PRECISION MEDICINE
Pharmacogenomics Collaborative Research – A Tribal Perspective
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Confederated Salish and Kootenai Tribes
Tribal Territories in Montana
Boundaries as defined by the Fort Laramie Treaty of 1851, and the Flathead and Blackfeet Treaties of 1855.
- Reservations today shown in red.
- Star indicates location of tribal capital.
• CSKT Tribal Health Department
• University of Montana Skaggs School of Pharmacology
• University of Washington School of Pharmacy
• Southcentral Foundation, Anchorage, Alaska
• Yukon-Kuskokwim Health Corporation serving the Yup’ik People living in the Yukon Kuskokwim Delta in Alaska
• Group Health Cooperative, Seattle (affiliate, not direct partner in current grant)
ORIGIN STORY

• UM and local oncologist recognized lack of representation of American Indian patients in studies
• They were doing clinical trials on cancer medications
• Wondered if there would be a difference in the AI population they served
• Approached Tribal Health with this question in 2007
• Small study (unpublished) funded by local Institute (Montana Cancer Institute Foundation grant) to begin looking at specific P450 enzymes to determine if there was any genetic variability
• Dr. Erica Woohahl joined the UM School of Pharmacy shortly after partnership formed

• NIH U01 grant for a large multi-center Community Based Participatory Research project funded in 2010
  • Resulted Northwest Area Pharmacogenomics Research Network (NWA-PGRN)
  • Established Community Pharmacogenomic Advisory Council (CPAC) in 2010

• P01 Funding for additional related projects in 2016 – five year grant
COMMUNITY BASED PARTICIPATORY RESEARCH

CBPR offers a model for pursuing trustworthy research with AI/AN communities.
COLLECTING SAMPLES IN THE COMMUNITY
CURRENT ACTIVITIES

Community-based activities

• Solicit input from CSKT members and leaders about the precision medicine research partnership and best practices for this type of research in the community.
• Tribal priorities for precision medicine research
• Identify educational and training needs
• Discuss how the research could be implemented in Tribal Health clinics
• Discuss policies related to data stewardship and return of results to research participants

• Goals:
  • Continuation of monthly Community Pharmacogenetics Advisory Council (CPAC) meetings
  • Seek community expertise about precision medicine research in three settings:
    1. Local discussions at each partner site: 1) CSKT people in Montana and 2) Yup’ik people in Alaska and 3) Southcentral Foundation patients in Alaska
    2. Cross-site discussions across all three partner sites
    3. National discussions: host a national meeting about precision medicine research with AIAN communities (follow-up meeting to the one held in February 2012 described in the “Exploring Pathways to Trust: A Tribal Perspective on Data Sharing” paper below)

• Participants:
  • CPAC members and Tribal Health and Tribal Council participants
**CURRENT ACTIVITIES**

**Genetic and environmental effects of antiplatelet therapies (i.e. aspirin)**

Genetics and diet can have a major effect on how well antiplatelet therapies work.

- **Goals:**
  
  Understand the role of genetics and dietary intake of fatty acids on aspirin therapy

- **Participants:**
  
  - 250 blood samples from CSKT participants for sequencing of select genes and measuring biomarkers of fatty acid dietary intake and platelet function.
  
  - 50 CSKT participants in a study to measure diet effect on response to aspirin (the 50 participants will be selected from the 250 participants above: 25 people with low biomarkers for fatty acid consumption and 25 people with high biomarkers). A blood sample will be taken before and after participants take one week of aspirin.
CURRENT ACTIVITIES

Management of warfarin (coumadin) therapies and other drugs used for anticoagulation

• Genetics and diet can have a major effect on how well anticoagulant therapies work.

• Goals:
  • Understand the role of genetics and dietary intake (particularly vitamin K intake primarily from green leafy vegetables) in long-term management of anticoagulant therapy.
  • Discuss and develop strategies for in-house testing of genetic and dietary markers to guide physicians’ dosing of warfarin and other anticoagulant medications.

• Participants:
  • Identify CSKT participants who will be started on warfarin therapy. Measure baseline INR (a measurement of coagulation) and vitamin K levels at time of recruitment, and follow INR over the course of 2 years or the discontinuation of warfarin treatment.

• Discuss with Tribal Health providers and staff about the possibility of establishing in-house testing capabilities for the future.
CURRENT ACTIVITIES

Management of vitamin D deficiency and impact on health outcomes

• Understand how vitamin D deficiency impacts a variety of health outcomes (i.e. cardiometabolic diseases, mental health, osteoporosis, cancer).
• Primary sources of vitamin D are diet and sunlight exposure

• Goals:
  • Understand genetic differences in vitamin D processing in the body.
  • Examine differences in vitamin D levels due to the variations in diet (traditional vs. modern diet) and sunlight exposure (seasonal differences in winter and summer).

• Participants:
  • Analyze the genes important in vitamin D processing in CSKT participants that may alter how much vitamin D a person has in their system.
  • Measure vitamin D levels in CSKT participants seasonally. Participants will have vitamin D measured twice: once in winter, once in summer.
  • Evaluation strategies to treat vitamin D deficiency, for instance vitamin D supplements or combination of traditional foods.
CURRENT PROGRESS

Participants:
• 521 CSKT participants recruited for blood draws
• 42 CSKT participants recruited for focus groups
• 17 health care providers (Tribal Health and non)
• 4 CSKT participants recruited for tamoxifen study
• 77 CSKT participants recruited for antiplatelet therapy and vitamin D study
Community Pharmacogenetics Advisory Council (CPAC):

- Established in November 2010
- 48 CPAC meetings
- Genetic Education Workshop – May 2011
- Digital storytelling Workshop – February 2012
- Genetic Education Workshop – March 2017
- Rotating membership
CURRENT PROGRESS: PUBLICATIONS

Genetic sequencing of four cytochrome p450 enzymes:
• “Pharmacogenetics in American Indian Populations: Analysis of CYP2D6, CYP3A4, CYP3A5, and CYP2C9 in the Confederated Salish and Kootenai Tribes”
  • Accepted April 24, 2013 in Pharmacogenetics and Genomics

Tribal perspectives on sharing of genetic data - paper came from the Exploring Pathways to Trust meeting February 15-17, 2012 in Suquamish, WA
• “Exploring Pathways to Trust: A Tribal Perspective on Data Sharing”
  • Accepted April 7, 2014 in Genetics in Medicine

Description of academic-community pharmacogenetic partnerships in Montana and Alaska:
• “Pharmacogenetic Research in Partnership with American Indian and Alaska Native Communities”
  • Accepted May 30, 2014 in Pharmacogenomics
CURRENT PROGRESS: PUBLICATIONS

Health care provider interviews on pharmacogenetic testing in rural and tribal settings
• “Pharmacogenomics in diverse practice settings: implementation beyond major metropolitan areas”
• Accepted December 3, 2014 in Pharmacogenomics

Description of CPAC partnership with interviewers from CPAC members, researchers, and physicians
• “Partnership with the Confederated Salish and Kootenai Tribes: Establishing an Advisory Committee for Pharmacogenetic Research”
• Accepted April 15, 2015 in Progress in Community Health Partnerships: Research, Education, and Action

Genetic testing to improve tamoxifen treatment in breast cancer patients
• Manuscript preparation underway
LESSONS LEARNED

• CBPR model ideal for engaging tribal communities
  • CPAC
  • Engagement of Tribal Council
  • Local Tribal Health Department equal partner
• Appears that genetic variations in one tribal could have clinical significance
  • The first report of gene resequencing of drug-metabolizing enzymes (specifically cytochrome P450s) in an AIAN community
  • Tamoxifen findings pending publishing
• Questions remain around data sharing, sampling storage/disposal and return of results
  • Ongoing discussions in CPAC and goal of current project to bring stakeholders together for further discussion
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Questions??