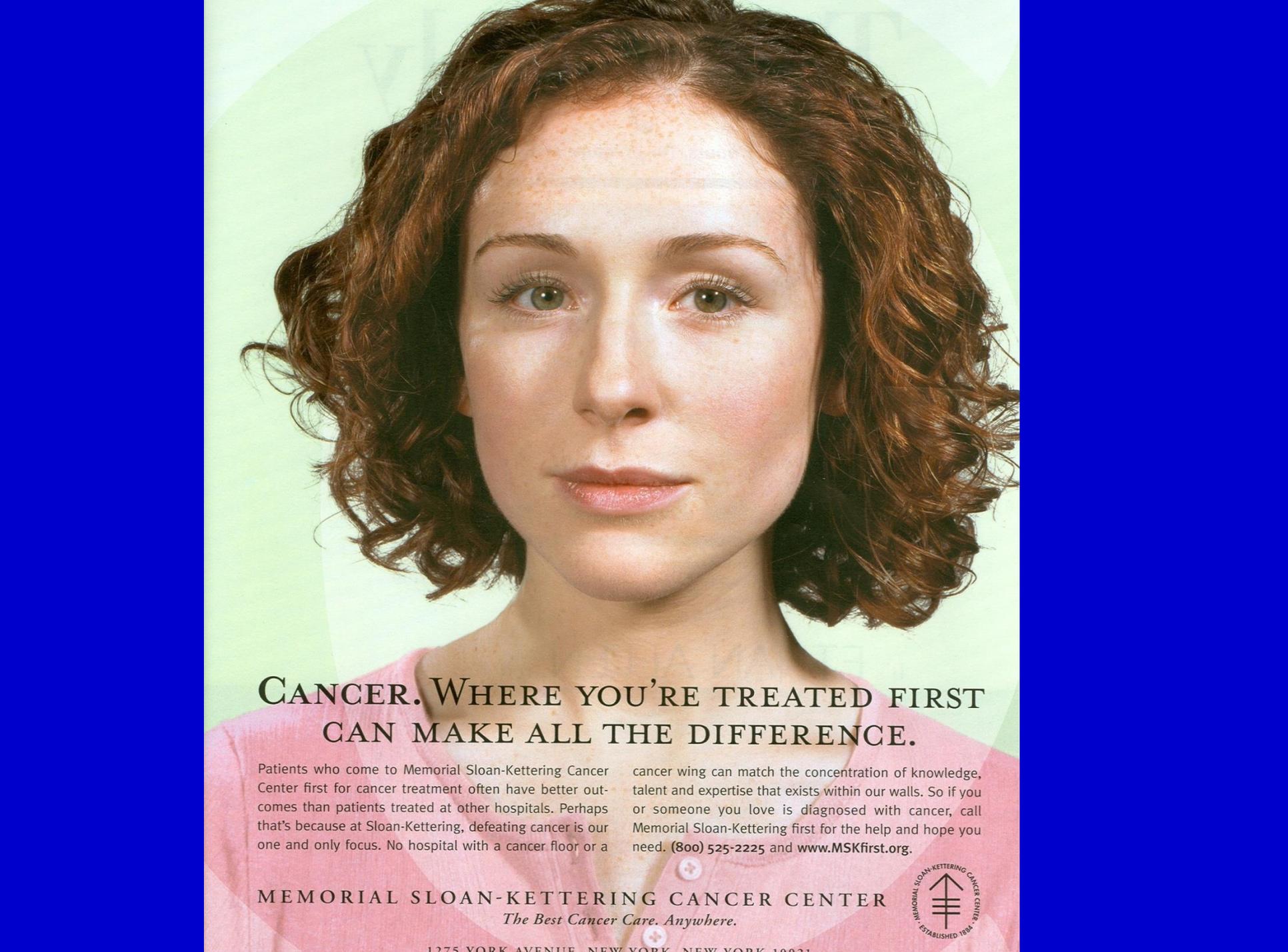
At Memorial Sloan-Kettering Cancer Center, our physicians have unsurpassed expertise in caring for patients with ovarian cancer. As national leaders in ovarian cancer care and research, we offer advanced surgical and medical options to maximize the chances for cure. Our surgeons lead the way in using minimally invasive surgery to shorten hospital stays and recovery times, and we have a team of medical oncologists who specialize in treating only gynecologic cancer. Remember, the doctors at Memorial Sloan-Kettering treat more cancer patients in a year than most doctors treat in a lifetime. So if the diagnosis is cancer, call us first for the help—and hope—you need. 1-800-525-2225 and www.MSKfirst.org.

MEMORIAL SLOAN-KETTERING CANCER CENTER

The Best Cancer Care. Anywhere.



1275 YORK AVENUE, NEW YORK, NEW YORK 10021
OUTPATIENT FACILITIES ALSO LOCATED IN NEW JERSEY, WESTCHESTER AND LONG ISLAND



**CANCER. WHERE YOU'RE TREATED FIRST
CAN MAKE ALL THE DIFFERENCE.**

Patients who come to Memorial Sloan-Kettering Cancer Center first for cancer treatment often have better outcomes than patients treated at other hospitals. Perhaps that's because at Sloan-Kettering, defeating cancer is our one and only focus. No hospital with a cancer floor or a

cancer wing can match the concentration of knowledge, talent and expertise that exists within our walls. So if you or someone you love is diagnosed with cancer, call Memorial Sloan-Kettering first for the help and hope you need. (800) 525-2225 and www.MSKfirst.org.

MEMORIAL SLOAN-KETTERING CANCER CENTER

The Best Cancer Care. Anywhere.

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**CANCER. WHERE YOU'RE TREATED FIRST
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cancer wing can match the concentration of knowledge, talent and expertise that exists within our walls. So if you or someone you love is diagnosed with cancer, call

A central moral dilemma:

- **To what extent are health disparities the result of unequal distribution of resources, and thus a consequence of varied social and economic background (or racism)?**
- **To what extent are variations in health outcomes the result of inherent characteristics of individuals?**

JAMA 2004

Genetic Research and Health Disparities

Pamela Sankar, PhD

Mildred K. Cho, PhD

Celeste M. Condit, PhD

Linda M. Hunt, PhD

Barbara Koenig, PhD

Patricia Marshall, PhD

Sandra Soo-Jin Lee, PhD

Paul Spicer, PhD

DISPARITIES IN HEALTH STATUS have increased in the United States in the last 50 years despite remarkable advances in our ability to prevent, diagnose, and treat disease.¹ The poor are the least likely to have benefited from progress in medi-

Alleviating health disparities in the United States is a goal with broad support. Medical research undertaken to achieve this goal typically adopts the well-established perspective that racial discrimination and poverty are the major contributors to unequal health status. However, the suggestion is increasingly made that genetic research also has a significant role to play in alleviating this problem, which likely overstates the importance of genetics as a factor in health disparities. Overemphasis on genetics as a major explanatory factor in health disparities could lead researchers to miss factors that contribute to disparities more substantially and may also reinforce racial stereotyping, which may contribute to disparities in the first place. Arguments that promote genetics research as a way to help alleviate health disparities are augmented by several factors, including research funding initiatives and the distinct demographic patterns of health disparities in the United States.

JAMA. 2004;291:2985-2989

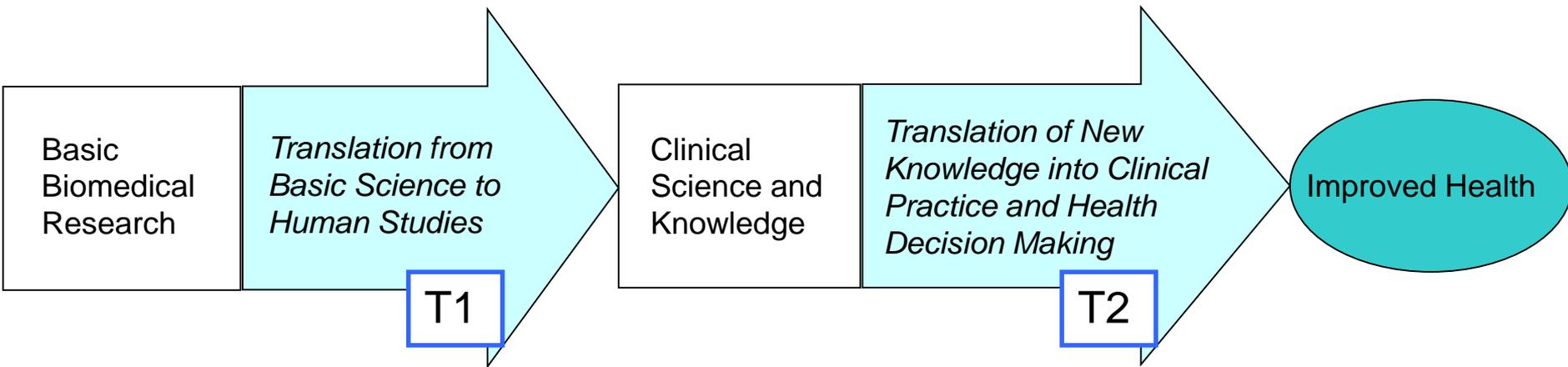
www.jama.com

Genomics: Currently THE Foundational Tool in Biomedicine

Impact of the Human Genome Project

- **Initial Message**
 - **Humans are 99.9% identical**
- **BUT, research focuses on minute differences**

Translational Research Continuum



Adapted from Sung, N.S. et al. JAMA 2003; 289: 1278-1287.

ELSI

Ethical, Legal, Social Implications

ELSI squeezing the pipeline?

Genomic
research



Slide Courtesy of W. Burke

- **What are the challenges to interdisciplinary dialogue?**
- **Why is this conversation so hard?**

Negotiating the “irritative phase”

- Independent research
- Multidisciplinary assessment

- **Irritative phase**

Debate & deliberation about assumptions, questions and methods, and their application to the problem



- Transdisciplinary research

Barrier: Diverse sources of power

Academic and social hierarchies

- “Hard” sciences > ethics/social sciences

Role-based

- Convening, decision-making, oversight authority
- Access to resources

Norm-based

- Hegemonic discourses – e.g., biomedical
- Default communication styles – e.g., confrontive vs. collegial

NEW TWISTS ON DNA • 100 YEARS AFTER THE WRIGHT BROTHERS

SCIENTIFIC AMERICAN

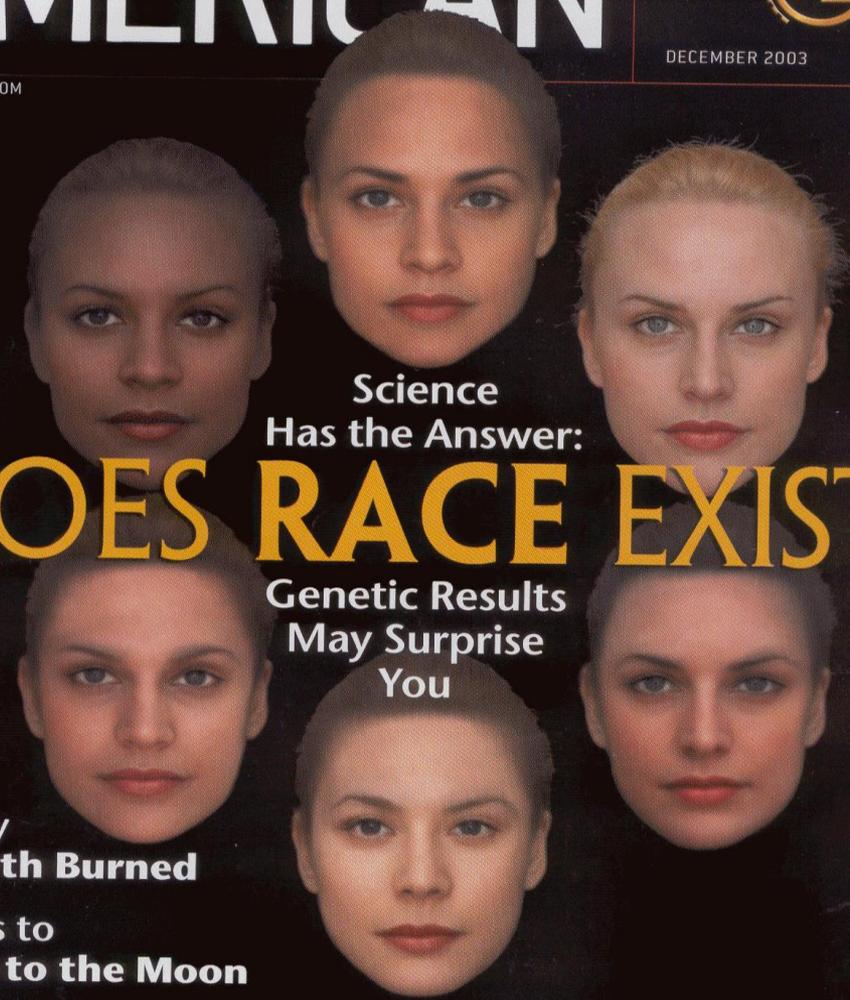
Tech Leaders
of 2003:
The
Scientific American



DECEMBER 2003

\$4.95

WWW.SCIAM.COM



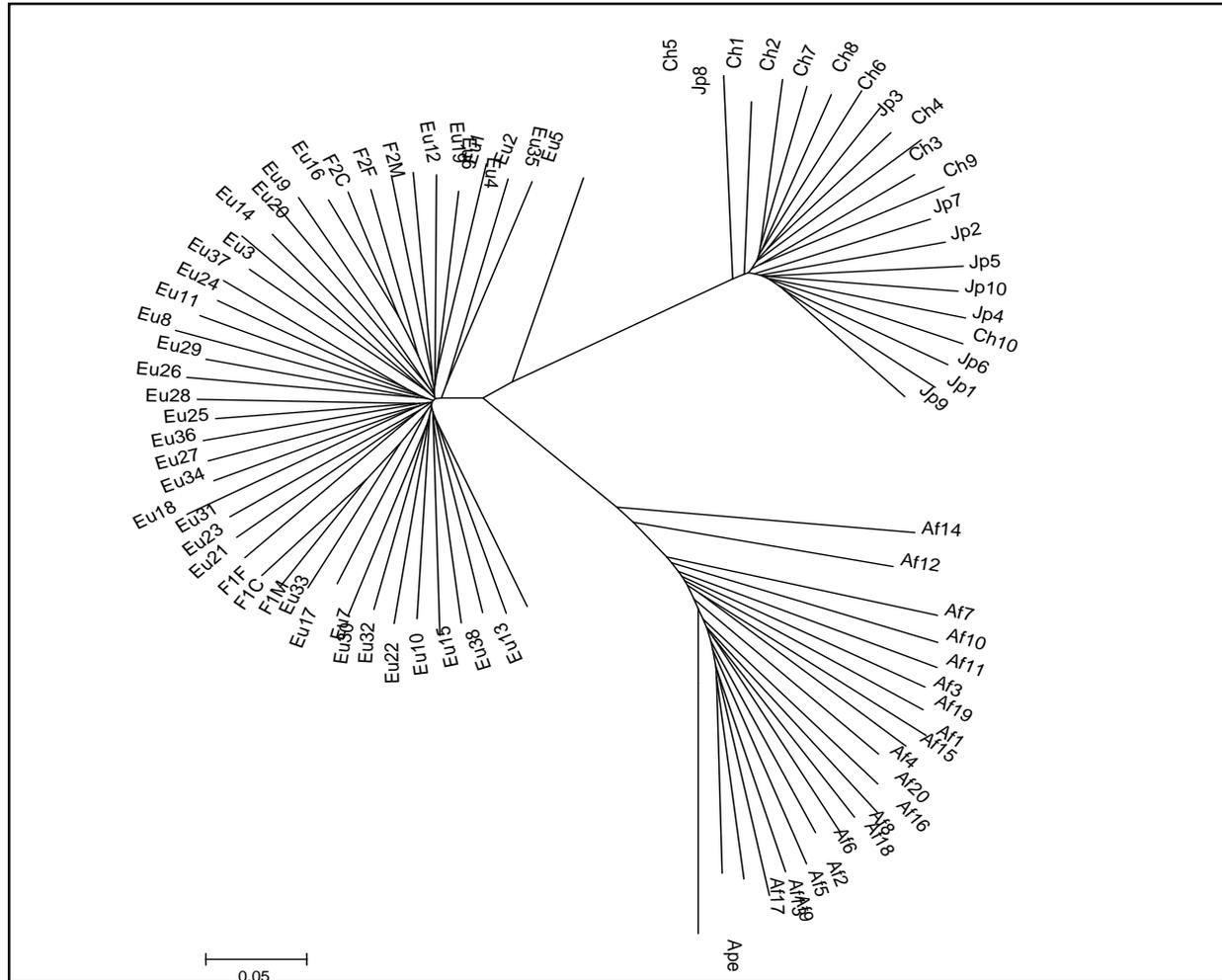
Science
Has the Answer:
DOES RACE EXIST?

Genetic Results
May Surprise
You

The Day
the Earth Burned

Reasons to
Return to the Moon

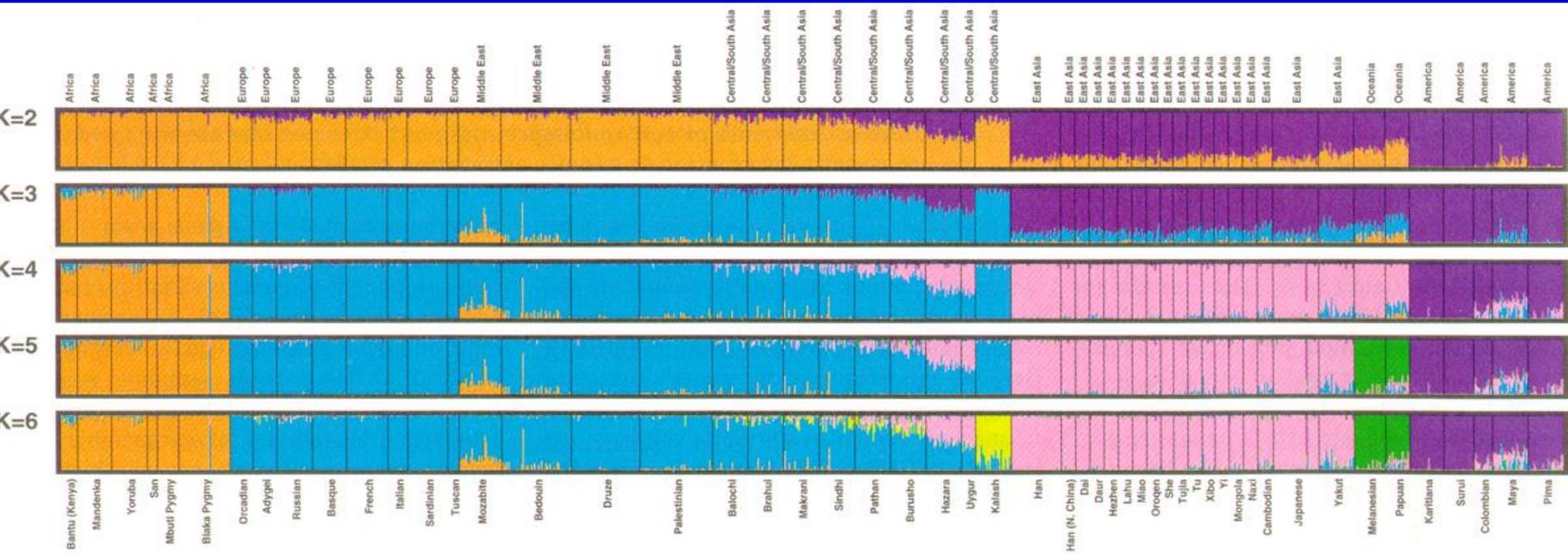
Genetic Variation of 78 individuals using 8,525 autosomal markers



Shriver, M. et al. Human Genomics 1(4): 274 (2004).

“Clustering of 1056 individuals based on >325 genetic markers”

Rosenberg, N. et al. *Science* 298(5602), 2002



Marcus Feldman, 2010

- **After reviewing the available data pertaining to human genetic diversity, and asking how these data relate to the definition and meaning of racial classification, we have shown that people can be assigned to ancestry clusters that usually agree with their self-identified ethnicity.**

Marcus Feldman, 2010

- We have also shown that only a small fraction of all genomic variation is responsible for the visible morphological differences such as skin color, facial features, or hair form that are commonly used to assign people to different races...we suggest that a more accurate name for such genetically defined clusters—rather than race or ethnicity—might be “**ancestry groups.**”

Francis Collins
The Language of Life (2010)

- “....what does DNA tell us about our traditional way of categorizing ourselves?” (p. 144)
- “There are no human races in the strict biological sense. We humans represent a wonderful continuum of marvelous diversity....” (p. 162)

“This is a (insert patient’s age, presumed race, and sex) who presents with a chief complaint of...”

The NEW ENGLAND JOURNAL of MEDICINE

SOUNDING BOARD

Collection of Data on Patients’ Race and Ethnic Group by Physician Practices

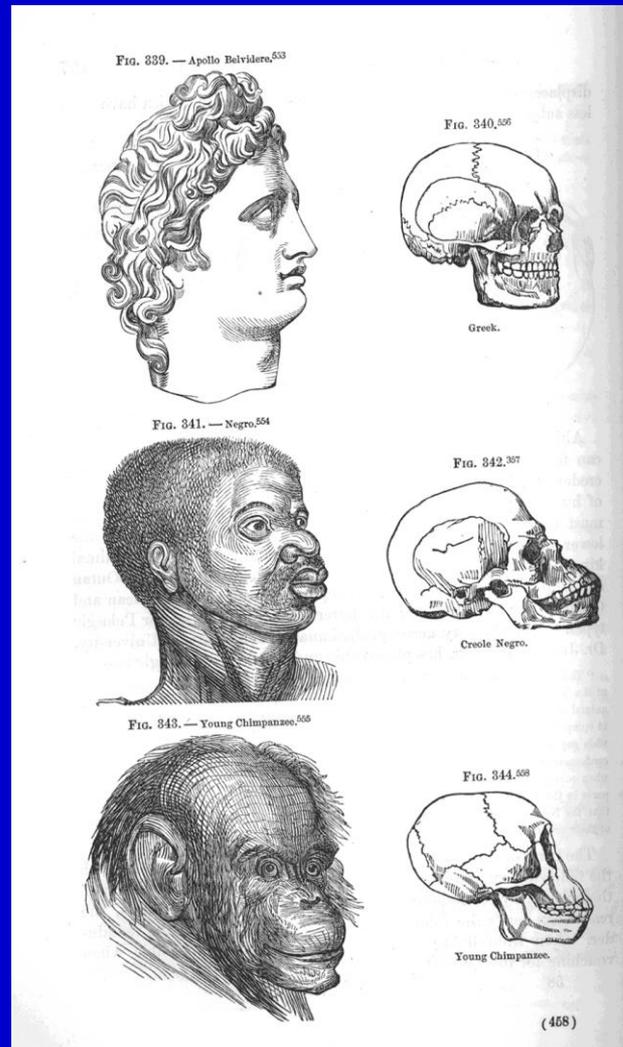
Matthew K. Wynia, M.D., M.P.H., Susan L. Ivey, M.D., and Romana Hasnain-Wynia, Ph.D.

These concerns are reflected in debates during the past two decades on whether to note the patient’s race or ethnic group at the outset of clinical case presentations (e.g., “This 44-year-old black man presents with fever and a cough”). This practice has been criticized for conveying more subtle social biases than actionable medical information.²⁵⁻²⁷ Some clinicians have noted that, insofar as one’s race, ethnic group, or ancestry might correlate with dietary habits, cultural norms, or other factors that could influence treat-

ment, the patient’s race might belong in the “history of present illness or social history” section of a case presentation and might be framed more properly as information on ethnic background or culture.²⁶ Even so, a demographic category to encapsulate a complex set of cultural and social factors would comprise an incomplete, and perhaps misleading, medical history. In the care of an individual patient, it is more important to know his or her personal health-related values, beliefs, and priorities than the average of such factors within any ethnic or racial group to which the patient might belong.

Where Does “Caucasian” Come From?

The Use of Science to Justify Theories of Racial Hierarchy



Johann Friedrich Blumenbach

(1752 – 1840)

On the Natural Varieties of Mankind

- **“The white colour holds the first place, such as is that of most European peoples.”**
- **Caucasian: “I have taken the name of this variety from Mount Caucasus, both because its neighborhood, and especially its southern slope, produces the most beautiful race of men, I mean the Georgian.”**

THE
HISTORY OF
WHITE PEOPLE

NELL IRVIN
PAINTER

Race is “Real”

- Race is not a thing—it is a social relation
- “...race is an idea, not a fact, and its questions demand answers from the conceptual rather than the factual realm.”

–Nell Irvin Painter

Problems in Classification

What exactly is a “Race”

- **U.S. OMB Labels**

(White, American Indian or AN, Asian, Black or AA, Native Hawaiian or Other Pacific Islander)

- **are POLITICAL, not biologically valid categories**

OMB Directive 15 & “Bad Science”

"These classifications should not be interpreted as being scientific or anthropological in nature, nor should they be viewed as determinants of eligibility for participation in any federal program. They have been developed in response to needs expressed by both the executive branch and the Congress to provide for the collection and use of compatible, nonduplicated, exchangeable racial and ethnic data by Federal agencies."

Guidelines of the International Committee of Medical Journal Editors (2003)

- **“When authors use variables such as race and ethnicity, they should define how they measure the variables and justify their relevance.”**

Variant Frequencies Differ by Ancestry

15% higher incidence of triple negative breast cancer in African Americans

Nat Genet. 2011 Oct 30;43(12):1210-4. doi: 10.1038/ng.985.

A common variant at the TERT-CLPTM1L locus is associated with estrogen receptor-negative breast cancer.

Haiman CA¹, Chen GK, Vachon CM, Canzian F, Dunning A, Millikan RC, Wang X, Ademuyiwa F, Ahmed S, Ambrosone CB, Baglietto L, Balleine R, Bandera EV, Beckmann MW, Berg CD, Bernstein L, Blomqvist C, Blot WJ, Brauch H, Buring JE, Carey LA, Carpenter JE, Chang-Claude J, Chanock SJ, Chasman DI, Clarke CL, Cox A, Cross SS, Deming SL, Diasio RB, Dimopoulos AM, Driver WR, Dünnebieer T, Durcan L, Eccles D, Edlund CK, Ekici AB, Fasching PA, Feigelson HS, Flesch-Janys D, Fostira F, Försti A, Fountzilas G, Gerty SM; Gene Environment Interaction and Breast Cancer in Germany (GENICA) Consortium, Giles GG, Godwin AK, Goodfellow P, Graham N, Greco D, Hamann U, Hankinson SE, Hartmann A, Hein R, Heinz J, Holbrook A, Hoover RN, Hu JJ, Hunter DJ, Ingles SA, Irwanto A, Ivanovich J, John EM, Johnson N, Jukkola-Vuorinen A, Kaaks R, Ko YD, Kolonel LN, Konstantopoulou I, Kosma VM, Kulkarni S, Lambrechts D, Lee AM, Marchand LL, Lesnick T, Liu J, Lindstrom S, Mannermaa A, Margolin S, Martin NG, Miron P, Montgomery GW, Nevanlinna H, Nickels S, Nyante S, Olswold C, Palmer J, Pathak H, Pectasides D, Perou CM, Peto J, Pharoah PD, Pooler LC, Press MF, Pykäs K, Rebbeck TR, Rodriguez-Gil JL, Rosenberg L, Ross E, Rüdiger T, Silva Idos S, Sawyer E, Schmidt MK, Schulz-Wendtland R, Schumacher F, Severi G, Sheng X, Signorello LB, Sinn HP, Stevens KN, Southey MC, Tapper WJ, Tomlinson I, Hogervorst FB, Wauters E, Weaver J, Wildiers H, Winqvist R, Van Den Berg D, Wan P, Xia LY, Yannoukakos D, Zheng W, Ziegler RG, Siddiq A, Slager SL, Stram DO, Easton D, Kraft P, Henderson BE, Couch FJ.

Dorothy Roberts
Fatal Invention, 2011

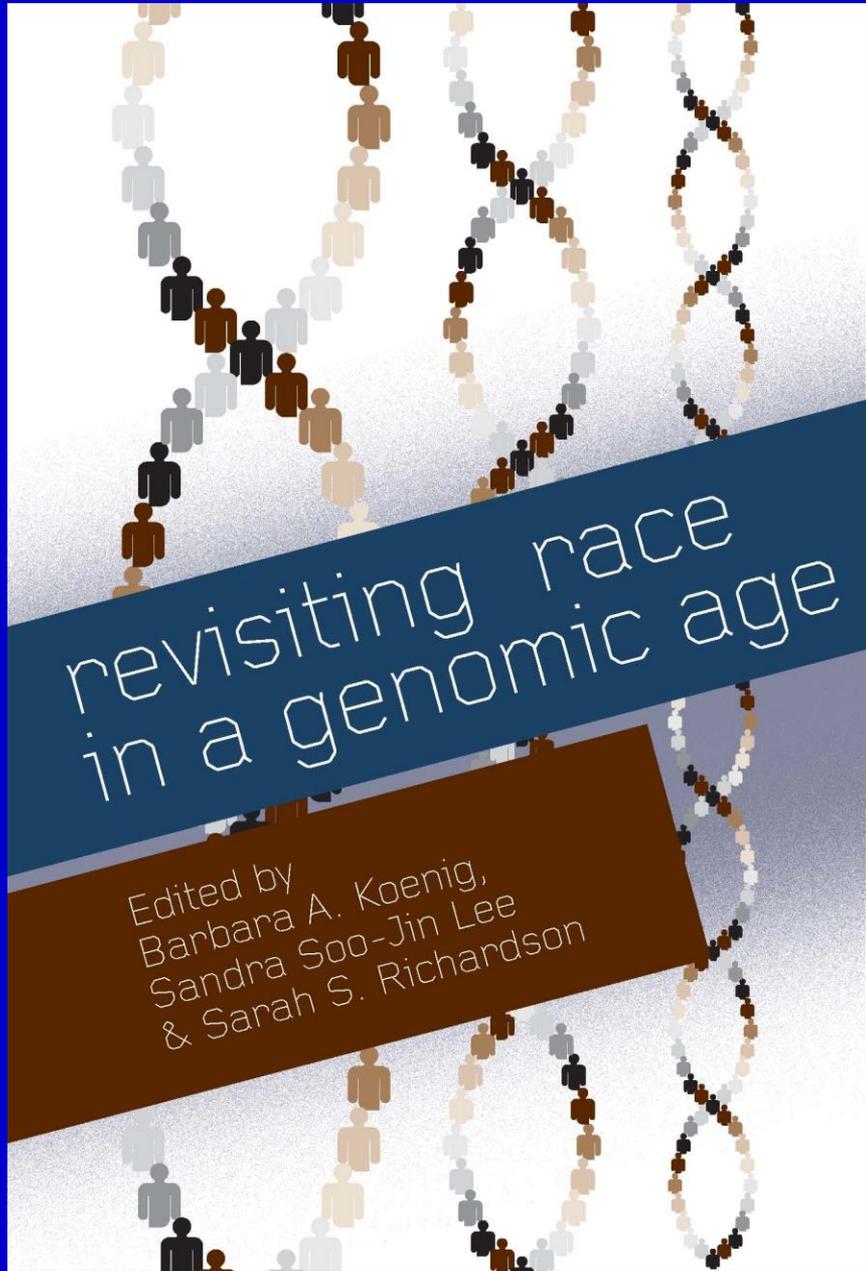
- **“As interest in health disparities converges with the genomic science of race, a new brand of racial stereotyping is gaining hold in biomedical research.” p. 111**
- **“So far, genetic technologies are reinforcing race, not transcending it.” p. 210**

Race in U.S. Context

**Governor McDuffie of South Carolina,
Message to the legislature.**

**Reprinted in *Boston Liberator*,
Dec. 12, 1835**

“The African negro is destined by Providence to occupy a condition of servile dependency...It is marked on the face, stamped on the skin, and evinced by the intellectual inferiority and natural improvidence of the race...They are in all respects—physical, moral, and political—inferior to millions of the human race...[and] are doomed to this hopeless condition by the very qualities which unfit them for a better life.”



revisiting race
in a genomic age

Edited by
Barbara A. Koenig,
Sandra Soo-Jin Lee
& Sarah S. Richardson

Genome Biology 2008

The ethics of characterizing difference: guiding principles on using racial categories in human genetics

Sandra Soo-Jin Lee¹, Joanna Mountain^{2,3}, Barbara Koenig⁴, Russ Altman⁵, Melissa Brown⁶, Albert Camarillo⁷, Luca Cavalli-Sforza³, Mildred Cho¹, Jennifer Eberhardt⁸, Marcus Feldman⁹, Richard Ford¹⁰, Henry Greely¹⁰, Roy King¹¹, Hazel Markus⁸, Debra Satz¹², Matthew Snipp¹³, Claude Steele⁸ and Peter Underhill³

Stanford “Statement”

Scientists and humanists are divided on the question of whether racial categorization is an appropriate and innocent means of organizing potentially useful genetic data or a pernicious reification of historically destructive typologies. Yet this debate is rarely joined. Genetic researchers do not have the opportunity to discuss the implications of their work with scholars of race and racial hierarchy. Likewise, philosophers, historians, and social scientists may not be familiar with recent research on human genetic variation.



GENETICS IS ABOUT TO GET PERSONAL

☛ don't panic, we're here to help

23andMe is a privately held company developing new ways to help you make sense of your own genetic information.

Even though your body contains trillions of copies of your genome, you've likely never read any of it. Our goal is to connect you to the 23 paired volumes of your own genetic blueprint (plus your mitochondrial DNA), bringing you personal insight into ancestry, genealogy, and inherited traits. By connecting you to others, we can also help put your genome into the larger context of human commonality and diversity.

Toward this goal, we are building on recent advances in DNA analysis technologies to enable broad, secure, and private access to trustworthy and accurate individual genetic information. Combined with educational and scientific resources with which to interpret and understand it, your genome will soon become personal in a whole new way.

To hear about new developments as they happen, sign up here:

Mayo Clinic Proceedings 2011

ORIGINAL ARTICLE

Impact of Direct-to-Consumer Predictive Genomic Testing on Risk Perception and Worry Among Patients Receiving Routine Care in a Preventive Health Clinic

KATHERINE M. JAMES, MPH; CLAYTON T. COWL, MD, MS; JON C. TILBURT, MD, MPH;
PAMELA S. SINICROPE, DRPH; MARGUERITE E. ROBINSON, MAR, MA; KATRIN R. FRIMANNSDOTTIR, PhD;
KRISTINA TIEDJE, PhD; AND BARBARA A. KOENIG, PhD

[my home](#)

health and traits

health and traits

These tables list those [clinical reports](#) we consider most notable based on your genetic information.

Move your mouse over the colored bars or icons for a glance at your data. Click the name of any disease or trait for your full report.

- Clinical Reports
- Research Reports

ancestry

- Maternal Line
- Paternal Line
- Ancestry Painting
- Global Similarity

genome sharing

- Manage Sharing
- Compare Genes
- Family Inheritance

23andWe

- My Surveys (28)
- Our Research Mission
- Featured Research

community

- 23andMe Community
- Parkinson's Disease
- Pregnancy
- Senior Games

account

Clinical Reports

Research Reports (86)

Show data for:

Disease Risks ?

| | |
|---|----------------------|
|  | Type 1 Diabetes |
|  | Crohn's Disease |
|  | Rheumatoid Arthritis |
|  | Type 2 Diabetes |
|  | Parkinson's Disease |

[See all 10 risk](#)

Carrier Status ?

Hemochromatosis Variant Present

Sickle Cell Anemia & Malaria Resistance

This person possesses one or more genetic variants linked to a particular condition, but is not necessarily affected by it. These variants could be inherited by this person's children.

[Read more »](#)

Variant Present

Variant Absent

Variant Absent

Variant Absent

[3 carrier status...](#)

Traits ?

| | |
|-------------------------|-----------------|
| Alcohol Flush Reaction | Does Not Flush |
| Bitter Taste Perception | Can Taste |
| Earwax Type | Wet |
| Eye Color | Likely Brown |
| Lactose Intolerance | Likely Tolerant |

[See all 10 traits...](#)

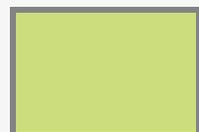
Drug Response ?

| | |
|----------------------------------|-----------|
| Warfarin (Coumadin®) Sensitivity | Increased |
| Abacavir Hypersensitivity | Typical |
| Clopidogrel (Plavix®) Efficacy | Typical |
| Fluorouracil Toxicity | Typical |

Barbara Koenig



Europe 96%



Africa 3%



Asia 1%



Not Genotyped

my home

health and traits

Clinical Reports

Research Reports

ancestry

Maternal Line

Paternal Line

Ancestry Painting

Global Similarity

genome sharing

Manage Sharing

Compare Genes

Family Inheritance

23andWe

My Surveys (28)

Our Research Mission

Featured Research

community

23andMe Community

Parkinson's Disease

Pregnancy

Senior Games

account

Inbox

My Profile

Settings

Browse Raw Data

23andMe Labs

Help/Contact Us

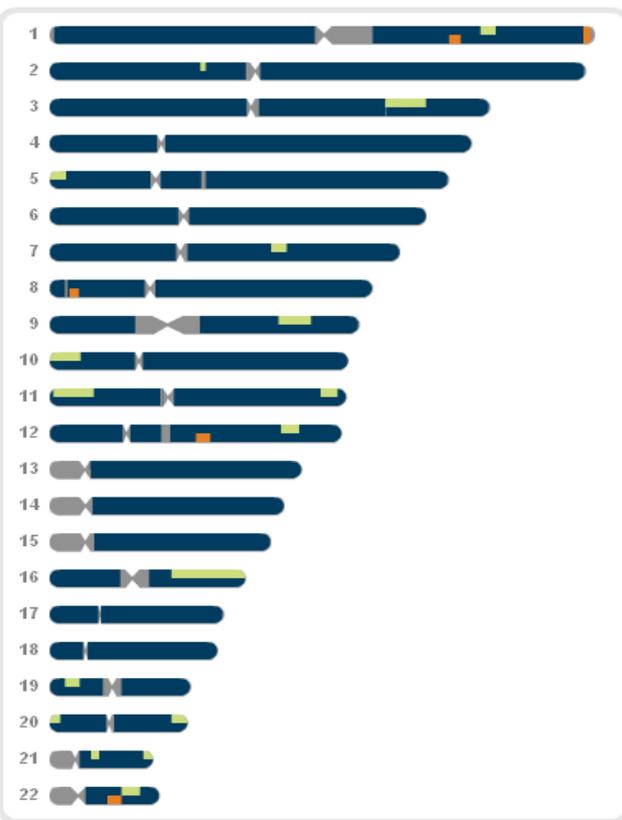
ancestry painting

Trace the ancestry of your chromosomes, one segment at a time. Last updated [April 23, 2008](#).

Chromosome View

-  Solid segments indicate that both chromosomes come from the same geographic region. [See a Cambodian Woman's painting.](#)
-  Dual-colored segments indicate chromosomes from different geographic regions. [See an African American Man's painting.](#)

Select a person:



Barbara Koenig

 Europe 96%

 Africa 3%

 Asia 1%

 Not Genotyped

Worldwide Examples

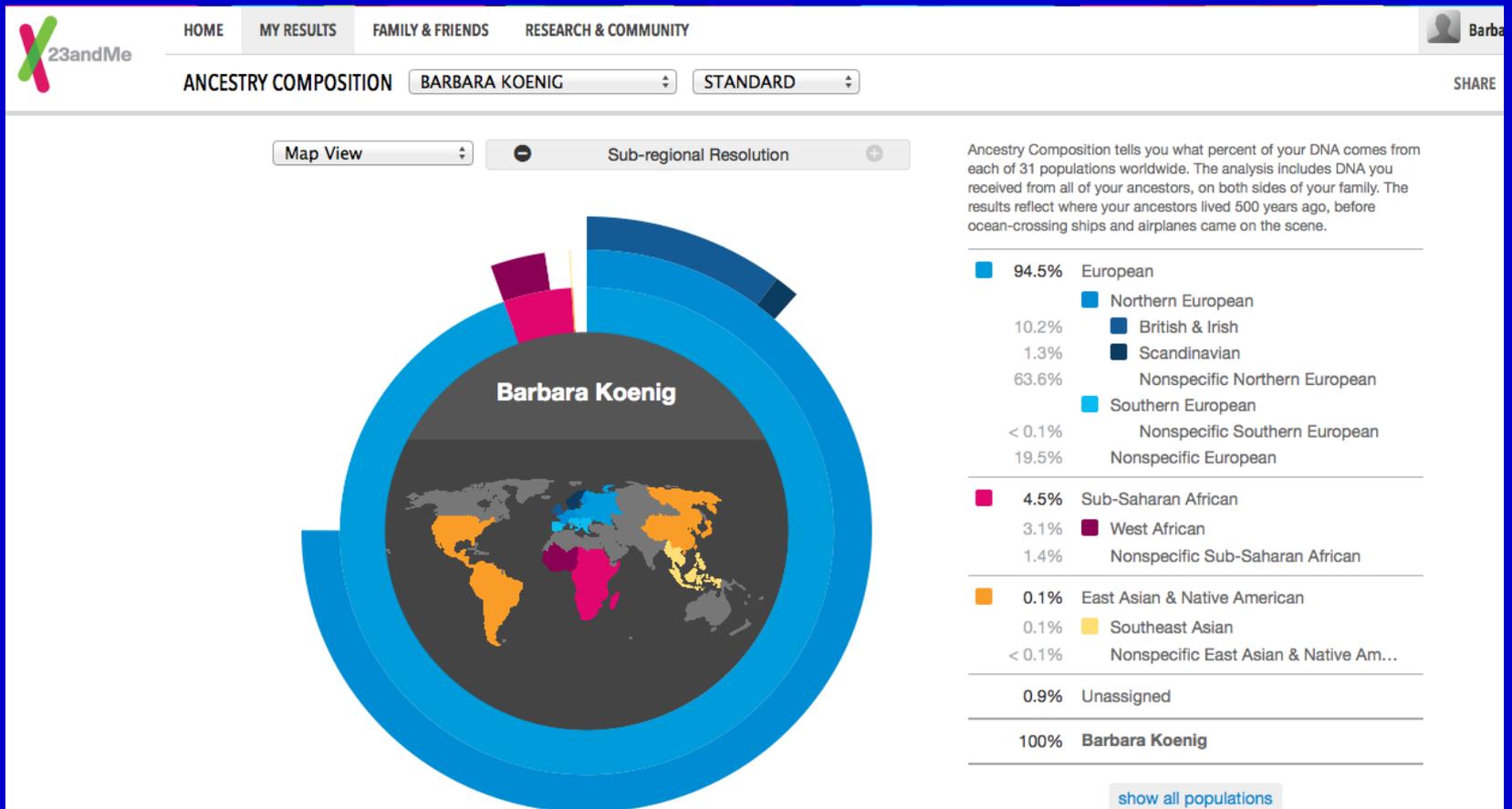
Click on the icons in the map below to see example paintings of individuals from across the globe.



Tell Me About...

- [...using Ancestry Painting.](#)
- [...the three reference populations.](#)
- [...why only three populations are used.](#)
- [...the people linked to my account.](#)
- [...why it says I'm European/African/Asian when I'm really an American/Australian/South African.](#)
- [...how the percentages are calculated.](#)
- [...where the X and Y chromosomes are.](#)

Map View



Chromosome View

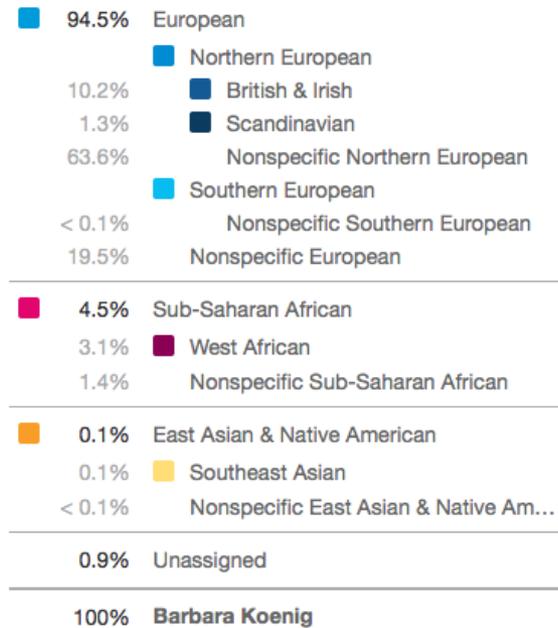
Chromosome View



Sub-regional Resolution



Ancestry Composition tells you what percent of your DNA comes from each of 31 populations worldwide. The analysis includes DNA you received from all of your ancestors, on both sides of your family. The results reflect where your ancestors lived 500 years ago, before ocean-crossing ships and airplanes came on the scene.



[show all populations](#)





U.S. Airforce Academy



Conclusion???? Social Context!!!!

- **Biological processes are known only through socially constructed categories.**

Best Practices in Describing Human Difference in Genomics Research?

Recommendations for Discussion

- Use “ancestry” (or biogeographical ancestry) to describe actual genetic variation
- Use “race” when studying health status in societies characterized by racial hierarchies
- Use “ethnicity” or “ethnocultural” to refer to lifestyle, diet, values, etc.

Recommendations for Discussion

- **In publications:**
 - **Explain how all categories of human difference were ascertained (e.g. self report, assignment by clerks, ancestry informative markers)**
 - **Avoid conflating biological and social categories**

How Should we Deal with Existing Data Sets (& the EMR)

- How to deal with race labels (?)
- State the limitations whenever you use the data (?)

How to answer the “race” question in genetics research?

The “wrong question” : *Should we use race in research?*

The “right question ” : *Under what conditions should we use race?*

- Clarifying, Engaging, Productive Debate

Can a “polysemic” concept of race prevail?

Challenges to Inter-disciplinary Conversation

- **Difficulty in discussing the “meaning” of classificatory schemes**
 - **Can data generate neutral descriptors of population categories?**
- **Scientists advance an “anti-racist” agenda through their work with “racialized” populations**
- **Rigidity of classificatory regimes**

Challenges to Inter-disciplinary Conversation

- New “Race Working Group” at UCSF to focus on APOL1 example
 - Jointly envisioned research using the Kaiser Permanente “Research Program on Genes, Environment, and Health” (a diverse 110K biobank linked to medical records)