



Race/Ethnicity and Genetics

Defining the population to be studied and the interpretation of group/population genomic data

- **Charles N. Rotimi, PhD**
 - **Director:** Center for Research on Genomics and Global Health
 - **Senior Investigator:** Inherited Disease Research Branch

Defining the population to be studied

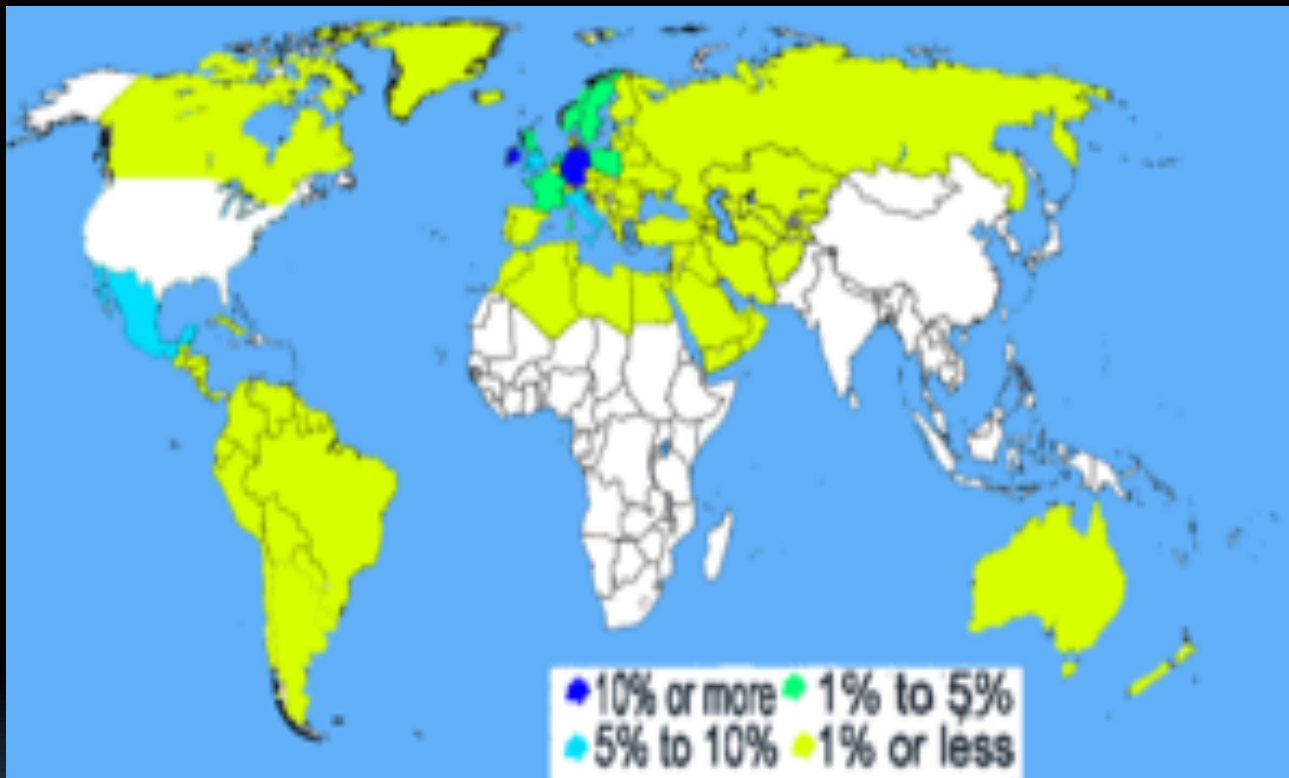
Concept of identity is fluid and time dependent

1. Continental
2. National
3. Ethnic/tribal
4. Admixture (recent and ancient)
5. Ancestry (for political and other reasons, individual and group ancestry are defined in sometimes on predictable ways)



Africa or Sub-Saharan Africa

Countries from which White Americans claim their ancestry



The government defines White people as "people having origins in any of the original people of **Europe, the Middle East, or North Africa**"

RACIAL CATEGORIZATION — IN THE 2010 CENSUS —

Professor Lee noted that the U.S. population has changed dramatically since the first census of 1790, and that the manner in which the census is collected has changed accordingly.¹⁰ She stated that almost every census for the past two hundred years has collected racial data differently than the census before it-

What does the Census Bureau mean by race?

Census Bureau collects race data in accordance with US OMB guidelines and these data are based on self-identification.

The racial categories included in the census generally reflect a social definition of race recognized in this country, **and not an attempt to define race biologically, anthropologically or genetically.**

People may choose to report more than one race to indicate their racial mixture, such as “American Indian and White.”

People who identify their origin as Hispanic, Latino, or Spanish may be of any race.

--- race item include both racial and national origin or socio-cultural groups. **You may choose more than one race category.**

2010 US Census form

→ NOTE: Please answer BOTH Question 8 about Hispanic origin and Question 9 about race. For this census, Hispanic origins are not races.

8. Is Person 1 of Hispanic, Latino, or Spanish origin?

- No, not of Hispanic, Latino, or Spanish origin
- Yes, Mexican, Mexican Am., Chicano
- Yes, Puerto Rican
- Yes, Cuban
- Yes, another Hispanic, Latino, or Spanish origin — *Print origin, for example, Argentinean, Colombian, Dominican, Nicaraguan, Salvadoran, Spaniard, and so on.* ↴

9. What is Person 1's race? Mark one or more boxes.

- White
- Black, African Am., or Negro
- American Indian or Alaska Native — *Print name of enrolled or principal tribe.* ↴

- | | | |
|---|--|--|
| <input type="checkbox"/> Asian Indian | <input type="checkbox"/> Japanese | <input type="checkbox"/> Native Hawaiian |
| <input type="checkbox"/> Chinese | <input type="checkbox"/> Korean | <input type="checkbox"/> Guamanian or Chamorro |
| <input type="checkbox"/> Filipino | <input type="checkbox"/> Vietnamese | <input type="checkbox"/> Samoan |
| <input type="checkbox"/> Other Asian — <i>Print race, for example, Hmong, Laotian, Thai, Pakistani, Cambodian, and so on.</i> ↴ | <input type="checkbox"/> Other Pacific Islander — <i>Print race, for example, Fijian, Tongan, and so on.</i> ↴ | |

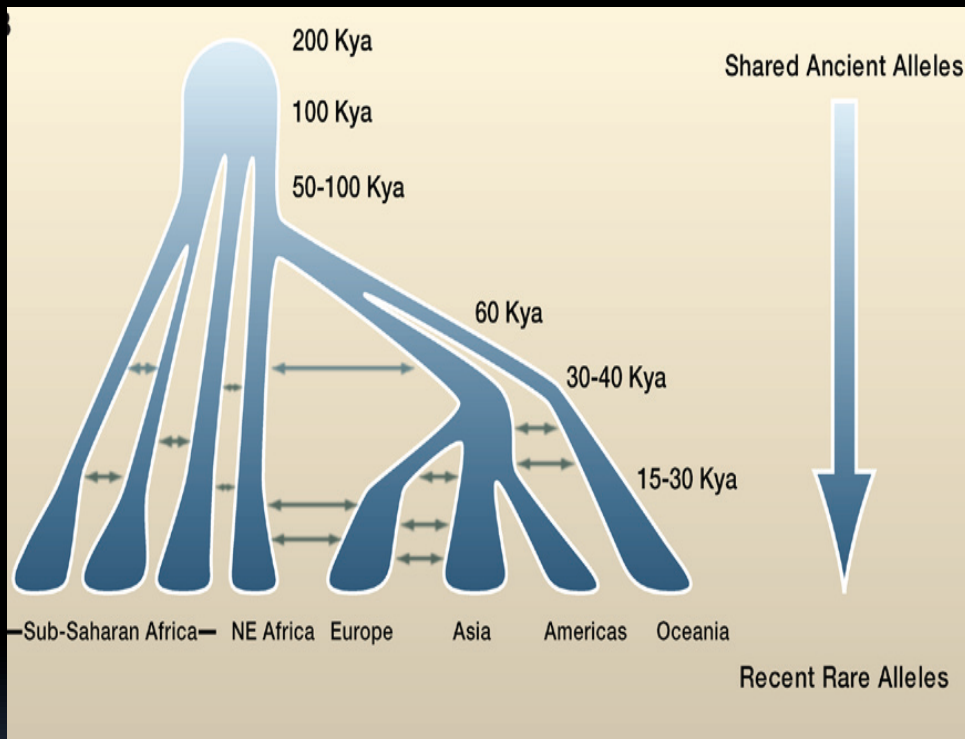
- Some other race — *Print race.* ↴

1790 census
– only three
categories –
white
Black
Indian

Reflecting
the political
reality of
slavery

Human Migrations and Genetic Diversity

Origins of common and rare alleles



The oldest human alleles originated in Africa well before the diasporas of modern humans.

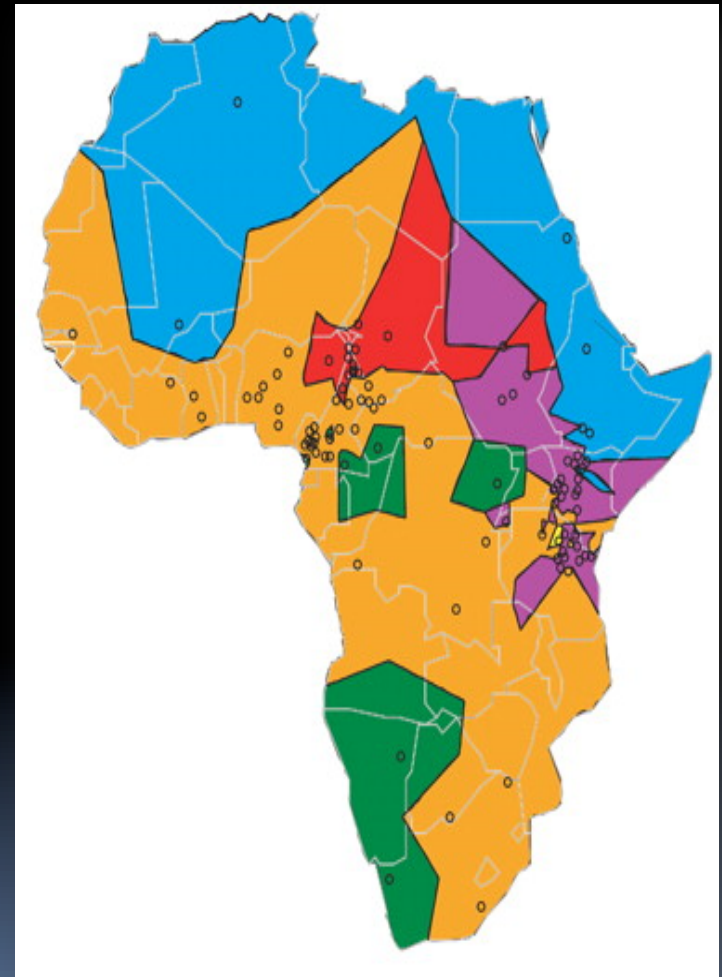
These oldest alleles are common in all populations worldwide. **Approximately 90% of the variability in allele frequencies is of this sort.**


Development of agriculture in the past 10,000 years and of urbanization and industrialization in the past 700 years led to rapid populations growth and the appearance of vast numbers of new alleles, each individually rare and specific to one population or even to one family.

The Genetic Structure and History of Africans and African Americans

Sarah A. Tishkoff,^{1,2*} Floyd A. Reed,^{1†‡} Françoise R. Friedlaender,^{3‡} Christopher Ehret,⁴

- **Conclusion –**
- **High level of mixed ancestry in most populations – reflecting historic migration across the continent**



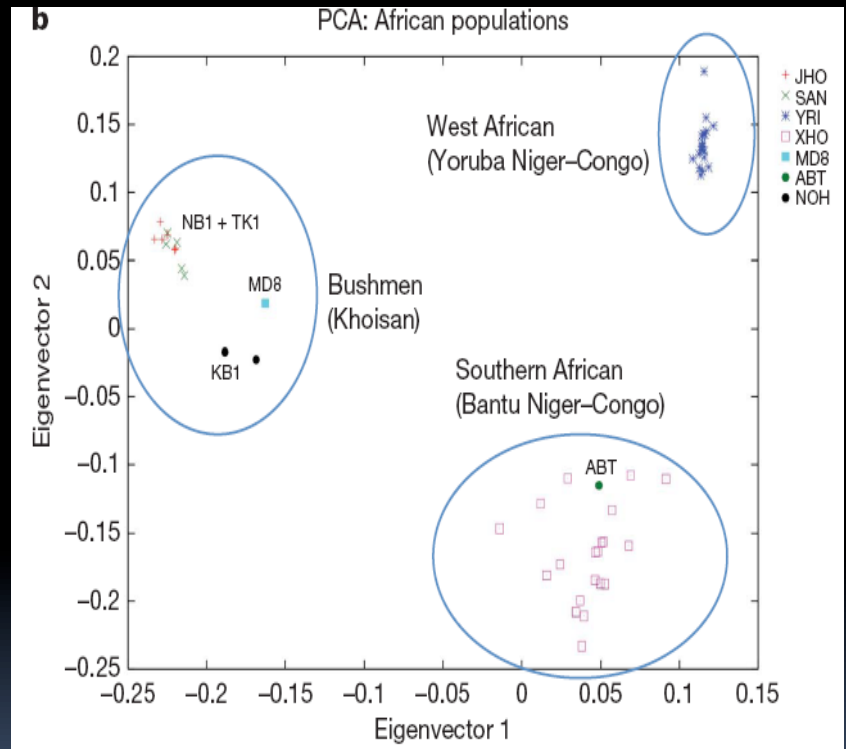
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- Genetic Diversity - African Populations

Complete Khoisan and Bantu genomes from southern Africa

Stephan C. Schuster^{1*}, Webb Miller^{1*}, Aakrosh Ratan¹, Lynn P. Tomsho¹, Belinda Giardine¹, Lindsay R. Kasson¹,



- | | |
|---|--|
| ■ Tuu speaker | ■ Arid climate |
| ■ Ju/'hoansi | ■ Desert |
| ■ !Kung (Etosha) | ■ Khoisan language |
| ■ Xhosa/Tswana | ■ Niger-Congo language |



Complete Khoisan and Bantu genomes from southern Africa

Stephan C. Schuster^{1*}, Webb Miller^{1*}, Aakrosh Ratan¹, Lynn P. Tomsho¹, Belinda Giardine¹, Lindsay R. Kasson¹,

"On average, there are more genetic differences between any two Bushmen in our study than between a European and an Asian---".

The study identified 1.3-million genetic variants that scientists previously had not observed. These genetic variations reveal that Southern Africans are quite distinct genetically from Europeans, Asians, and West Africans.

Pharmacogenomics

**The danger of group labeling of
genetic variation**

Variable Drug Response

- How do we interpret differential drug response by “groups” when “group” definition is imprecise, fluid and time dependent?
- Can we tell how an individual will respond based on group data?

Confusion: Group identity is confused with group ancestry. For example, the group identity “African Americans” does not reflect a single path of ancestry.

Who is Black?



Genetic Screening to Prevent Abacavir Hypersensitivity (AHS) Reaction

HLA-B*5701 - negative predictive value of 100% for patch-test-confirmed AHS for both Whites and Blacks

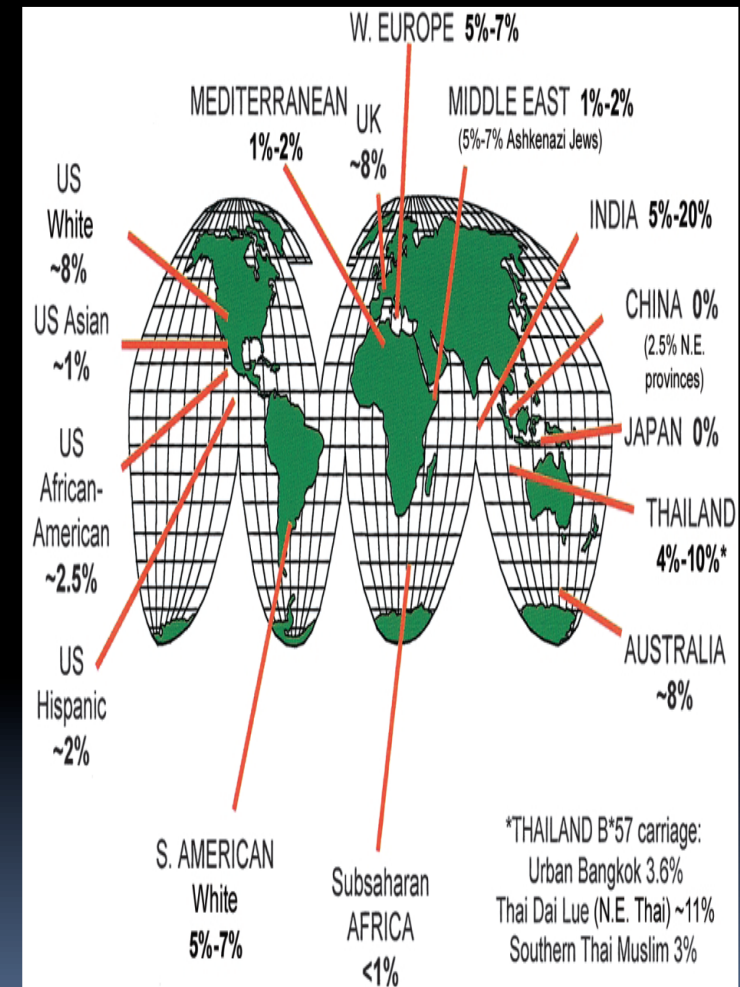
Indians - highest freq of 17.6% - 20%.

Africa - 13.6% (Maasai), 0% (Yoruba).

Europe – 3.4% (Tuscans), 5.8% (Utah).

The label “Africans” or “Blacks” renders radically different allele frequencies invisible.

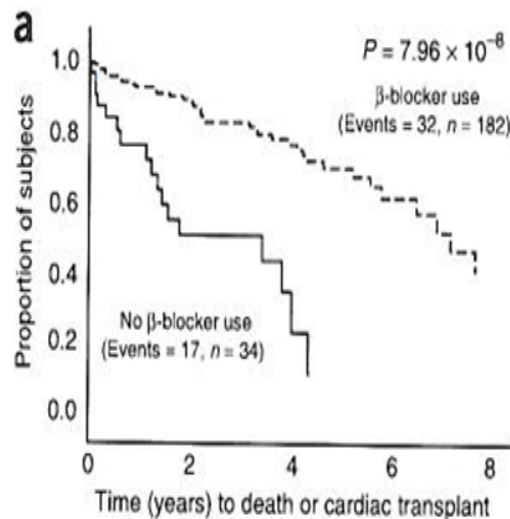
Consequence - Wrong public health decision about who to screen.



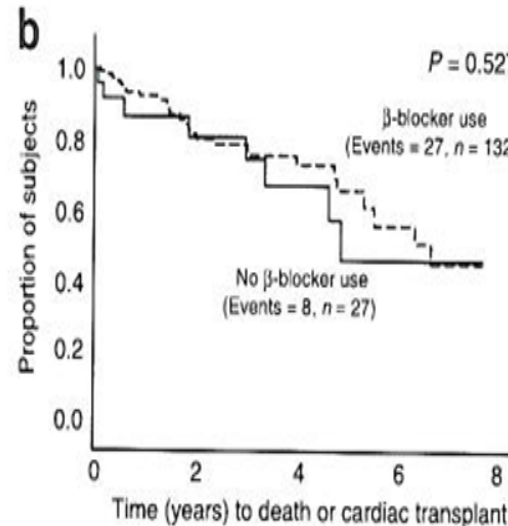
A GRK5 polymorphism that inhibits β -adrenergic receptor signaling is protective in heart failure

1. G protein-coupled receptor kinases (GRKs) desensitize β -adrenergic receptors (β ARs).
2. Re-sequencing of GRK5 revealed a nonsynonymous polymorphism - leucine is substituted for glutamine at position 41; GRK5-Leu41 allele is common in AA (~40%).
3. Results offer an explanation for the confusion in the findings of clinical trials of β -blocker. **β -blockers are absolutely effective in AA without the variant.**

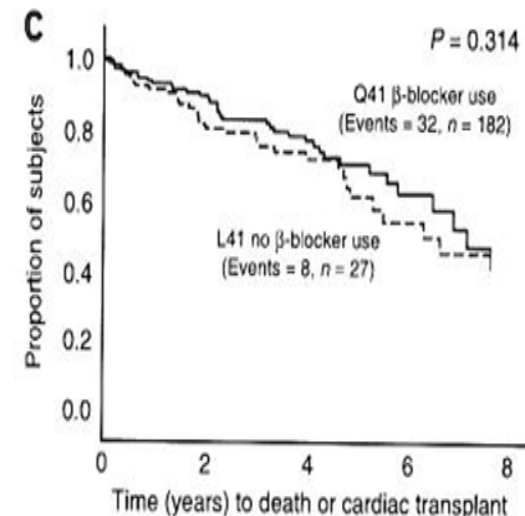
GRK5-Q41 only - with and without β -blocker use



GRK5-L41 only - with and without β -blocker use



GRK5-Q41 only txt with β -blocker vs GRK5-L41 only



Genome-wide patterns of population structure and admixture in West Africans and African Americans


Katarzyna Bryc^a, Adam Auton^a, Matthew R. Nelson^b, Jorge R. Oksenberg^c, Stephen L. Hauser^c, Scott Williams^d, Alain Froment^e, Jean-Marie Bodo^f, Charles Wambebe^g, Sarah A. Tishkoff^{h,1,2}, and Carlos D. Bustamante^{a,1,3}

That some individuals who self-identify as African American show almost no West African ancestry and others show almost complete West African ancestry has implications for pharmacogenomics studies and assessment of disease risk. Although individuals with very low West African or very low European ancestry may be expected by chance after several generations of admixture, these individuals are most likely descendants of individuals of European ancestry or recent African immigrants, respectively. Assuming these individuals are not simply mislabeled, it appears that the range of genetic ancestry captured under the term *African American* is extremely diverse, which suggests caution should be used in prescribing treatment based on differential guidelines for African Americans (45).



Take Home Message

Individuals cannot be treated as representative for all those who physically resemble them, or have some of the same ancestry.





A Project of the American Anthropological Association

“Race, in countries like the US at least, is a fuzzy social construct by which people with one or two superficial similarities are often clumped together. It reflects simplistic cultural habits reinforced by the questionable practices of government statisticians and medical researchers, among others. Ethnic binning may simplify thought processes and, in some cases, negate them altogether. But using genetics to define race is like slicing soup. You can cut wherever you want, but the soup stays mixed.”