Otis W. Brawley, MD, MACP, FASCO, FACE

Chief Medical and Scientific Officer
American Cancer Society

Professor of Hematology, Medical Oncology,
Medicine, and Epidemiology
Emory University
Genomic Medicine in the 21st Century and A Brief History of Health Disparities

From the perspective of a Cancer Doc
Disclosures

• Employment:
  – American Cancer Society
  – Emory University

• Consulting
  – Turner Broadcasting (CNN)
  – National Institutes of Health
  – Centers for Disease Control
  – Department of Defense
My Task

• Importance of equitable access to genetic/genomic services
• Define “disparities in health”
• Discuss fears and concerns
• Outline some areas for further study
Genetics

The study of heredity, or how the characteristics of living things are transmitted from one generation to the next.

Genomics

The study of genes and their functions, and related techniques.

WHA 57.13: Genomics and World Health, Fifty Seventh World Health Assembly Resolution; 22 May 2004
Genetics vs Genomics

The **main difference** is that genetics scrutinizes the functioning and composition of the single gene whereas genomics addresses all genes and their inter relationships in order to identify their combined influence on the growth and development of the organism.
Genetics/Genomics

• Risk of Disease
  – BRCA mutations - Breast Cancer
  – HBB mutations - Sickle Cell Trait/Anemia
  – CFTR mutations - Cystic Fibrosis

• Defining type of disease and response to treatment
Rudolph Ludwig Karl Virchow
1821 - 1902
A 19\textsuperscript{th} Century Definition of Cancer

- Cancer is uncontrolled cell growth, uncontrolled mitoses
- Cancerous cells spread and interfere with bodily functions.
Adenocarcinoma
A 21st Century Definition of Cancer

Involves histology and genomics

An understanding of the varying biologic behaviors of cancer based on histology and genomics.

Numerous molecular targets have and are being defined. Some are drugable targets.
Non Small Cell Lung Cancer

- No mutation detection: 37%
- KRAS: 25%
- EGFR (sensitizing): 15%
- ALK: 8%
- EGFR (other): 6%
- Mutation in >1 gene: 4%
- BRAF: 2%
- PIK3CA: 1%
- MET: 1%
- NRAS: 1%
- MEK1 <1%
- HER2: 2%
Oncotype Dx
for hormone receptor positive Her 2 Neu negative breast cancer

21 Gene Array Test Determines Therapy

Chemotherapy and Hormones

Hormones

Oncotype Dx can prevent 70,000 American women from receiving chemotherapy in 2018
The American Healthcare System

Inefficient!!!

• Some over consume resources
  (This can be harmful to the over-consumer)

• Some under consume resources
  (This is the cause of disparities)

• Healthcare outcomes could be better
  (People die needlessly)
The American Healthcare System

The True Cost of an Inefficiency

• More than 25,000 Americans die annually due to lack of healthcare

• More than 75,000 Americans die annually due to poor quality healthcare

• Thousands suffer because healthcare is not available to them

IOM 2006, Sathcer and Pamies 2006
The Most Important Question in Healthcare

How can we provide adequate high quality care (to include preventive services) to populations that so often do not receive it?
What if we applied what we already know about cancer?
Applying Known Science (Prevention and Treatment)

- 610,000 Americans will die of cancer this year.

- If all Americans had the cancer death rate of college educated Americans then 152,000 (25%) would not die.
There has been a 49% decline in age adjusted colorectal cancer death rates since 1981. The shaded states have <30% decline.
There has been a 39% decline in age adjusted colorectal cancer death rates since 1989.

The shaded states have <30% decline.
Access to Care

• It is not just having insurance

• It is healthy habits and access to:
  – Prevention
  – Screening
  – Diagnosis
  – Treatment
A Brief History of A Discipline

- Minority Health
- Special Populations
- Health Disparities
- Health Equity
Disparities in Health

Populations can be defined or categorized by:

- Gender
- Race
- Ethnicity and Culture
- Area of geographic origin
- Socioeconomic Status
- Urban vs Rural
Minority Health

The Civil Rights Movement of the 1950’s and 1960’s.

Realization that there were Black/White differences in cancer death rate and survival.


Minority Health

The Civil Rights Movement of the 1950’s and 1960’s.

• Increasing awareness of Sickle Cell Disease as a genetic disease associated with African ancestry

• Increasing awareness of different risk in other diseases by race.
   - Hypertension
   - Certain Cancers
   - Diabetes
Race Medicine

An old concept!!!

Used to justify slavery

Used to justify the Tuskegee Syphilis Experiment
Race Medicine

The concept that diseases differ amongst the races due to ”genetic” differences amongst populations.

The word “genetic” has baggage!!! It is a buzzword to disenfranchised people.
Race Medicine

The concept of biologic differences led to the thought that disparities exist because our treatments do not work in Blacks.

We have to test our treatments in Blacks!

Few said or say disparities exist because Blacks do not get the treatment!!
The NIH Revitalization Act of 1993

“Minorities must be included in Federally sponsored clinical trials.”

“In phase III trials, there must be valid subset analysis of the differences among the races.”
The NIH Revitalization Act of 1993

Subset analysis by race, ethnicity and gender are required of all phase III clinical studies with initial funding after 1995.

Peer review must assess each funded project for inclusion and subset analysis.

This creates some serious scientific and ethical issues.
Scientific and Ethical Issues

• The law implies that race is a biological categorization and disparities are due to “genetic” differences among the races!!!

• The law encourages researchers to “encourage” minority participation.
Scientific and Ethical Issues

For those who know how to design clinical trials:

• Subset analysis should be avoided as they can be very wrong!

• Subset analysis often require over-sampling. An ethical issue, putting the minorities at greater risk and violating equipoise.
Scientific and Ethical Issues

Subset analysis should be avoided as they can be very wrong!

The case against tamoxifen in the treatment of black women with breast cancer.

The original randomized trial was before the ER Receptor assay (a genetic test) was available.

– In a world without a defined estrogen receptor and a law requiring a valid subset analysis.
  • Tamoxifen is of little use in Black Women
– In a world with an estrogen receptor
  • Tamoxifen is a good drug for Black women and women of all races with ER Positive breast cancer
Race

Carl Linnaeus – Systema Naturae, 1735

Caucasian
Negroid
Mongoloid
Race

Defined by US Office of Management and Budget every ten years.

– Sociopolitical and not biologic according to OMB definition

– Rejected by Anthropological community as non-scientific

– Race changes over time*
Population Differences in Disease Outcome

Race is not a good surrogate for genetics/genomics.

We should strive for genetic/genomic diversity in clinical studies.
Area of Geographic Origin and Genetics

Can correlate with family/genetics/tribe

• Sickle Cell Trait – Mediterranean Basin and sub-Saharan Africa

• Cystic Fibrosis – Northern Europe

• EtOH dehydrogenase deficiency – East Asia

• The Askenazi-Jewish Mutations of BRCA (one has been traced to a woman alive about 100 to 200AD. This brings about concept of family)
Area of Geographic Origin and Genetics

• 12% of the Thai population and a smaller portion of the Malaysian population have a genomic predisposition to a skin reaction Stevens-Johnson Syndrome when administered carbamazepine (Tegretol)

• Identifying these people can save lives by preventing use of drugs known to cause Stevens-Johnson Syndrome

• Populations profiling, is it ethical?
Population Science

– Genomics may:
  – Define populations at risk of disease
  – Define subsets of disease
  – Predict response to treatment

– Genomics is a scientific/objective way of defining or categorizing populations
“The ultimate goal is for medicine to become so personalized from a “fingerprint” of one’s biologic makeup, not from racial typecasting.”

Keith Norris, MD
The Most Important Question in Health Disparities Research

How can we provide adequate high quality care (to include preventive services) to populations that so often do not receive it?
Otis W. Brawley, MD, MACP, FASCO, FACE

Chief Medical and Scientific Officer
American Cancer Society

Professor of Hematology, Medical Oncology,
   Medicine, and Epidemiology
Emory University