



University of Colorado
Anschutz Medical Campus

Genetics and Inclusion of Indigenous Populations

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Ethical and Regulatory Aspects of Clinical Research

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uhealth



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COLORADO CENTER FOR PERSONALIZED MEDICINE

From the Rez to a PhD and beyond



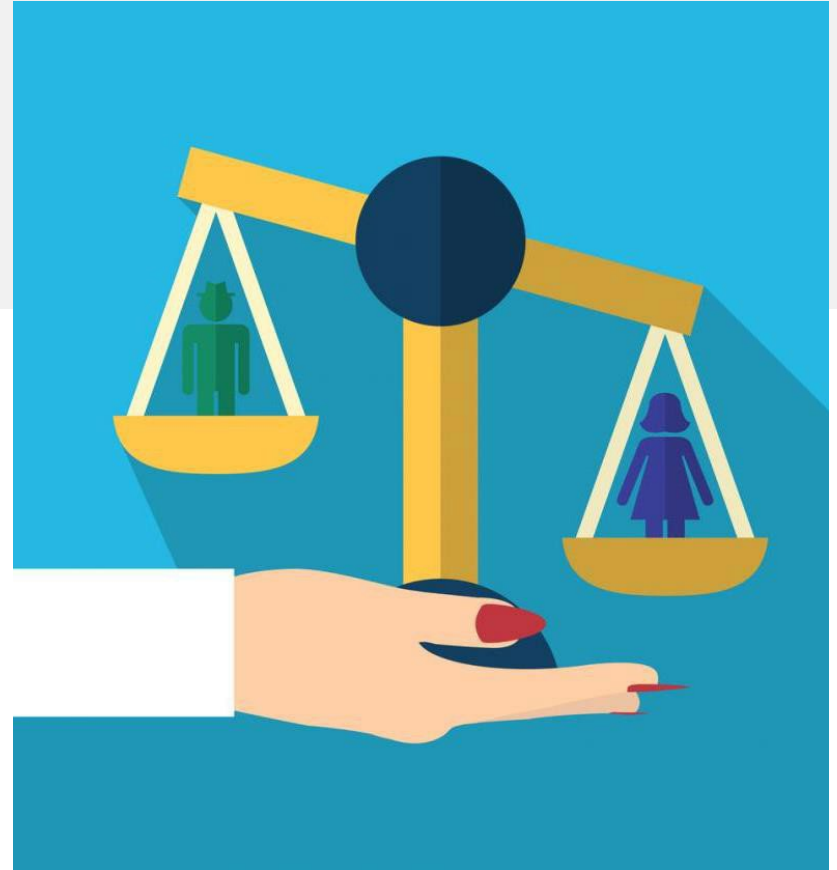
Focusing on questions that matter to my communities

- Focus on pharmacogenomics, bioethics, and community engagement
- Created community connections
- Really thought about what mattered in Native communities



Navigating an unequal playing field in STEM

- Financial woes
- Emotional distress
 - Self-doubt and uncertainty
 - Imposter Syndrome
 - Pressure, stress, loneliness
- Great sacrifices despite privileged experiences
 - Being away from home and family
 - Language/culture/traditions
- Unequal networks, training, and expectations



<http://www.thebigidea.co.uk/cost-gender-inequality/>

Changing the academy

Research has too often been done *to* and *about* Indigenous peoples, rather than *for*, *with*, or *by* Indigenous peoples.

- Tsose et al., 2021

My research program is broadly motivated by:

- Supporting equity, equality, and inclusion of diverse populations in genomic research
- Addressing disparities in health and health care
- Enhancing ethical research with Indigenous and other historically underrepresented communities

Bringing my culture into the laboratory



February 18, 2020: <https://news.cuanschutz.edu/>



Home > News > Blessing Ceremony Opens New Genomics and Health Research Lab

Blessing Ceremony Opens New Genomics and Health Research Lab

Researcher wants to ensure she shows respect for the Native Americans with whom she plans to collaborate



Claw Indigenous Genomics and Ethics Laboratory

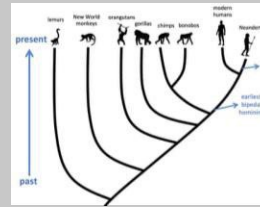
Pharmacogenomics research in diverse populations

1. Nicotine metabolism personalized medicine

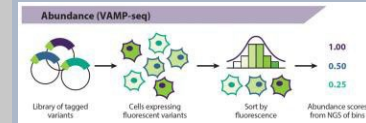
2. Cytochrome P450 Diversity



3. Evolution of Pharmacogenes



4. Understanding variants with multiplex assays



Cultural and bioethical research with Indigenous populations

5. Navajo Perspectives on genetic research



6. Ancient DNA ethics

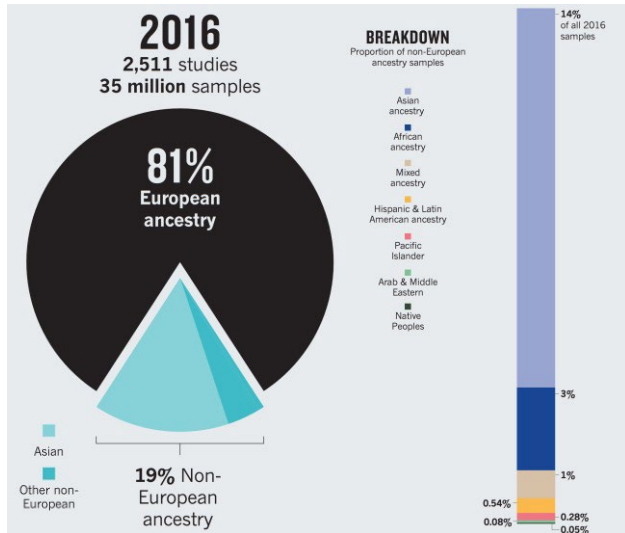


NATIVE AMERICAN DNA

7. Impacts and mentorship of Indigenous trainees



Underrepresentation in Genomic Research



- Biased understanding of which variants are important
- Potential for new health care inequalities



Bustamante et al., *Nature*, 2011; Popejoy and Fullerton, *Nature*, 2016; Mills and Rahal, *Comm. Biology*, 2019

There is a disconnect between genetic and genomic research and Indigenous communities



Members of the Havasupai Tribe, shown in 2010 looking at blood samples previously taken from them, had to fight for access to their samples.

A moratorium on Genetic Research conducted within the Navajo Nation was approved in April 2002.



Inbreeding Coefficients of the Ramah Navaho Population

A STUDY OF THE BLOOD GROUPS AMONG THE AMERICAN INDIANS

CLARA NIGG

From the Department of Bacteriology, University of Kansas, Lawrence

Received for publication August 1, 1925

In 1923 Coxa and Delbert (1) studied the percentage distribution of the four Landsteiner blood groups in the North American Indians in order to investigate the question of the relation of the American Indian race to the northeastern Asiatic races (Chinese, Japanese, Koreans), since it has been thought that the American Indian is of Mongolian origin. Their results in a series of 802 full-blooded Indians showed the following occurrence: group I 77.7 per cent, group II 20.2 per cent, group III 2.1 per cent, group IV one individual.

J.N. SPUHLER¹ AND CLYDE KLUCKHOHN²

Hereditary Nonpolyposis Colorectal Cancer in a Navajo Indian Family

Henry T. Lynch, Thomas J. Drouhard, Guy S. Schuelke, Karen A. Biscione, Jane F. Lynch, and B. Shannon Danes

Personalized Medicine - Pharmacogenetics

Personalized or Precision Medicine is an emerging field that uses an individual's genetic profile, environment, and lifestyle to aid in the diagnosis, prevention, and treatment of diseases.

BioMe™ BioBank Program

Your History Is Our Future™



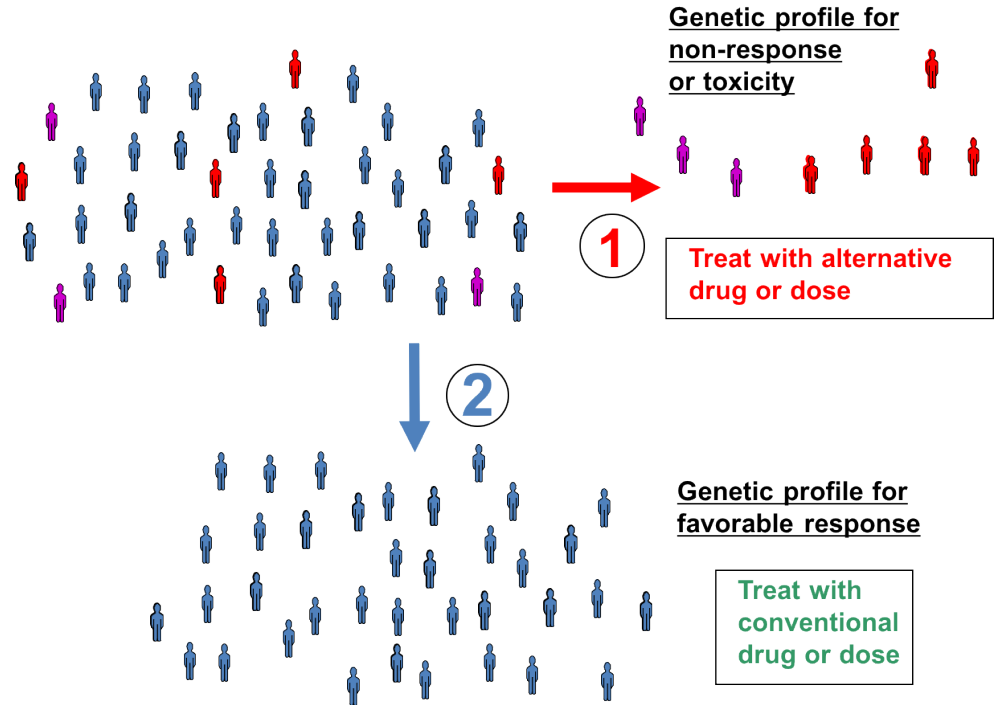
Colorado Center for Personalized Medicine

Biobank

Pharmacogenomics is the foundation for personalized medicine.

Diverse Populations and Promise of PGx

- Promote personalized medicine to optimize the quality of patient care
- Guide selection of best drug and dose for an individual
- Minimize adverse drug reactions
- Potential to improve health outcomes and reduce the cost of care



Genomic medicine for underserved communities

As more genomic studies are pursued,

- How can research be done in a respectful and culturally appropriate way with Native communities?
- How can we, as researchers, institutions, and funders, engage Native communities and tribes in genomic research?

As health applications are developed from genomic research,

- How can we assure that everyone benefits?
- How can we assure that disadvantaged populations are not harmed?

Precision Medicine may widen, not reduce, health disparities.

Past history

Benefits

Tribal sovereignty

Data-sharing policies



Consent

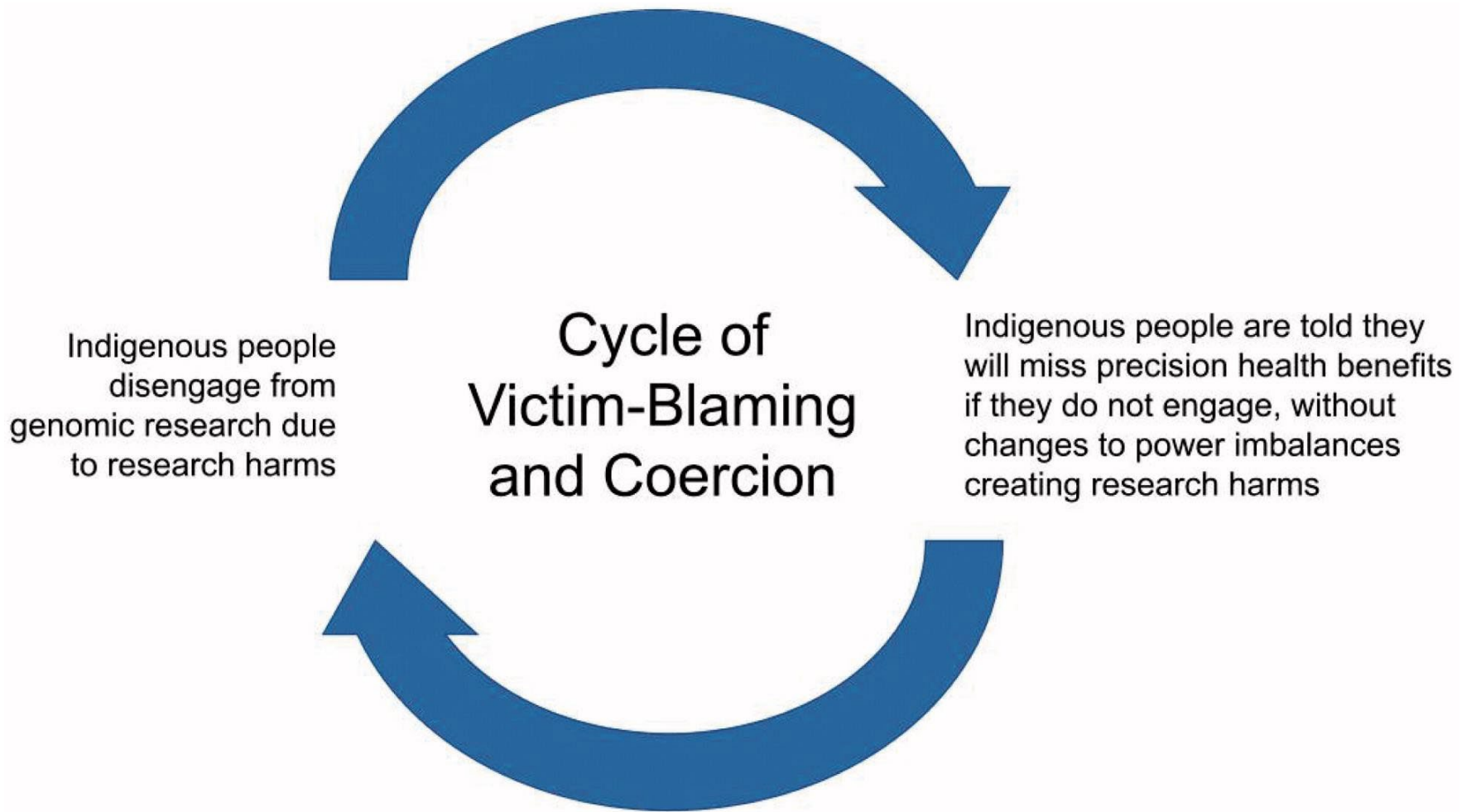
Intellectual property

Structural barriers

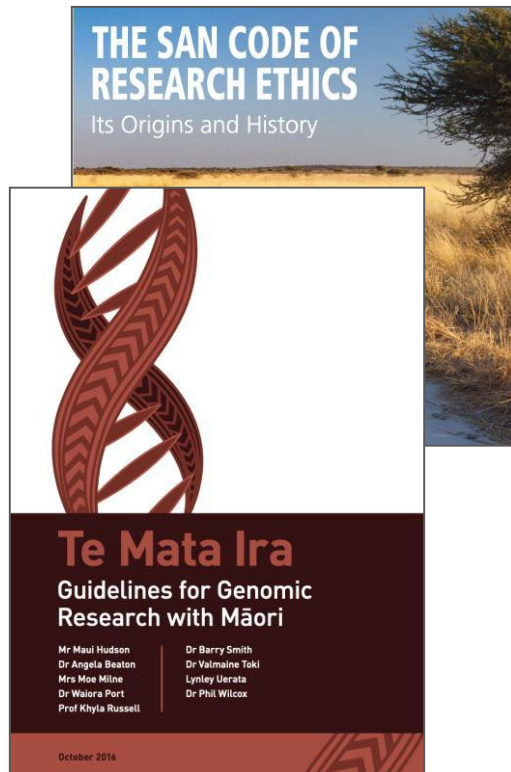
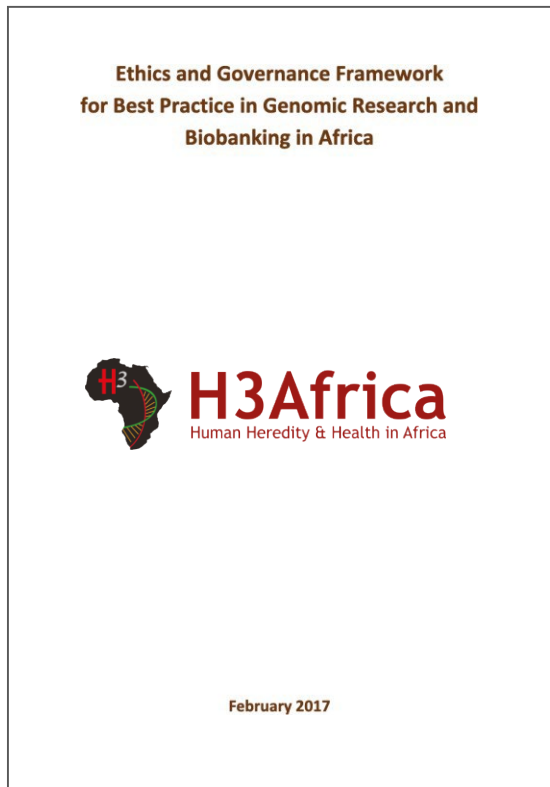
Social and racial barriers

COVID-19 Further Strains Care Disparities Among Native Americans

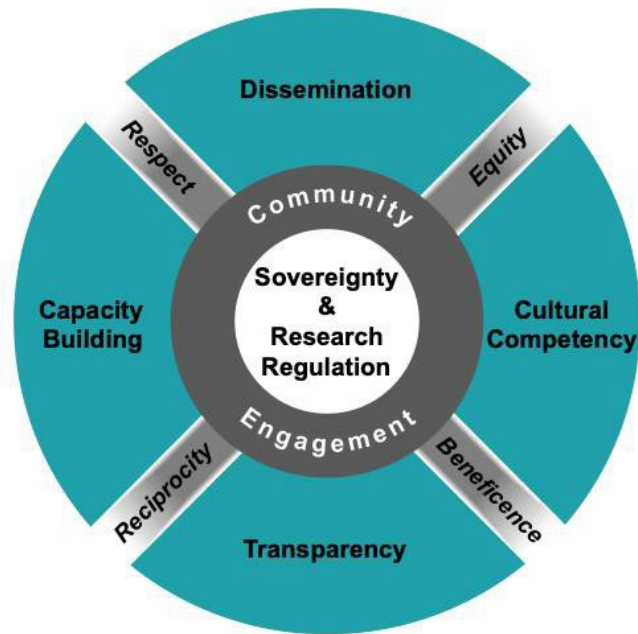
Community-based Genomic Research Approach



Recent advancement of community-specific research ethics guidelines



**Enhancing ethical genomic research
with Indigenous communities**



Moving toward Community-based Genomic Research



The Summer Internship for Indigenous Peoples (SING) Consortium hosts workshops to engage students and tribal members in genomics.

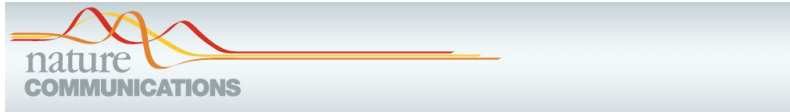


A collaborative approach to research

Challenge:
What would/does your study look like when community is involved?



Ethical research in Contemporary and Ancestor Indigenous populations








PERSPECTIVE

DOI: 10.1038/s41467-018-05188-3

OPEN

A framework for enhancing ethical genomic research with Indigenous communities

Katrina G. Claw ¹, Matthew Z. Anderson ^{2,3}, Rene L. Begay ⁴, Krystal S. Tsosie ^{5,6}, Keolu Fox⁷, Summer internship for Indigenous peoples in Genomics (SING) Consortium & Nanibaa' A. Garrison ^{8,9}

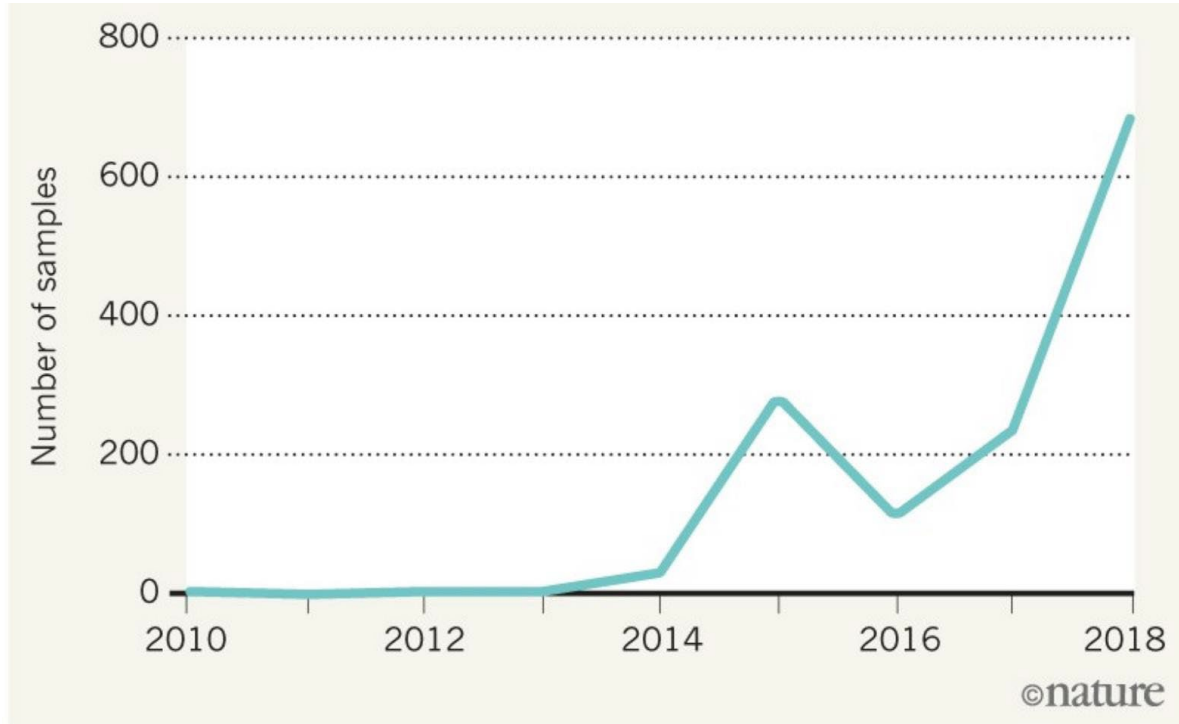
ASHG GUIDANCE

Fostering Responsible Research on Ancient DNA

Jennifer K. Wagner,^{1,2,3,14,*} Chip Colwell,^{2,4} Katrina G. Claw,^{2,5} Anne C. Stone,^{2,6} Deborah A. Bolnick,^{2,7,8} John Hawks,^{2,9} Kyle B. Brothers,^{1,2,10,14} and Nanibaa' A. Garrison^{1,2,11,12,13,14}



Research using ancient DNA has increased rapidly in the last 8 years



Sources: E. Callaway *Nature* **555**, 573–576 (2018); David Reich



NAGPRA was enacted in 1990 to return cultural items and ancestors to Native American tribes.

Ancient Populations: Responsible aDNA Research

- Indigenous concerns about aDNA
- Existing policies related to paleogenomics
- Practical Guidance on Responsible Research
 - Recommendations
 - Key questions for *Geneticists* and *Communities*
 - Case Studies

Recommendations

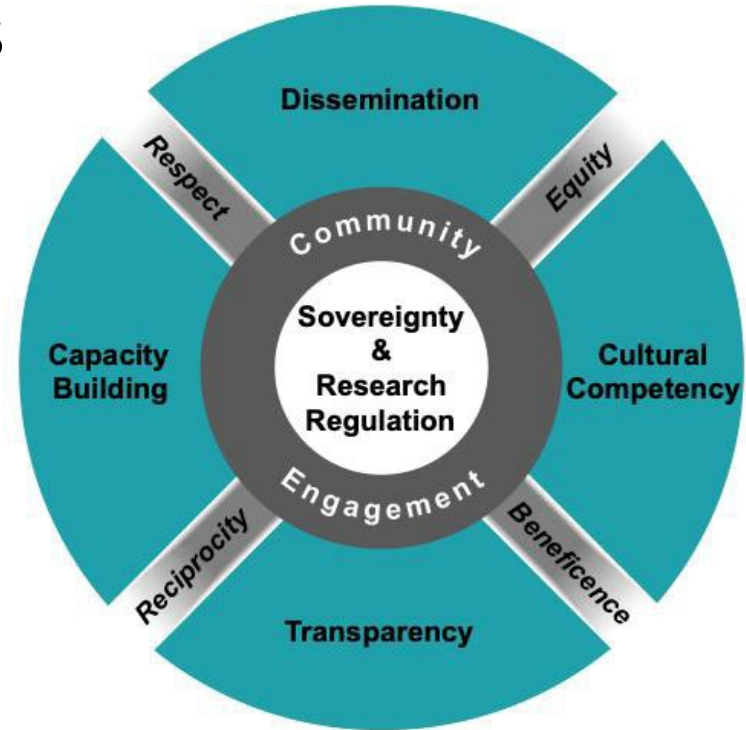
1. Formally Consult with Communities
2. Address Cultural and Ethical Concerns
3. Engage the Community and Support Capacity Building
4. Develop Plans to Manage Data and Report Results
5. Develop Plans for Long-term Responsibility and Stewardship

aDNA
Ethics

<http://www.adnaethics.org/>

Enhancing ethical genomic research with Indigenous communities

1. Understand existing regulations
2. Foster collaboration
3. Build cultural competency
4. Improve transparency
5. Support capacity
6. Disseminate research findings

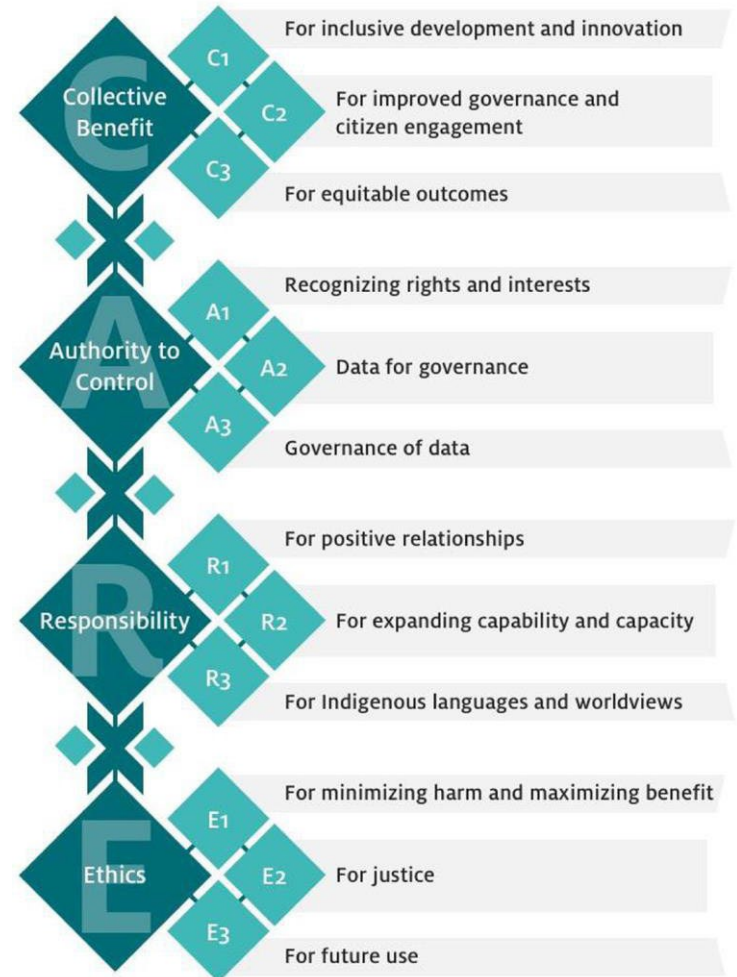


Principles proposed to support greater Indigenous diversity and inclusion in genomic research



Indigenous genomic data sovereignty and governance in PM

- Collection, ownership and application of data and specimens
- Consider data *stewardship* rather than *ownership*
- DNA on Loan concept

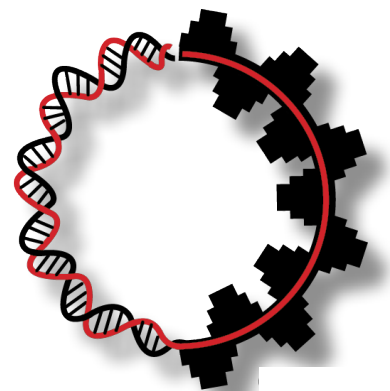


The CARE Principles for Indigenous Data Governance

Inclusion and ethics in Indigenous communities

- A shift toward Community-based Genomic Research is needed
- Multiple guidelines/principles can be used to engage in ethical genomic research
- Ensure that Indigenous communities govern and benefit from genetic and genomic research

Ahéhee' (Thank you)



Claw lab members: Carissa Sherman, Leah Nez, Amber Nashoba, and Kaja Aagaard

Tribal partners:

Southcentral Foundation, Strong Heart Study, Confederated Salish and Kootenai tribes, Navajo Nation, Metlakatla First Nations, individual tribal members

CU Boulder

Fernando Villanea

U. Illinois

Ripan Mahli

SING Consortium

aDNA ethics group

UCLA

Nanibaa' Garrison

U. Montana

Erica Woodahl

NWA-PGRN

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