Pharmacogenetic research in partnership with American Indian and Alaska Native communities

Pharmacogenetics is a subset of personalized medicine that applies knowledge about genetic variation in gene–drug pairs to help guide optimal dosing. There is a lack of data, however, about pharmacogenetic variation in underserved populations. One strategy for increasing participation of underserved populations in pharmacogenetic research is to include communities in the research process. We have established academic–community partnerships with American Indian and Alaska Native people living in Alaska and Montana to study pharmacogenetics. Key features of the partnership include community oversight of the project, research objectives that address community health priorities, and bidirectional learning that builds capacity in both the community and the research team. Engaging the community as coresearchers can help build trust to advance pharmacogenetic research objectives.

Keywords: Alaska Native • American Indian • community-based participatory research • genetics • indigenous populations • North American Indians • pharmacogenetics • pharmacogenomics • underserved populations

Pharmacogenetic research seeks to identify genetic contributors to interindividual variability in drug disposition and response, with the goal of developing tests that can be used to individualize therapy and improve patient outcomes [1–3]. Some pharmacogenetic tests are already in wide use and many promising applications are under active study. As with other areas of medical innovation, however, access for historically underserved populations is a concern. Medically underserved populations in the USA are designated by four criteria: lower number of primary care physicians per 1000 people, increased infant mortality rate, higher percentage of the population with incomes below the poverty level and higher percentage of the population aged 65 years or over, as compared with the average [4]. These populations have disproportionate representation of minority groups, including African–Americans, Hispanic Americans, and American Indian and Alaska Native (AI/AN) people.

Several barriers could prevent or limit the implementation of pharmacogenetics

among underserved communities. Some of these include awareness and preparedness of primary care physicians, difficulties incorporating pharmacogenetics into clinical practice decision-making, and lack of funding and reimbursement for test costs. Mistrust of genetic research, including concerns about privacy, misuse of DNA specimens and fear of stigmatizing interpretations of genetic information, can be a barrier to the use of pharmacogenetics in minority populations [5–8]. Among AI/AN communities in particular, two well publicized cases have spurred misgivings about genetic research: the Havasupai in Arizona (AZ, USA) and the Nuu-Chah-Nulth in British Columbia (Canada) both agreed to specific genetic studies but later discovered that other unauthorized studies were conducted with their samples, some of them offensive to the communities [9,10]. These examples reverberated among AI/AN and First Nations communities and resulted in a resolution of the National Congress of American Indi-

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ans affirming tribal ownership of health-related data [11]. They also added to a legacy of mistrust resulting from a long history of governmental actions aimed at appropriation of tribal lands, abrogation of sovereignty and forced acculturation [12]. Inappropriate, exploitive and harmful research was a part of this legacy [13,14]. While this history has led to an appropriate mistrust of research unrelated to tribal interests, AI/AN communities are supportive of research that addresses their priorities, when it is carried out with appropriate tribal oversight [12]. Unlike other types of genetic studies, such as migration and consanguinity studies undertaken with the Havasupai samples, pharmacogenetic research represents an opportunity to address health concerns [7]. Pharmacogenetic testing holds the potential to optimize dosing for individual patients in order to improve drug response and limit adverse drug reactions, but appropriate testing protocols cannot be defined without knowledge about the prevalence of pharmacogenetic traits within the population.

Pharmacogenetics with AI/AN communities

Substantial heterogeneity has been observed across world populations in the genes that predict drug dosing, response and toxicity [15,16]. Little is known, however, about the prevalence of pharmacogenetic variation in AI/AN populations. A review of genetic variability in CYP450 drug-metabolizing enzymes among indigenous people in the Americas identified a small number of studies that documented differences in allele frequencies among indigenous populations compared with other populations [17]. Unfortunately, the data were sparse, particularly for North America; the search identified only two Canadian studies and no US studies.

Since AI/AN populations have traditionally not been a part of pharmacogenetic research, the possibility for implementing pharmacogenetic testing to guide drug therapy is limited. There are 5.2 million AI/AN people in the US living in the west (40.7%), south (32.8%), midwest (16.8%) and northeast (9.7%) [18]. The incidence of several common diseases requiring chronic or long-term drug therapy, including diabetes, cardiovascular disease and many cancers, is disproportionately high in AI/AN communities [19–21]. Communities are motivated to identify solutions to these health disparities, but wary of researchers who may have research interests poorly aligned with community needs [22–24].

Community-based participatory research (CBPR) offers a model for pursuing trustworthy research with AI/AN communities through the institution of partnerships between researchers and community leaders for the design and implementation of a research agenda [25–27]. CBPR values communities as partners in all

aspects of the research process, helps to assure that research is aligned with the health priorities of a community, and also lends itself to powersharing and bidirectional learning and teaching [25,28–32]. While most genetic research does not currently address questions with direct application to healthcare, pharmacogenetic research is an exception, because it provides the foundation for clinical applications that could be of particular benefit should the results be shown to improve drug response and avoid adverse drug reactions. Thus, pharmacogenetics fits well within a research agenda focused on the needs of communities experiencing health disparities.

In an effort to develop constructive approaches to the inclusion of AI/AN populations in pharmacogenetic research, community and academic partners in Alaska (AK, USA), Montana (MT, USA) and Washington (WA, USA) have joined together to form the Northwest-Alaska Pharmacogenomics Research Network (NWA-PGRN). The NWA-PGRN partners include the Confederated Salish and Kootenai Tribes (CSKT, MT, USA), Southcentral Foundation (SCF, AK, USA), Yukon-Kuskokwim Health Corporation (YKHC, AK, USA), Montana Cancer Institute Foundation (MT, USA), Group Health Research Institute (WA, USA), Center for Alaska Native Health Research (CANHR) at the University of Alaska Fairbanks (AK, USA), University of Montana (MT, USA) and University of Washington (WA, USA) [7]. A key feature of each of the academic–community partnerships is the use of CBPR methods to assure that the research is based on the expertise of all partners and focused on benefiting AI/AN people. We report here on the approaches we have used and the initial results of these efforts.

Academic–community partnerships to study pharmacogenetics

The academic–community partnerships within the NWA-PGRN share a history of working together before discussions about pharmacogenetic research occurred, each of which are discussed later in more detail. No research activities were initiated without full discussion of the potential clinical benefit of pharmacogenetics and after we had reached agreement with our partners that the research was of value to them. Owing to the partnerships we have developed that inform our research approach, we have not faced issues or resistance to community participation and support for the pharmacogenetics research.

Tribal authorities provide oversight of the pharmacogenetic research process at each community partner site, and the procedures for review and approval of new projects, grant applications, manuscript submissions and presentations differ. Each community partner

chooses whether to participate in specific aims of the research project, works with researchers to tailor the research to their health priorities and has the authority to stop the research. The community approval and oversight processes for the different sites within NWA-PGRN are summarized in [Table 1](#).

The partner site in Montana began through discussions between researchers at the University of Montana and Montana Cancer Institute Foundation and healthcare providers at CSKT Tribal Health and Human Services. CSKT providers identified research in pharmacogenetics as a way to address health disparities in their community, particularly in the area of cancer treatment. The CSKT people reside on the Flathead Reservation in northwestern Montana and are comprised of three tribes, the Bitterroot Salish, Upper Pend d'Oreille and the Kootenai. Research is conducted at various sites on and off the Reservation including Tribal Health clinics, powwows and health and career fairs. The CSKT do not have their own institution

review board (IRB), so the University of Montana IRB reviews, approves and monitors human subjects research, with additional levels of tribal oversight and approval that include research approval by the CSKT Tribal Council.

In Alaska, one of the partner sites is SCF, a healthcare system owned, administered by and serving AI/AN people living in Anchorage, the Matanuska–Susitna Valley and nearby villages. The SCF system includes a research department that, among other research objectives, implements pharmacogenetic research. Tribal authorities via the SCF Board of Directors require research at SCF to include both a community-based review as well as a human subjects review. In addition, an executive committee of the organization provides oversight of all research activities.

The second partner site in Alaska arose from a long-standing partnership between CANHR at the University of Alaska Fairbanks and Yup'ik communities within the Yukon-Kuskokwim (YK) Delta. CANHR

Table 1. Community approval and oversight processes at the three community sites within the Northwest-Alaska Pharmacogenomics Research Network.

NWA-PGRN community partner	Approval processes
CSKT (MT, USA)	<p>Institutional review board approval from the University of Montana (MT, USA)</p> <p>Continuous consultation with the Community Pharmacogenetics Advisory Council to provide tribal input in research design, review manuscripts, approve new study objectives, and discuss strategies for dissemination of research progress and findings</p> <p>Department Head and Medical Director from CSKT Tribal Health and Human Services review study aims to make sure research goals align with their health priorities and review manuscripts to ensure results are presented in a culturally appropriate manner</p> <p>CSKT Tribal Council reviews and approves research proposals, grant submissions and publication of research results</p>
SCF (AK, USA)	<p>Concept proposal submitted by SCF research team to designated tribal leadership to ensure proposed study is in line with mission and vision of the institution</p> <p>Protocol drafted by SCF research team with input from academic partners, SCF customer-owners, tribal leadership, and SCF management to ensure institutional support and resources necessary for implementation</p> <p>Proposal submitted to Alaska Area institutional review board</p> <p>SCF Research Oversight Committee, SCF Executive Board, and Alaska Native Tribal Health Consortium reviews and approves research</p> <p>Research status updates provided to the tribal leadership and community</p> <p>Continuous consultation with the tribal leadership in the design and execution of research and dissemination of results</p> <p>Abstracts and manuscripts submitted to tribal leadership</p>
YKHC (AK, USA)	<p>Institutional review board approval from the University of Alaska Fairbanks (AK, USA)</p> <p>Medical Director of YKHC presents research proposals to the YKHC Human Studies Committee for review and approval and recommendations are made to the Executive Board of Directors for final approval</p> <p>All manuscripts and presentations are reviewed by the YKHC Human Studies Committee for cultural appropriateness and approved by the Executive Board of Directors</p> <p>Consultation with the Community Planning Group for tribal guidance in dissemination of research progress and findings</p>

CSKT: Confederated Salish and Kootenai Tribes; NWA-PGRN: Northwest-Alaska Pharmacogenomics Research Network; SCF: Southcentral Foundation; YKHC: Yukon-Kuskokwim Health Corporation.

has been conducting health and genetic research in the delta for more than 10 years. Much of the research has been foundational, with the eventual goal of translation into specific ways to improve disease prevention and treatment. CANHR investigators and the community identified pharmacogenetic research as a promising and feasible way to achieve some of those objectives. With implementation of the research agenda, human subject protocols are reviewed and approved by the University of Alaska Fairbanks IRB, the YKHC Human Studies Committee and the YKHC Executive Board of Directors, which consists of tribal representatives elected by the 58 tribes of the YK Delta region. Additionally, each community is represented by a federally recognized tribal council that also reviews and approves research.

The sites in Montana and Alaska work together with researchers in Washington at the University of Washington and Group Health Research Institute. The three community partners in the NWA-PGRN work with the researchers to identify the research priorities, research methods and forms of dissemination. Communities also identify whether they want to participate in each research objective. The partnership is one of reciprocity and bidirectional learning in which community members educate researchers on appropriate research practices and the potential of the research to impact their communities, while simultaneously building capacity to support or lead health research within the community. Lastly, all public presentations and publications derived from the research partnership in Montana and Alaska undergo tribal review and approval.

One way in which CBPR practices have been used within the NWA-PGRN is the formation of community advisory groups to strengthen the academic–community partnerships. These advisory groups assure tribal input into the research project and facilitate the dissemination of research findings within the partnering community. These groups are called the Community Pharmacogenetics Advisory Council (CPAC) for the CSKT working with the University of Montana and the Community Planning Group (CPG) for the YK communities working with CANHR. The interactions between researchers and the community advisory groups provide a forum to discuss tribal interest in pharmacogenetic research, culturally appropriate research practices and the potential for the use of pharmacogenetic testing in healthcare settings. An important aspect of these groups is the bidirectional learning between researchers and the community. To increase community knowledge and involvement in the pharmacogenetics project, members of the CPAC and CPG have participated in numerous informal

and formal educational workshops including Genetics Education for Native Americans (GENA®; Native American Cancer Initiatives, CO, USA) and nDigiDreams Digital Storytelling (NM, USA). In addition, researchers learn from community members about their culture, the health priorities that are important locally, and ways to disseminate research results that are culturally appropriate and understandable to the community.

We have worked to identify unique potential barriers and facilitators for use of pharmacogenetics in healthcare through discussions with AI/AN community members. As an example, SCF undertook focus groups with its customer–owners, to determine the acceptability of pharmacogenetic testing as part of the healthcare delivered at SCF facilities [6]. Participants viewed pharmacogenetics as a two-edged sword that could improve healthcare but also poses potential harm. These included opportunity costs and misuses of genetic information leading to community or tribal stigmatization. Participants identified strong and effective community oversight of research and clinical care as the best way to assure that this technology is used in appropriate ways [6]. In addition to the SCF focus groups, the CPAC and CPG have endorsed the potential value of pharmacogenetic testing, if it can be shown to have clinical utility. These views underscore the importance of the research we are undertaking: that clinical benefit must be clearly established in research studies prior to the use of pharmacogenetic tests in the clinic.

Lack of common language to talk with community partners about pharmacogenetic research is another barrier that has emerged from our interactions. For example, the CPG, comprised of past participants in CANHR's genetic studies, has been working with researchers to discuss more effective ways to talk about genetic research and progress. The absence of certain scientific terminology in the Yup'ik language has challenged effective and accurate communication. Nonetheless, these discussions have led to a deeper understanding of Yup'ik knowledge of inheritance and the development of common linguistic tools to talk about genetic research. Additionally, the CPG are identifying culturally relevant and feasible ways to communicate with community members and their healthcare providers about pharmacogenetic research; this is challenged by the fact that the Yup'ik population of the YK Delta is distributed into multiple, geographically isolated villages.

With community approval from each partner site, we are pursuing research aimed at characterizing the genetic variation in AI/AN populations that influences drug disposition and response. Recently, we

published one of the first reports of genetic variation in an AI population, based on resequencing of four major human CYP450 drug-metabolizing genes (*CYP2D6*, *CYP3A4*, *CYP3A5* and *CYP2C9*) in the CSKT population to characterize all variants [33]. Together these CYP450s account for more than 75% of all phase I drug metabolism, and thus are important contributors to interindividual differences in drug response and toxicity. Allele frequencies of common variants in the CSKT population (*CYP2D6**4 and *41 [20.86 and 11.23%, respectively]; *CYP2C9**2 and *3 [5.17 and 2.69%, respectively]; and *CYP3A5**3 [92.47%]) were similar to frequencies observed in Europeans. *CYP3A4**1G was found more frequently (26.81%), however, and there was low linkage between *CYP3A4**1G and *CYP3A5**1, which is unique compared with other world populations. Together, *CYP3A4* and *CYP3A5* metabolize approximately 50% of all drugs and are the primary routes of elimination for one-third of them. The clinical consequence of the *CYP3A4**1G variant is not completely understood, but it is a focus of future research with the CSKT. The high prevalence of the *CYP3A4**1G variant in the CSKT population may affect metabolism of many different therapeutics and thus understanding its clinical significance may provide the opportunity for individualized dosing in patients carrying this allele. These data strongly suggest that there can be clinically meaningful heterogeneity between indigenous communities in North America and other world populations, and that allele frequencies in one population cannot be used as an accurate surrogate for allele frequencies in another.

Measures are taken at all three sites in Montana and Alaska to secure blood, DNA and other study data. At consent, participants are assigned a unique identification number. All biological samples, demographic data (i.e., gender, age and tribal affiliation) and qualitative data are identified only by this number. A confidential database linking identifying information is kept either on a separate secure server or in a separate, locked file cabinet from the de-identified data. The investigators do not have access to participant names and there is no chance of the participants being individually identified in any publications. Blood and DNA samples are stored frozen in secure biorepositories at the University of Montana, University of Washington, Alaska Native Tribal Health Consortium (AK, USA) or CANHR.

Dissemination of the research results to the communities is an important part of the partnership in pharmacogenetics and the researchers have worked with the respective tribal authorities to determine how the results should be shared. In Montana, we have used multiple methods to communicate the results to the community, including regular articles in the tribal

newspaper, the Char-Koosta News, and written summaries and formal presentations of the research findings to the CPAC, CSKT Tribal Health and Human Services and CSKT Tribal Council. One example of dissemination of the research occurred when the CSKT Tribal Council asked that the results of the CYP450 sequencing study be published in the Char-Koosta News; the article was written by the CSKT Tribal Health Public Information Officer who is also a member of the CPAC [34]. In Alaska, clinically actionable findings are presented on an individual and community level. At SCF, formal presentations are made to leaders through core business groups and committee meetings throughout the organization. The public relations department provides additional guidance on information and materials disseminated to the community, which are communicated via mailings and community newsletter dissemination. In the YKHC, formal presentations are given, in Yup'ik, describing how the research will be disseminated in each study community in the YK region. The CPG and a Ciuliat group of Yup'ik bicultural consultants are actively involved in developing culturally appropriate ways to disseminate research progress and results.

Tribal members from the communities are engaged in the implementation and fieldwork for the project across the three sites to develop research capacity within tribal organizations. CSKT Tribal Health staff and the CPAC work with University of Montana investigators in recruitment of participants for different aims of the project, development of research methods and enrollment criteria and sample collection. At SCF, AI/AN investigators are involved in all aspects of the study from development to implementation and analysis, which capitalizes on the many roles people play within the study and their community. The CPG and Ciuliat group work together with CANHR investigators to explore Yup'ik understanding of heredity and guide data collection. Local field research assistants in the YK Delta are also involved with recruitment and data collection.

Our work with AI/AN populations highlights the importance of population-specific genetic research for defining the array of variants relevant to drug response and toxicity. Pharmacogenetic testing has the potential to improve healthcare by increasing the safety and efficacy of drug treatment. Lack of knowledge about pharmacogenetic variation in minority populations, however, limits the possibility of achieving benefits from pharmacogenetic testing. Our findings suggest that the study of genetic variation in different populations is required for an accurate understanding of allelic frequencies, and demonstrate the need for broader population-specific research for reducing health disparities and improving public health.

Future perspective

In order for pharmacogenetics to reach clinical usefulness for all people, efforts are needed to ensure the inclusion of minority, sometimes geographically isolated, and historically medically underserved populations, who are currently under-represented in genetic research. Important elements in pursuing this research objective include the development of research partnerships that share oversight of the research process with community partners, and bidirectional learning that allows for capacity development at both academic and community settings. This approach, facilitated by the methods of community-based participatory research, can build the trust and knowledge necessary to enable productive, meaningful pharmacogenetic research.

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Executive summary

Pharmacogenetics with American Indian & Alaska Native communities

- There is a need for research in underserved communities to ensure effective implementation of pharmacogenetic tests.
- Considerable genetic heterogeneity between American Indian and Alaska Native populations is likely and the variation needs to be characterized for optimal design of pharmacogenetic tests that deliver the most benefit to drug therapy outcomes.

Academic–community partnerships to study pharmacogenetics

- Including tribal communities as partners in the research process is key to inclusion of these underserved populations in pharmacogenetic research.
- The approach and design of research should address community health priorities and should incorporate investigation of barriers, including resource and educational needs.

References

Papers of special note have been highlighted as:

• of interest; •• of considerable interest

- Eichelbaum M, Ingelman-Sundberg M, Evans WE. Pharmacogenomics and individualized drug therapy. *Annu. Rev. Med.* 57, 119–137 (2006).
- Evans WE, Relling MV. Pharmacogenomics: translating functional genomics into rational therapeutics. *Science* 286(5439), 487–491 (1999).
- Lesko LJ, Schmidt S. Individualization of drug therapy: history, present state, and opportunities for the future. *Clin. Pharmacol. Ther.* 92(4), 458–466 (2012).
- US Department of Health and Human Services. Medically Underserved Areas & Populations (MUA/PS). www.hrsa.gov/shortage/mua/
- Bustamante CD, Burchard EG, De La Vega FM. Genomics for the world. *Nature* 475(7355), 163–165 (2011).
- Discussion of the need for racial and ethnic diversity in genetic research.
- Shaw JL, Robinson R, Starks H, Burke W, Dillard DA. Risk, reward, and the double-edged sword: perspectives on pharmacogenetic research and clinical testing among Alaska Native people. *Am. J. Public Health* 103(12), 2220–2225 (2013).
- Perceptions of pharmacogenetic research among Alaska Native people.
- Boyer BB, Dillard D, Woodahl EL, Whitener R, Thummel KE, Burke W. Ethical issues in developing pharmacogenetic research partnerships with American Indigenous communities. *Clin. Pharmacol. Ther.* 89(3), 343–345 (2011).
- Ethical considerations in developing partnerships with American Indian and Alaska Native people to study pharmacogenetics.
- Goldenberg AJ, Hartmann CD, Morello L, Brooks S, Colon-Zimmermann K, Marshall PA. Gene–environment interactions and health inequalities: views of underserved communities. *J. Community Genet.* 4(4), 425–434 (2013).
- Bommersbach J. Arizona's broken arrow. *Phoenix Magazine* November, 134–144 (2008). www.janabommersbach.com/pm-fea-nov08.php
- Wiwchar D. Genetic Researcher Uses Nuu-Chah-Nulth Blood For Unapproved Studies In Genetic Anthropology. Ha-Shilth-Sa – A First Nations Newspaper.

- www.hashilthsa.com/archive/news/2013-07-22/genetic-researcher-uses-nuu-chah-nulth-blood-unapproved-studies-genetic-anth
- 11 National Congress of American Indians. Resolution #TUL-05–059: Tribal Ownership of Health-Related Data. www.ncai.org/resources/resolutions/tribal-ownership-of-health-related-data
 - **Resolution adopted by the National Congress of American Indians to address tribal ownership of health-related, including genetic, data.**
 - 12 James R, Tsosie R, Sahota P *et al.* Exploring pathways to trust: a tribal perspective on data sharing. *Genet. Med.* doi:10.1038/gim.2014.47 (2014) (Epub ahead of print).
 - **Tribal perspectives on sharing of genetic data.**
 - 13 Mosby I. Administering colonial Science: nutrition research and human biomedical experimentation in aboriginal communities and residential schools, 1942–1952. *Histoire Sociale* 46(91), 145–172 (2013).
 - 14 Manson SM, Garrouette E, Goins RT, Henderson PN. Access, relevance, and control in the research process: lessons from Indian country. *J. Aging Health* 16(5 Suppl.), S58–S77 (2004).
 - 15 The International HapMap Consortium. The International HapMap Project. *Nature* 426(6968), 789–796 (2003).
 - 16 Whirl-Carrillo M, McDonagh EM, Hebert JM *et al.* Pharmacogenomics knowledge for personalized medicine. *Clin. Pharmacol. Ther.* 92(4), 414–417 (2012).
 - 17 Jaja C, Burke W, Thummel K, Edwards K, Veenstra DL. Cytochrome p450 enzyme polymorphism frequency in indigenous and native American populations: a systematic review. *Community Genet.* 11(3), 141–149 (2008).
 - **Review of genetic variability amongst indigenous people in the Americas.**
 - 18 The American Indian and Alaska Native Population: 2010 Census Briefs. www.census.gov/prod/cen2010/briefs/c2010br-10.pdf
 - 19 Roubideaux Y. Perspectives on American Indian health. *Am. J. Public Health* 92(9), 1401–1403 (2002).
 - 20 Warne D, Kaur J, Perdue D. American Indian/Alaska Native cancer policy: systemic approaches to reducing cancer disparities. *J. Cancer Educ.* 27(Suppl. 1), S18–S23 (2012).
 - 21 Indian Health Service fact sheets. Indian health disparities. www.ihs.gov/newsroom/factsheets/disparities/
 - 22 Hiratsuka V, Brown J, Dillard D. Views of biobanking research among Alaska Native people: the role of community context. *Prog. Community Health Partnersh.* 6(2), 131–139 (2012).
 - 23 Hiratsuka VY, Brown JK, Hoeft TJ, Dillard DA. Alaska Native people's perceptions, understandings, and expectations for research involving biological specimens. *Int. J. Circumpolar Health* 71, 18642 (2012).
 - 24 Smith HS. An Alaska Native leader's views on health research. Presented at: *15th International Congress Circumpolar Health*. AK, USA, 5–10 August 2012.
 - 25 Minkler M. Ethical challenges for the “outside” researcher in community-based participatory research. *Health Educ. Behav.* 31(6), 684–697 (2004).
 - 26 Israel BA, Coombe CM, Cheezum RR *et al.* Community-based participatory research: a capacity-building approach for policy advocacy aimed at eliminating health disparities. *Am. J. Public Health* 100(11), 2094–2102 (2010).
 - 27 Izumi BT, Schulz AJ, Israel BA *et al.* The one-pager: a practical policy advocacy tool for translating community-based participatory research into action. *Prog. Community Health Partnersh.* 4(2), 141–147 (2010).
 - 28 Mohatt GV, Plaetke R, Klejka J *et al.* The Center for Alaska Native Health Research Study: a community-based participatory research study of obesity and chronic disease-related protective and risk factors. *Int. J. Circumpolar Health* 66(1), 8–18 (2007).
 - 29 Mohatt GV, Hazel KL, Allen J, Stachelrodt M, Hensel C, Fath R. Unheard Alaska: culturally anchored participatory action research on sobriety with Alaska Natives. *Am. J. Community Psychol.* 33(3–4), 263–273 (2004).
 - 30 Mohatt GV. The community as informant or collaborator? *Am. Indian Alsk. Native Ment. Health Res.* 2(3), 64–70 (1989).
 - 31 Lopez ED, Sharma DK, Mekiana D, Ctibor A. Forging a new legacy of trust in research with Alaska Native college students using CBPR. *Int. J. Circumpolar Health* 71, 18475 (2012).
 - 32 Hoeft TJ, Burke W, Hopkins SE *et al.* Building partnerships in community-based participatory research: budgetary and other cost considerations. *Health Promo. Pract.* 15(2), 263–270 (2014).
 - 33 Fohner A, Muzquiz LI, Austin MA *et al.* Pharmacogenetics in American Indian populations: analysis of *CYP2D6*, *CYP3A4*, *CYP3A5*, and *CYP2C9* in the Confederated Salish and Kootenai Tribes. *Pharmacogenet. Genomics* 23(8), 403–414 (2013).
 - **One of the first reports on pharmacogenetic variation in CYP450 drug-metabolizing enzymes in an American Indian population.**
 - 34 Azure BL. Pharmacogenetics research enters second phase. Char-Koosta News. www.charkoosta.com/2013/2013_02_28/Pharmacogenetics_research_2nd_phase.html