Genetic Research with Alaska Native People: Lessons Learned and Future Possibilities

National Institute on Minority Health and Health Disparities
Director’s Seminar Series - November 12, 2019

Denise A. Dillard, Ph.D., (Inupiaq) Director of Research

65,000 voices
Objectives

- Share lessons learned over a decade of engagement with the Alaska Native community about ethical, legal and social implications of genetic research.
- Present findings from recent and ongoing genetic research by Southcentral Foundation, a tribal health organization in Anchorage, Alaska.
- Present ideas to increase participation of individuals from groups typically underrepresented in genetic research.
Alaska Tribal Health System (ATHS)

- A voluntary affiliation of over 30 Alaskan tribes and tribal organizations providing health services to Alaska Native/American Indian people
- Each tribe or tribal health organization serves a specific geographical area
- The entire ATHS serves approximately 130,000 Alaska Native/American Indian people and provides comprehensive services across the entire continuum of care.
Alaska Tribal Health System

Facts
- 239 Federally Recognized Tribes (Villages)
- Over 60 Villages in the Southcentral/Anchorage Service Unit
- Alaska Native Health Board: Statewide health advocate voice
- Alaska Native Tribal Health Consortium: Statewide specialty and tertiary health care services Regional seat on board as governance
Alaska is larger than Texas, California and Montana combined.
History

1971 – Alaska Native Claims Settlement Act

1982 - Cook Inlet Region Inc. (CIRI) establishes SCF as a 501(c)(3) nonprofit

1985 - SCF enters into its first self-management contract (dental, optometry, community health) with the government

1998 - Assumes management of the region’s entire primary care system

1999 - Assumes co-ownership and co-management of services for the Alaska Native Medical Center

2000 - Introduces relationship-based Nuka System of Care: integrated care teams, same day access to care and much more

Today - Baldrige award recipient 2011 & 2017; 65,000 customer-owners; 1,600 employees (more than 50% Alaska Native or American Indian); 65+ programs
SCF Asked the Community
Unfriendly staff, long waits, no customer input, inconsistent treatment, dirty and run-down facilities
Access to Own Provider, Culturally Appropriate Care, Cleaner and Better Facilities
Nuka System of Care

- Value-driven system with customer-owners (patients) at the center
- Empanelment to a primary care team with family match encouraged
- Same-day access
- Data driven learning environment
Vision

A Native Community that enjoys physical, mental, emotional and spiritual wellness

Mission

Working together with the Native Community to achieve wellness through health and related services
Goals

Shared Responsibility
Commitment to Quality
Family Wellness
Operational Principles

Relationships between customer-owner, family and provider must be fostered and supported.

Emphasis on wellness of the whole person, family and community (physical, mental, emotional and spiritual wellness).

Locations convenient for customer-owners with minimal stops to get all their needs addressed.

Access optimized and waiting times limited.

Together with the customer-owner as an active partner.

Intentional whole-system design to maximize coordination and minimize duplication.

Outcome and process measures continuously evaluated and improved.

Not complicated but simple and easy to use.

Services financially sustainable and viable.

Hub of the system is the family.

Interests of customer-owners drive the system to determine what we do and how we do it.

Population-Based systems and services.

Services and systems build on the strengths of Alaska Native cultures.
History of Research in Alaska

- 1950s Air Force Aeromedical Laboratory Thyroid Function Study (Radioactive Iodine-131)
- 1979 Barrow Alcohol Study

“The Inupiat Eskimos of Alaska’s North Slope, whose culture has been overwhelmed by energy development activities, are ‘practically committing suicide’ by mass alcoholism… researchers said here yesterday. The alcoholism rate is 72 percent among the 2,000 Eskimo men and women in the village of Barrow, where violence is becoming the most frequent cause of death as a result of ‘the explosive and self-destructive abuse of alcohol,’ the researchers said. ‘Offshore oil development is expected to peak in 2010 or 2015’ … one of the researchers, said at a news conference. ‘We don’t see the Eskimos surviving till then. This is not a collection of individual alcoholics, but a society which is alcoholic, and therefore facing extinction.’”
SCF Governance of Research

- SCF research policy developed in 2005
  - Requires approval of research with SCF customer-owners, within SCF facilities, and/or involving SCF employees
  - Initial review by research committee with researchers, medical directors, and Vice Presidents
  - Approval by SCF Board of Directors (100% Alaska Native)

SCF Research Review Criteria

- Alignment with SCF vision, mission, key points, goals, and objectives.
- Appropriate depiction and involvement of AN/AI people.
- Appropriate topic selection and handling.
  - Sensitive topics
- Quality of research design.
- In compliance with SCF Guidelines for Researchers
SCF Research Review Process

- SCF review and approval must occur before any recruitment or data collection begins.
- Review and approval is required prior to any dissemination of findings.
- Review and approval is required for:
  - Research concept
  - Protocol
  - Presentation of preliminary findings
  - Final reports and manuscripts
SCF Research Department

- Established in 2007
- 25 employees
- 17 Alaska Native or American Indian

www.southcentralfoundation.com/services/research
Guided by three factors:

• Health priorities and interests of the customer-owner population.
• Guidance and direction from the board of directors and senior organizational leadership.
• Funding opportunities.
Ethical and Cultural Implications of Specimen Banking Among Alaska Native People


Background

- Biological samples have been used for research studies in Alaska for over 60 years.
- Samples have been stored in the Alaska Area Specimen Bank (AASB) since 1948.
- In 2004, Alaska Native Tribal Health Organizations assumed shared ownership and management of AASB with the Centers for Disease Control and Prevention’s Arctic Investigations Program.
Study Purpose

- Explore views of biobanking among Alaska Native community members and leaders across Alaska using community based participatory research (CBPR) approach.
Methods

- We approached tribal health organizations (THOs) to partner and guide the study in their regions.
- Community liaisons were hired to lead study recruitment.
- 29 focus groups were conducted in 14 locations -- participation from 82 community members and 81 tribal leaders.
- Data were analyzed in ATLAS.ti using a grounded theory approach.
What do Alaska Native people think about specimen collection

We talked to people in 14 communities across Alaska in gatherings called focus groups. We had focus groups with younger people, older people and Tribal leaders.

In each focus group, we asked questions such as:

“What do you think about researchers collecting specimens from you for studies?”

We also asked more specific questions like:

“What should happen to a specimen in the bank if the person who gave it passes away?”

We then looked at what people said for patterns or important ideas mentioned more than once.

WHAT DO YOU THINK ABOUT RESEARCHERS COLLECTING SPECIMENS?

People brought up many ideas when explaining what they thought. Some talked about past research or medical care in their community or family. Some felt mistreated by researchers, doctors, or others from the United States government.

Others mentioned their Alaska Native culture and that specimens were very special and not just blood.

Continued on page 4, “View”
There were concerns about the research that could be done in the future with new technology. Some were also concerned about research that singled out Alaska Native people.

People also said many things about how this kind of research may help Alaska Native people and their health. It could help now and in the future even if it didn’t help them personally.

WHAT WOULD YOU WANT TO KNOW WHEN DECIDING WHETHER TO JOIN A STUDY?

People said they would want to know many things when thinking about joining a research study using specimens.

- Many said they’d want to know more about the research when deciding whether to join.
- Most said they wanted to know what the results were when the study was done.
- Many people had questions about the specimens and how they’re stored in the bank.
- People were curious about how long a specimen is good for and how the bank keeps them safe.

WHO SHOULD GIVE PERMISSION?

We also asked questions about what should happen with specimens already in the specimen bank when permission isn’t clear. This would include when someone who gave the specimen passes away.

Some people thought the specimens should be destroyed and others thought the specimen bank should keep them.

More than a few people thought a family member or other chosen person should decide.

We also asked how tribal health organizations should be involved in giving permission to researchers.

Some people said each individual should make the decisions.

Others thought tribal health organizations should help decide what research should be done in the region.

We will share this information with tribal leaders who may use it to make future decisions about research.
Recommendations for Researchers

- Gain awareness of past research and surveillance projects.
- Actively dialogue with community leaders and community members about your research and other research conducted in the community.
- Work with the community to determine how to treat collected data and specimens with respect.
- Provide clear, jargon free information in the informed consent including a set data and specimen destruction date.
Recommendations for Researchers

- Give participants options through tiered or multi-layered consent
- Share information on the study progress throughout the study.
- Consider the return of individual results as well as sharing how individual contribution impacted the findings of the overall study.
- Have community leaders to review and comment on study findings prior to peer review publication and presentation.
Northwest-Alaska Pharmacogenomics Research Network (NWA-PGRN)

U01GM092676 Thummel & Burke (PIs)
NIGMS
2010-2015

- University of Washington
- University of Montana
- University of Alaska Fairbanks/Center for Alaska Native Health
- Confederated Salish and Kootenai Tribes
- Yukon-Kuskokwim Health Corporation
- Southcentral Foundation
Perspectives on Pharmacogenetic Research and Clinical Testing Among Alaska Native People

- Four focus groups (total N=32) with Alaska Native community members
- Views elicited about pharmacogenetic research in general and for treatment of cardiovascular disease, breast cancer, depression and nicotine addiction

Pharmacogenetics *generally endorsed* for potential rewards of improved individual health, health system sustainability, and community capacity building, *but...*

Pharmacogenetics also viewed as a “double-edged sword” with *potential to harm and heal* in Alaska Native communities.

Clinical utility and social acceptability of pharmacogenetics *requires 8 conditions be met* to ensure that potential rewards outweigh potential risks.
<table>
<thead>
<tr>
<th>Contingency Domain</th>
<th>PGx could be acceptable IF:</th>
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<tbody>
<tr>
<td>Efficacy</td>
<td>• It is more clinically effective than existing treatments</td>
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<tr>
<td>Access</td>
<td>• It does not result in rationing of primary healthcare services</td>
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<td>Scale</td>
<td>• It benefits the majority of patients with a particular condition.</td>
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<td>Values</td>
<td>• It does not conflict with personal or community worldviews</td>
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<td>Engagement</td>
<td>• It directly involves AN/AI people as drivers of PGx education, research and practice</td>
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<tr>
<td>Social Responsibility</td>
<td>• It does not perpetrate views of AN/AI people as “entitled” or receiving special benefits</td>
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<tr>
<td>Health Promotion</td>
<td>• It does not increase health disparities, as has occurred with other introduced technologies</td>
</tr>
<tr>
<td>Participant and Community Protection</td>
<td>• It is voluntary, confidential, and uses culturally appropriate consent with community oversight</td>
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“I think it (participation in pharmacogenetic research) should be voluntary, but the first thing I start thinking of is exactly who would be trying to look at in your health record, who is watching, who is looking at, if they’re doing genetic testing only on certain areas or certain people and not leaving it up to other people—just like I’ve heard about Natives being just tested in (other regions of Alaska). People working at that hospital know they’re doing this right now. And whether it’s voluntary or not, sometimes it’s just done anyway, in my opinion. And there’s, for me, a lot of privacy (concerns) on what else are they looking at . . . who would be watching the people that are supposedly watching us? Or, what is it used for? Is it used correctly?”

“Genetics is a lot of doors to be opened, to have that kind of research there is a very good thing I believe the hospital should really look into. I’d like to see something like that. I’m tired of seeing all this space age stuff happen in the Lower 48 and all over. Why don’t we lead the way, you know? Alaska leading the way in this genetic thing would be a good door to open for a hospital.”
Exploring Pathways to Trust

- Tribal perspectives on data sharing discussed at meeting sponsored by NWA-PGRN Feb 2012
- Strong support for efficient research which translates knowledge to benefit
- BUT… benefits of research often poorly defined, indirect & long-term versus immediate potential harms like stigma
- Data sharing policies fall under a trust relationship with the federal government requiring meaningful tribal consultation

Variation in Genes Controlling Warfarin Disposition and Response

- Convenience sample of Alaska Native/American Indian people 18 years of age or older (n=380 SCF, 250 Yukon Kuskokwim Delta)
- Subset (n=188 SCF, 94 YK-Delta) selected for deep sequencing of CYP2C9, VKORC1, CYP4F2, CYP4F11, and GGCX genes.

Variation in Genes Controlling Warfarin Disposition and Response

- Tiered consent - medical record review, storage in AASB with agreement to recontact for future use
- Consent identified specific genes
- No identifiers sent to UW or other laboratories
- Specimens returned or destroyed
- Self-reported heritage and classification into regions
- Agreement to terms of the SCF Research Agreement in terms of tribal review and approval, ownership
- Two relatively common, novel, potentially function-disrupting variants in CYP2C9 (M1L and N218I) which, along with CYP2C9*3, CYP2C9*2 and CYP2C9*29, predict decreased CYP2C9 activity.
- High frequencies of the lower-warfarin dose VKORC1 haplotype and the higher-warfarin dose CYP4F2*3 variant.
### CYP2C9: Regional Differences

<table>
<thead>
<tr>
<th>Allele</th>
<th>Interior</th>
<th>Northern</th>
<th>Southeast</th>
<th>Southwest</th>
<th>Western</th>
<th>AI</th>
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<tbody>
<tr>
<td>*2 (R144C)</td>
<td>4.1</td>
<td>1.2</td>
<td>3.6</td>
<td>5.9</td>
<td>2.1</td>
<td>8.3</td>
</tr>
<tr>
<td>*3 (I359L)</td>
<td>5.4</td>
<td>4.1</td>
<td>7.1</td>
<td>5.8</td>
<td>0.3</td>
<td>8.3</td>
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<tr>
<td>M1L</td>
<td>1.4</td>
<td>1.8</td>
<td>0.0</td>
<td>0.8</td>
<td>6.3</td>
<td>0.0</td>
</tr>
<tr>
<td>N218I</td>
<td>5.4</td>
<td>2.4</td>
<td>0.0</td>
<td>0.8</td>
<td>3.8</td>
<td>0.0</td>
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<tr>
<td>P279T</td>
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<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>2.1</td>
<td>0.0</td>
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- founder effects, genetic drift or selection can account for regional differences.
AN/AI customer-owners on long-term warfarin therapy (> 6 mo)

Buccal swab and medical record review for demographics, warfarin dose, comorbidities, medications

Targeted genotyping for variants in the VKORC1, GGCX, CYP2C9, CYP4F2 and CYP4F11 genes

Association between stable therapeutic dose and genetic variation, with adjustment for covariates

Heritage and Stable Warfarin Dose

**Hypothesis**: Difference in VKORC1 genotype frequencies in these heritage groups is driving the observed difference in stable warfarin dose.
VKORC1-1639 and Stable Warfarin Dose

- Heritage is no longer significant after controlling for VKORC1-1639 genotype
- 34% of dose variability explained by VKORC1 genotype

Trend with Stable Warfarin Dose (Significance)

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<tr>
<th></th>
<th>Multivariate</th>
<th>Univariate</th>
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<tr>
<td></td>
<td>-1.7 mg/day</td>
<td>-2.1 mg/day</td>
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<tr>
<td>(p = 1.4e-05)</td>
<td>(p = 1.3e-06)</td>
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VKORC1-1639 G>A Genotype

<table>
<thead>
<tr>
<th></th>
<th>G/G</th>
<th>G/A</th>
<th>A/A</th>
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<tr>
<td>n</td>
<td>9</td>
<td>25</td>
<td>16</td>
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Avg Daily Dose (mg)
Genetic Variation and Tamoxifen Metabolism

- 42 AIAN females receiving tamoxifen
- Associations between CYP genotype and steady-state plasma concentrations of:
  - Tamoxifen
  - Endoxifen
  - 4-hydroxytamoxifen (4-OH-Tam)

CYP2D6 and Tamoxifen

- AI/AN women with breast cancer who were intermediate and poor metabolizers of CYP2D6:
  - Had significantly lower plasma concentrations of metabolites, endoxifen and 4-OH-Tam
  - Had lower metabolic ratios, notably the endoxifen/tamoxifen metabolic ratio
  - May require increased tamoxifen dose, use of aromatase inhibitors, direct administration of endoxifen
Warfarin and Tamoxifen

- Novel variants submitted to dbSNP
- Genetic findings for warfarin supported what clinicians already knew
- No additional genetic testing for customer-owners on warfarin based upon research findings
- Standard clinical testing for variants among customer-owners with cancer
 Role genetics can play in substance abuse treatment among Alaska Native people
AN/AI’s dependent on nicotine regulate intake to maintain nicotine levels

Lower CYP2A6 activity (lower activity genotypes) associated with:
  - lower tobacco intake, dependence, and difficulty quitting
  - lower risk of lung cancer risk
Specific Aims

- **Aim 1:** Explore stakeholder preferences and needs regarding pharmacogenetics (PGX) & PGX use to guide tobacco cessation
- **Aim 2:** Identify and characterize polymorphic CYP2A6 and CYP2B6 variation
- **Aim 3:** Identify relative contributions of patient, clinical, and genetic factors to successful tobacco cessation
Perceptions of Pharmacogenetic Research to Guide Tobacco Cessation

- 20 AI/AN current or previous users of tobacco, 12 providers, 9 system leaders
- Viewed use of genetics in healthcare favorably but ‘hard to do right’
- Genetic research posed moderate degree of risk
  - Privacy, misuse, discrimination, conflict of interest, wasted resources, unanticipated findings

### Box 1. Paraphrased questions relevant to informed consent for pharmacogenetic research.

- How would the research staff collect the genetic material from the participant?
- How would the lab actually do the genetic testing?
- What would the study cost and how may the study improve medical expenditures in the future?
- How would the study respond to the organization’s whole health philosophy?
- How exactly would the information guide healthcare decisions?
- What is the history of previous pharmacogenetic research at the organization?
- On what medications has pharmacogenetic research already been conducted?
- How would the genetic information from the study be shared?
- Would the results be included in the electronic health record and who can see the results?
- What protections of genetic information are in place?
Pharmacogenetics of Nicotine Metabolism

- 521 Alaska Native/American Indian adults
- Completed demographic and tobacco use questionnaire, provided blood and urine specimen
- Sequenced CYP2A6 and CYP2B6 genes to identify known and novel gain, reduced, and loss-of-function alleles

- CYP2A6*4 and reduced function CYP2A6*9 alleles high frequency in Northern/Western subgroups and in Lower 48/Interior subgroups, respectively.

- Reduced function CYP2B6*6 observed in all subgroups.

- Novel, predicted reduced function CYP2B6 variant relatively high frequency Southeastern subgroup.
Explanatory Models of Alcohol Misuse and Sobriety

Aim 1

• Describe *explanatory models* of alcohol misuse and sobriety among Alaska Native people and other key stakeholders (providers and leaders) in a tribal health system.

Aim 2

• Examine the *acceptability and perceived utility of different treatment strategies* to reduce alcohol misuse and encourage sobriety.
Perceptions of Alcohol Misuse and Sobriety

- Individual interviews with 34 customer-owners 21 and older, 4 Tribal leaders
- Focus groups with 20 providers (medical, behavioral, substance abuse) and 12 clinical and administrative leaders

Major Themes

- **Colonialism** – harm due to forced relocation, boarding school, prohibitions against cultural practices and language, loss of traditional knowledge, introduction of alcohol
  - When you lose your family nucleus and you’re being bombarded by another culture to the point of breaking you to remake you in their image, it created tremendous trauma. And then this happened for generations . . . . (customer-owner)

- **Structural factors** - economic hardship; transportation challenges; lack of employment; local option laws; lack of sober spaces and activities
  - It seems like in the villages – ‘specially dry ones – people tend to overindulge. Many think, “Oh, it’s because you can’t bring it in. You have to quickly have it and get rid of it.” And it kinda becomes a culture, it seems like, of – that’s the norm. Like you just drink it ‘til it’s all gone. (customer-owner)
Major Themes

- **Social alienation** - feeling/perceiving a lack of belonging and connection with other people increases risk
  - *Maybe [people who misuse alcohol] feel that they don’t have anything to be sober for.* (customer-owner)

- **Social norms** - high prevalence of alcohol misuse and early childhood exposure, mass media and stereotypes, binge drinking associated with paydays, Alaska (not only Native) motif of “work hard, play hard”

- **Familial patterns** - intergenerational patterns of alcohol misuse, some avoid alcohol altogether
  - *A curse, handed down* (customer-owner)
Coping with negative emotions - modulate painful emotions/experiences, often due to past trauma, “self-medicating” PTSD or mood disorders
  • Numb the pain
Beliefs about alcohol and AN/AI people - ANAI people are uniquely vulnerable to AUD since biologically bodies can’t process alcohol, genetic risk, cultural lack of “knowing how to drink”
Explanatory Models

Adapted Broadus and Evans (2015) Public Attitudes About Alcohol (PAAS) instrument

<table>
<thead>
<tr>
<th>Our Model</th>
<th>Our Definition</th>
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<tbody>
<tr>
<td>Disease</td>
<td>Alcohol misuse occurs because of biological processes that we can adequately control only through abstinence and medical treatment. It is not about the individual making better choices (moral) or improving their coping or relationship skills (psycho-social) or changing their surroundings (environmental) or finding a good balance with alcohol (nature).</td>
</tr>
<tr>
<td>Environmental</td>
<td>Alcohol misuse occurs because of a person’s surroundings/place-based variables excluding influences of other people or social norms (psychosocial).</td>
</tr>
<tr>
<td>Moral</td>
<td>Alcohol misuse occurs because people make bad (immoral) choices that reflect poor self-control and/or wrong-headed values.</td>
</tr>
<tr>
<td>Nature</td>
<td>Alcohol misuse is a natural part of human experience that can correct itself without intervention and/or total abstinence.</td>
</tr>
<tr>
<td>Psychosocial</td>
<td>Alcohol misuse occurs because the person lacks adequate supportive individual coping skills and/or social roles or relationships.</td>
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</tbody>
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Predictors of Drug Response in Rural and AI/AN Populations

P01GM116691 Thummel & Burke (PIs)
NIGMS
2016-2021
What is the molecular mechanism behind altered bleeding time and does diet and gene variation affect antiplatelet drug response?

- Determine whether variation in CYP4F2 and PEAR1, RBC EPA+DHA concentration, and RBC d\textsuperscript{15}N is associated with plasma sP-selectin levels.
- Among groups with extreme RBC levels of EPA+DHA
  - Examine platelet EPA/DHA, TXB2 and 20-HETE concentrations and determine whether associations are modified by CYP4F2 genotype and dependent on CYP4F2 enzyme function.
  - Test platelet aggregation under basal and aspirin-treated conditions, and whether those associations are modified by CYP4F2 and PEAR1 gene variation.
Aim 1. Evaluate the impact of pre- and post-natal exposure to n-3 PUFAs, and the CPT1A arctic variant, on the health of Alaska Native infants.

Aim 2. Develop and evaluate a risk prediction model that identifies and quantifies the contribution of CPT1A genotype, n-3 PUFA status, and other known risk factors to infectious disease-related infant outcomes.
Community Engaged Research Towards Precision Medicine

R01HG009500 Hiratsuka, Boyer, Woodahl (PIs)
NHGRI/NIGMS
2017-2020

- Support Precision Medicine research through culturally respectful dialogue, empiric data collection, and deliberation with rural and urban AIAN community members and tribal representatives in Alaska and Montana.

- Address three complex and important challenges: (1) alignment of PMR with tribal health priorities; (2) return of PMR results to participants and communities; and (3) data stewardship
Lessons Learned

Acceptability varies according to:

- Who is conducting the research, who is considering participation, who is reviewing and approving the research;
- What is the focus of the research, what types of data are being requested;
- When research is occurring, when results may be applied for benefit;
- Where the research is being conducted, where data and specimens will be stored; and
- How the research is conducted from development of the idea to implementation.
Lessons Learned

May need to alter or omit practices considered standard elsewhere

- Non-tiered, broad consent
- Storage of specimens in national repositories
- Documenting pedigrees
- Genome-wide sequencing
- No return of individual or collective results
- Assessing stigmatizing conditions, use of stigmatizing language
- More limited assessment of contextual or environmental variables
Lessons Learned

- Alaska Native people and tribal health systems see the potential benefits of genetic research and don’t want to be left out
- Ongoing community engagement is required
- Academic-tribal partnerships can offer rich bidirectional learning and mutual benefit
- Resources required for research and to translate findings into clinical care must consider the needs of the whole Alaska Native community
Increasing Future Participation

- Respect tribal sovereignty
- Follow the lead of the community
- Be transparent
- Be humble
- Acknowledge harms
- Build local capacity
- Make a long-term commitment
- Be flexible and creative
Contact Information

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Aleut
Quyanaa
Alutiiq
Igamsiqanaghalek
Siberian Yupik
Gunalchéesh
Tlingit
Awa'ahdah
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Haida
Quyanaa
Alutiiq
Quyanaq
Inupiaq
Aw'aahdah
Eyak
Háw’aa
Haida
T’oyaxsm
Tsimshian
Gunalchéesh
Tlingit
Tsinaen
Ahtna Athabascan
Chin’an
Dena’ina Athabascan
Qağaasakung
Aleut
Quyanaa
Alutiiq
Quyanaq
Inupiaq
Aw’aahdah
Eyak
Háw’aa
Haida
Thank You!