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**“INFERRING GENETIC ANCESTRY:  
OPPORTUNITIES, CHALLENGES, AND  
IMPLICATIONS” A REVIEW**

# ETHICAL ISSUES RAISED BY GENEALOGICAL TESTING

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- ✗ Unresolved paternity
- ✗ Consent for testing
- ✗ Ownership of Samples
- ✗ Uncovering genetic disorders
  - + SRY Reversal / Klinefelter's Syndrome
- ✗ Unexpected Ancestry

# GENEALOGY VS. ANCESTRY TESTING

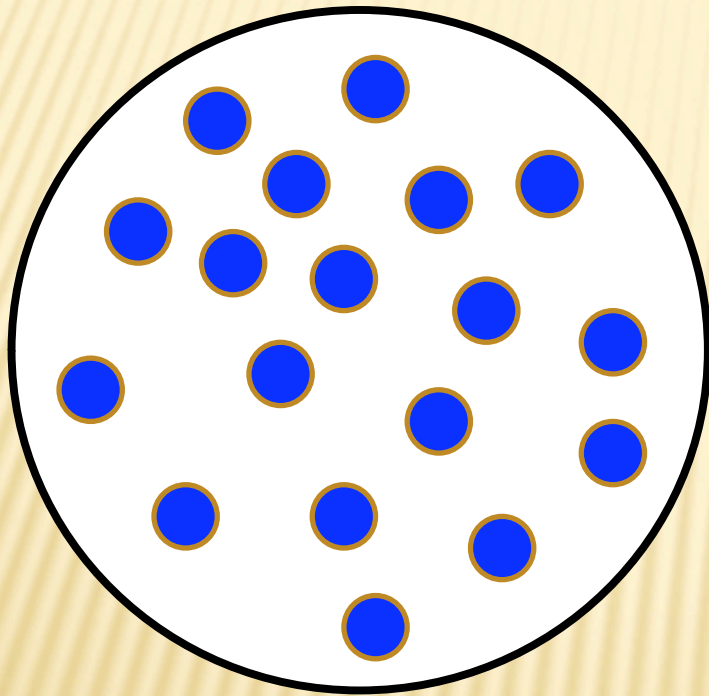
The tools for genealogical testing came from population genetics

In population genetics, the history of a population is inferred by constructing mathematical models of evolution and comparing it to the “behavior” of the population (what is observed in nature).

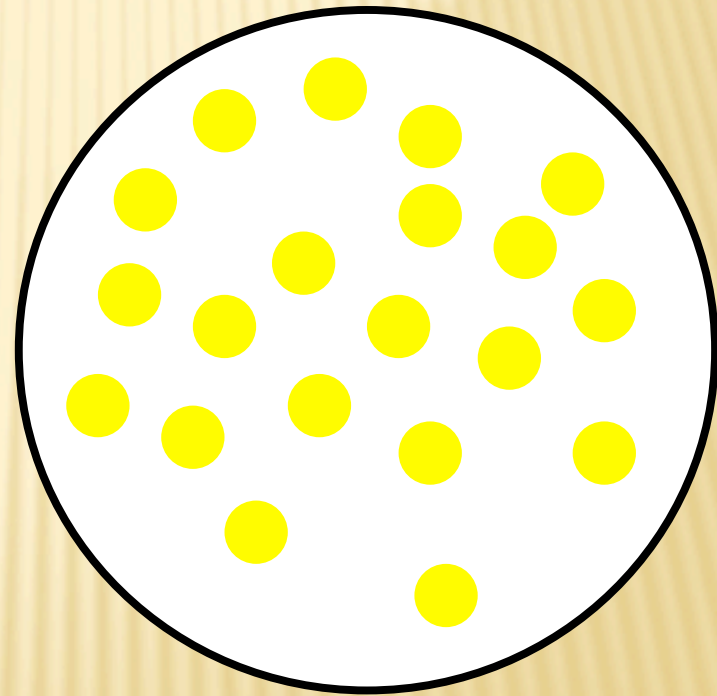
Ancestry testing applies population genetics to an individual sample

# POPULATION GENETICS

Population A

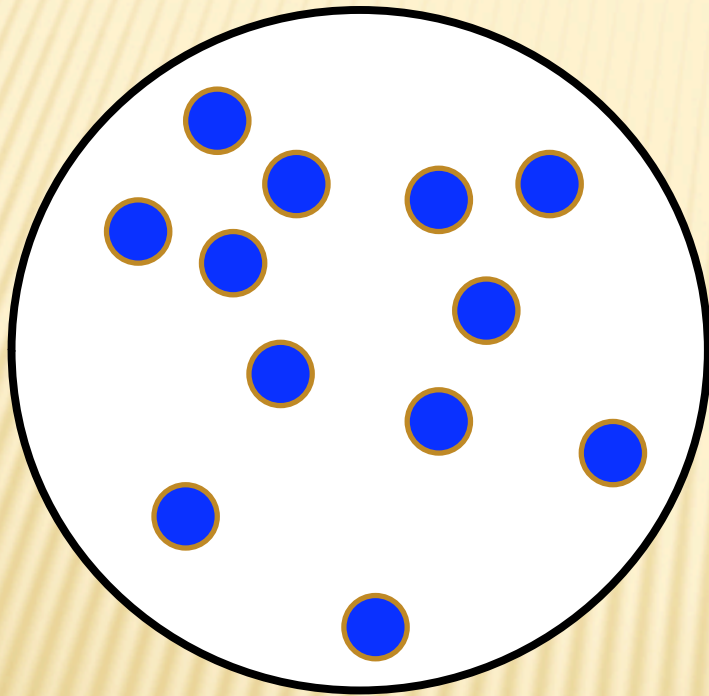


Population B

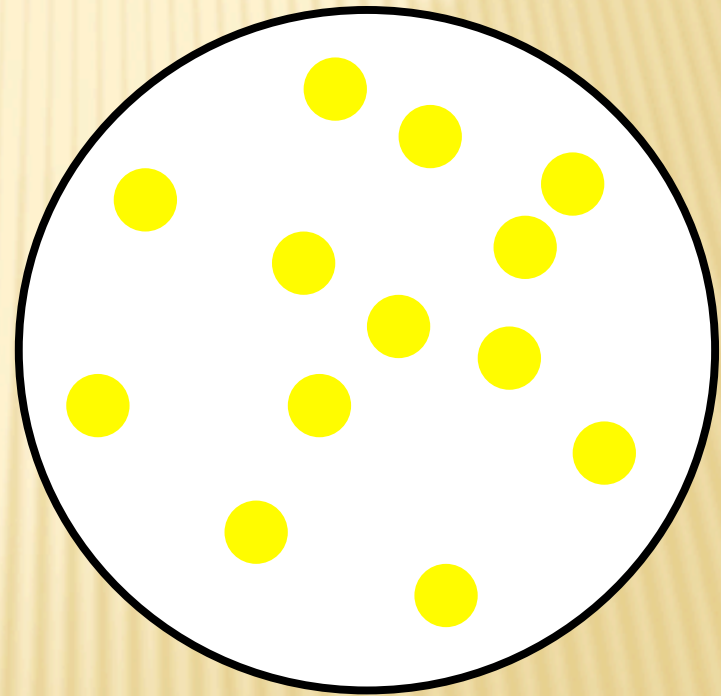


# SURVEY VS. CENSUS

Population A

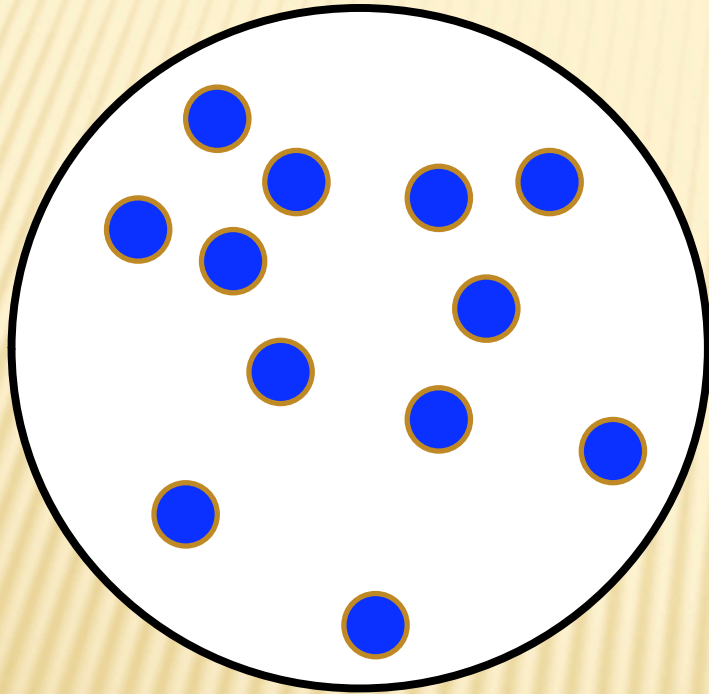


Population B

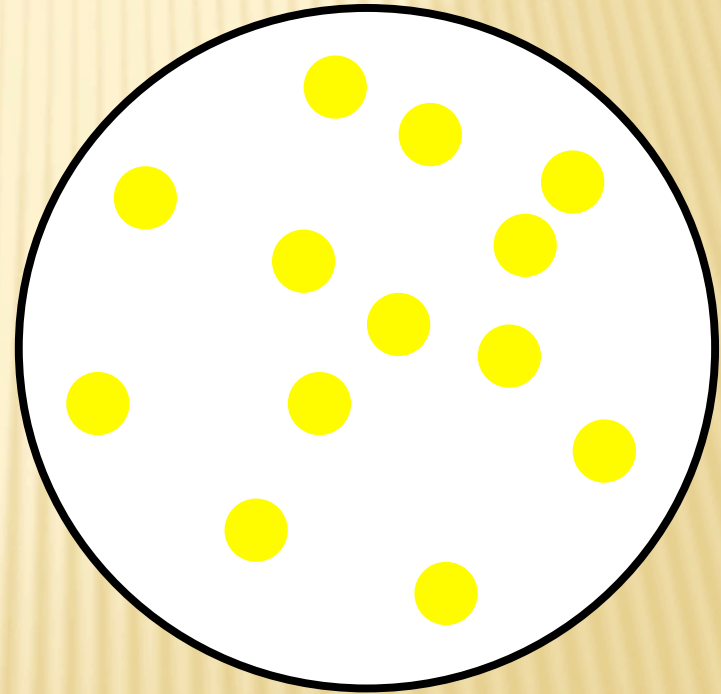


Sample = 

Population A

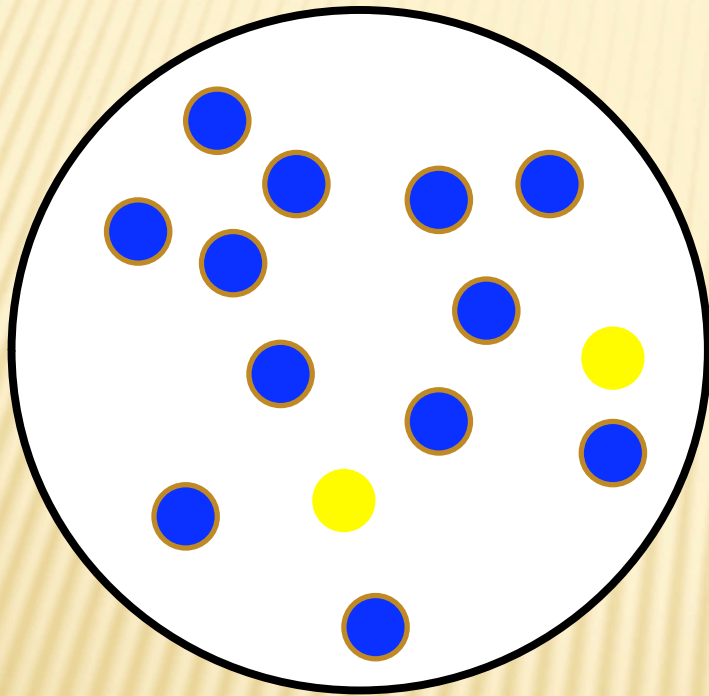


Population B

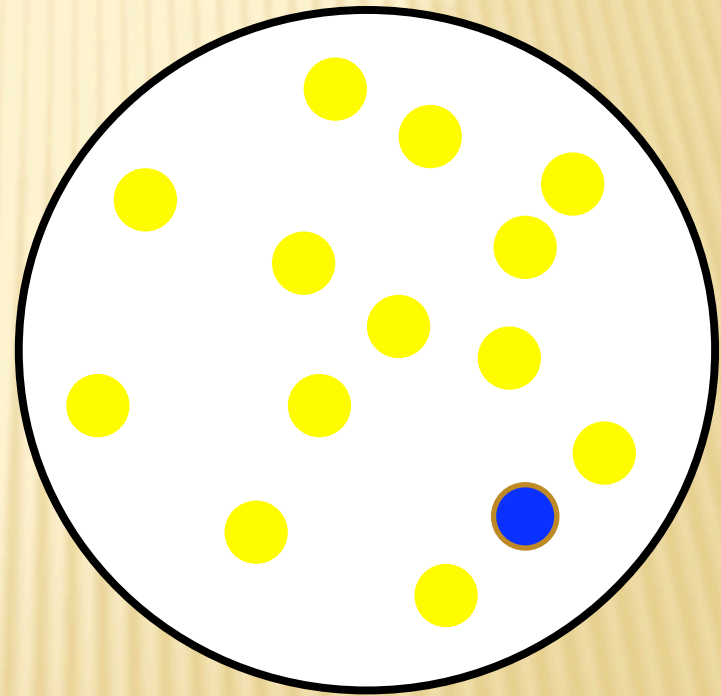


Sample = 

Population A



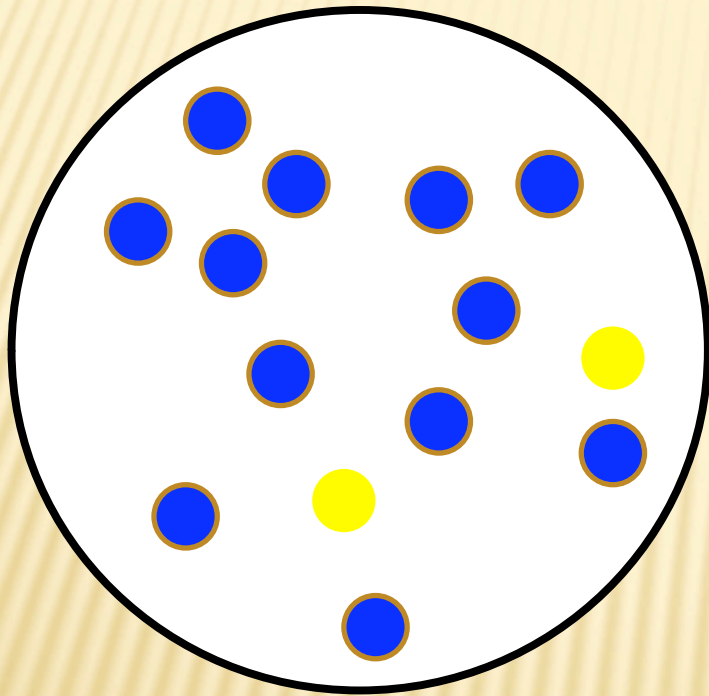
Population B



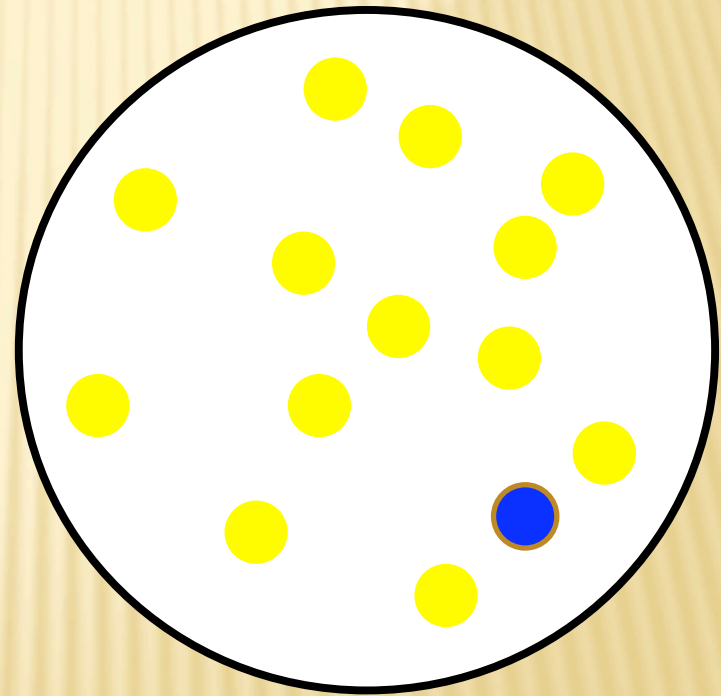
**Population vs. Individual**

Sample = 

Population A



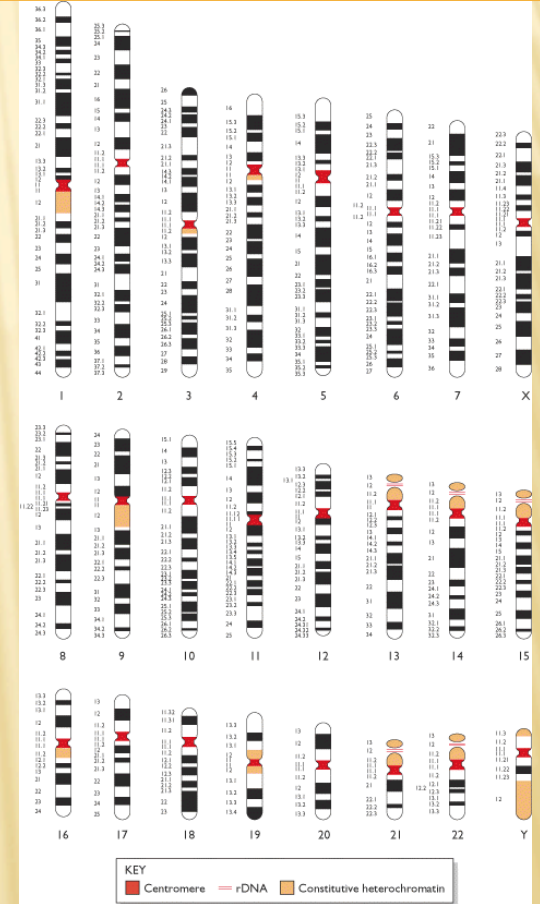
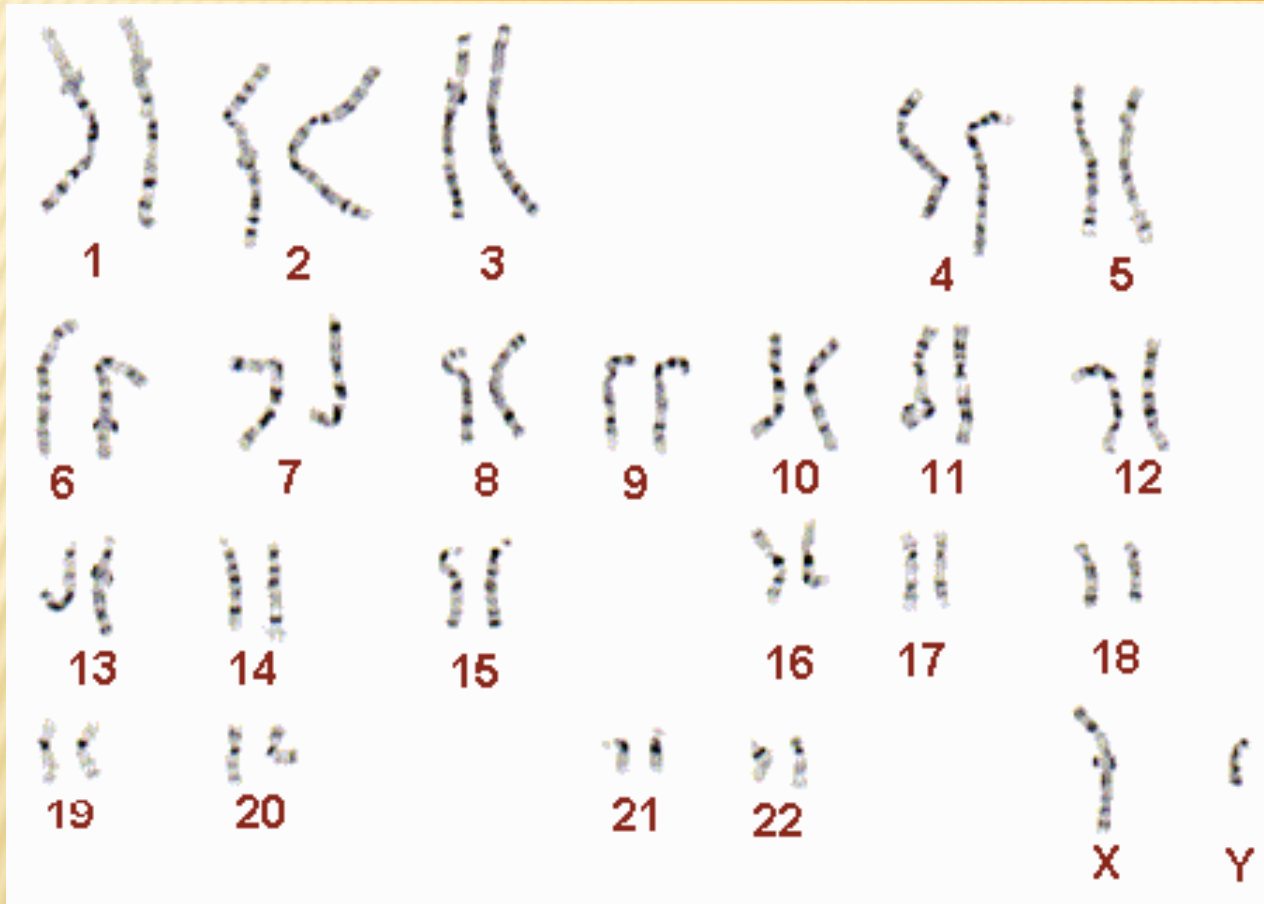
Population B




Haplotype  $\neq$  Population



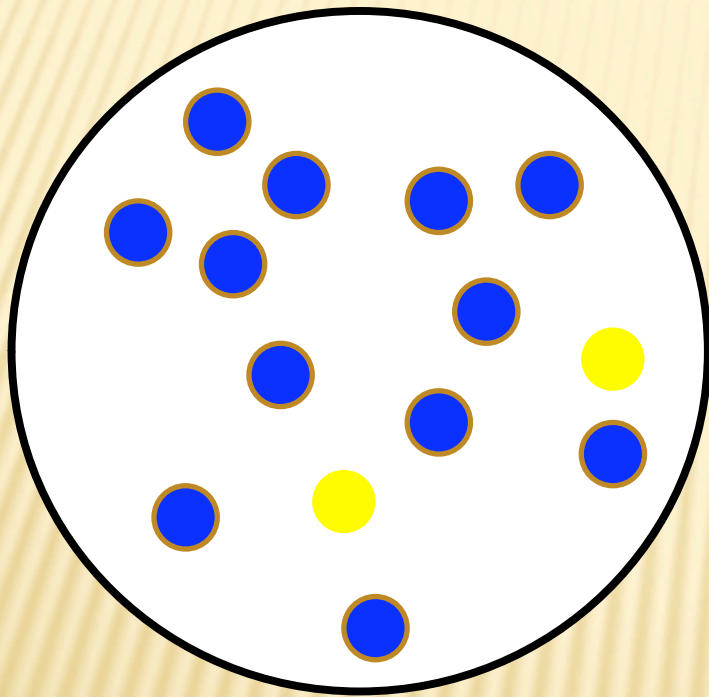
# YOUR GENOME



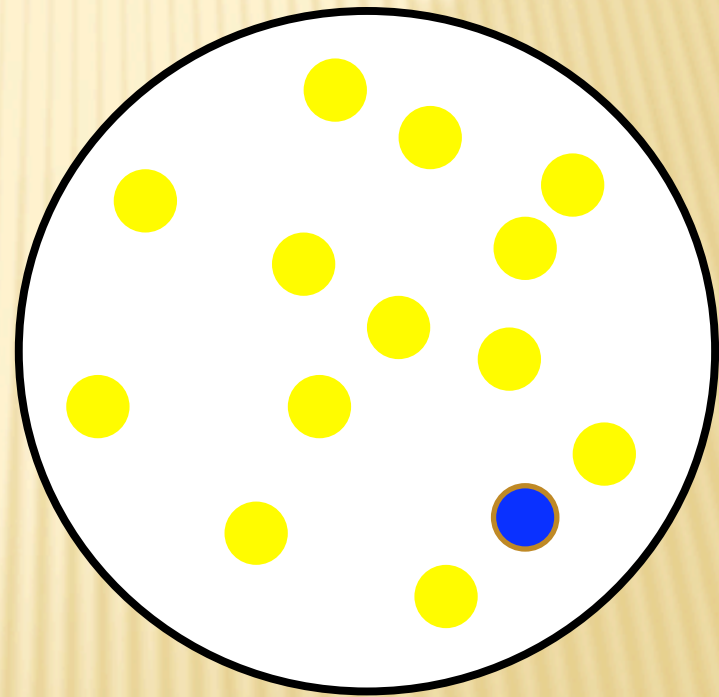
We have now entered the Genomics era

Sample = 

Population A



Population B



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# LIMITATIONS

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- ✘ The distribution of variation among human populations is still being researched
- ✘ What we historically have tested is only a part of an individual's genetic ancestry
  - + Y-Chromosome
  - + mtDNA
- ✘ An individual's genetic make up will likely represent a variety of lineages

# ACCURATE INTERPRETATION RELIES ON:

- ✘ The underlying patterns of variation
- ✘ How the diversity is surveyed
- ✘ Which populations are surveyed
- ✘ The statistical methods used to interpret the results

“Interpretation is always uncertain and statistical” (ASHG 2010)

# ASHG NOVEMBER 13, 2008

**The American Society of Human Genetics**  
*Ancestry Testing Statement*  
November 13, 2008

## **Scope**

Ancestry testing and ancestry estimation are utilized in a variety of settings. Ancestry testing is done on an individual basis, in an attempt to determine the ancestral origins or population(s) of origin for a person or family. Ancestry estimation is performed to infer biogeographical origins or admixtures of populations for research purposes. This document from the human genetics community focuses on issues pertaining to the assessment of genetic ancestry in both research and individual testing situations, the latter usually being performed in a commercial environment. We acknowledge that, in addition to these uses, genetic ancestry data are being utilized for other purposes. The forensic applications have drawn much attention, and along with other possible uses of these data, foster questions about privacy and the security of ancestry-related databases. It is yet unknown what the full potential of the applications and implications of genetic ancestry information might be, but The American Society of Human Genetics (ASHG) will continue to take a leadership role in discussions about the issues.

# SUMMARY

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- The concept of "ancestry"

“Genetic ancestry assessment often addresses the intermediate levels of ancestry that are usually imprecisely defined and identified.”

“every person has hundreds of ancestors going back even a few centuries and thousands of ancestors in just a millennium.”

“The genomic segments contributed by a particular ancestor are far from all being uniquely identifiable, so even if one’s genome has those specific genome contributions, identification of particular ancestry is always uncertain and statistical.”

# SUMMARY

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- Consumers and scientists have different reasons for pursuing assessment of genetic ancestry

“Most consumers are interested in using genetic ancestry testing to confirm or extend their knowledge of family genealogy.”

“population geneticists and anthropologists use these same technologies as used in DTC (direct-to-consumer) ancestry testing, but more often summarized on a population scale”

“Epidemiologists with an interest in identifying genetic associations with disease, in contrast, employ methods of ancestry inference either to control for complexities due to population stratification”

# SUMMARY

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- assessment of confidence or accuracy

“A major concern about the DTC ancestry testing business is that there is no quality assurance guarantee, and there is not even a mechanism to couple market performance with anything relating to accuracy.”



# SUMMARY

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- Recommendations

1. Because the science of ancestry determination has limitations, greater efforts are needed on the part of both industry and academia to make the limitations of ancestry estimation clearer to consumers, the scientific community, and the public at large. In turn, the public has the responsibility to avail themselves of information regarding ancestry testing and strive to better understand the implications and limitations of these assessments.

# SUMMARY

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- **Recommendations**

2. Additional research is required to further understand the extent to which the accuracy of genetic ancestry estimation is influenced by the individuals represented in existing databases, geographical patterns of human diversity, marker selection and statistical methods.

# SUMMARY

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- **Recommendations**

3. The complex consequences of ancestry estimation for people, families, and populations need to be assessed and guidelines should be developed to facilitate explanation and/or counseling about ancestry estimation in research, DTC and health care settings.

# SUMMARY

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- Recommendations

4. Scientists inferring genetic ancestry should consult or collaborate with scholars who have expertise in the historical, sociopolitical and cultural contexts needed to inform the processes and outcomes of their research and commercial efforts.

# SUMMARY

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- **Recommendations**

5. Mechanisms for greater accountability of the DTC ancestry testing industry should be explored.

# ASHG MAY 14, 2010

**COMMENTARY**

## Inferring Genetic Ancestry: Opportunities, Challenges, and Implications

Charmaine D. Royal,<sup>1,\*</sup> John Novembre,<sup>2</sup> Stephanie M. Fullerton,<sup>3</sup> David B. Goldstein,<sup>1</sup>  
Jeffrey C. Long,<sup>4</sup> Michael J. Bamshad,<sup>5</sup> and Andrew G. Clark<sup>6</sup>

Increasing public interest in direct-to-consumer (DTC) genetic ancestry testing has been accompanied by growing concern about issues ranging from the personal and societal implications of the testing to the scientific validity of ancestry inference. The very concept of “ancestry” is subject to misunderstanding in both the general and scientific communities. What do we mean by ancestry? How exactly is ancestry measured? How far back can such ancestry be defined and by which genetic tools? How do we validate inferences about ancestry in genetic research? What are the data that demonstrate our ability to do this correctly? What *can* we say and what can we *not* say from our research findings and the test results that we generate? This white paper from the American Society of Human Genetics (ASHG) Ancestry and Ancestry Testing Task Force builds upon the 2008 ASHG Ancestry Testing Summary Statement in providing a more in-depth analysis of key scientific and non-scientific aspects of genetic ancestry inference in academia and industry. It culminates with recommendations for advancing the current debate and facilitating the development of scientifically based, ethically sound, and socially attentive guidelines concerning the use of these continually evolving technologies.

# SUMMARY

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- There are now approximately 40 companies, based in various countries, that currently provide genetic ancestry testing to the public.
- The use of multiple marker systems
  - Y chromosome
  - mtDNA
  - Autosomal SNPs
- most DTC tests for ancestry offer lineage testing that uses mtDNA and Y-chromosome markers, DTC testing with autosomal markers, especially with whole-genome SNP chips, is becoming more common

# AUTOSOMAL SNPS

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- An interpretation of admixture from multiple populations
- Currently reference populations are not yet complete
- Inferences at this time will be limited by the existing reference data
- Testing services must communicate the level of uncertainty in the presentation of the inference



# SUMMARY

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- There is a potential to infer health or racial identity from the interpretation of this information
- Knowledge about genetic ancestry, particularly if undesirable and unexpected, can lead to the reshaping of group, familial, or personal identity.

## Positive or Negative

- Genetic ancestry inference could reveal the nuances of ancestry and dispel the notion of race in humans and/or the practice of equating race with ancestry
- inaccurate concept of human variation and increases the possibility of stigmatization and discrimination

# SUMMARY

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- **Recommendations**

1. Leadership of the human-genetics community, diverse in its interests and its own identities, should develop mechanisms for promoting thoughtful and rigorous use of genetic ancestry estimation in academic research
2. Interested scientific and scholarly societies should collaborate to convene a national roundtable discussion of DTC genetic ancestry testing.

**WHAT DO YOU THINK?**

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**THANKS!**

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