**Precision Medicine with American Indian and Alaska Native People**

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**Abstract**

Precision medicine seeks to identify sources of interindividual variability in genes, environment, and lifestyle to tailor disease treatment and prevention. Participation of diverse racial and ethnic communities in precision medicine research is an essential first step in the path to realizing the promise of precision medicine and preventing worsening of minority healthcare disparities. Our strategy for increasing participation of diverse populations in precision medicine research is to include communities in the research process using principles of community-based participatory research. We have established community-academic partnerships with American Indian and Alaska Native (AIAN) people living in Alaska and Montana to provide a trustworthy foundation for implementation of precision medicine. AIAN people experience numerous health disparities, yet health research addressing these concerns is limited, and resulting culturally appropriate interventions based on community research priorities are rare. The partnership between the University of Montana and the Confederated Salish and Kootenai Tribes on the Flathead Reservation in western Montana was established more than 10 years ago and is one of only a few partnerships in the US focused on precision medicine research with AIAN communities. One focus of the research partnership is pharmacogenomics, which is an application of precision medicine that uses knowledge about genetic variation to help guide optimal dosing. We published the first comprehensive resequencing of the major cytochrome P450s (CYPs) genes in an American Indian population. Characterizing the frequency of common variation and identification of novel gene variants in CYP drug-metabolizing enzymes among AIAN people – variants that are predicted to influence drug safety and efficacy – highlight the importance of including diverse populations in genetic research. Another emphasis in the partnership is gene-environment interactions such as dietary intake of polyunsaturated fatty acids and genetic factors as predictors of response to antiplatelet therapy and how diet, genetics, and sunlight contribute to vitamin D homeostasis and optimal health in AIAN people. Vitamin D sufficiency is of particular concern for tribal populations living in northern latitudes where sunlight exposure is reduced in winter months. We have also conducted qualitative assessments with healthcare providers about the clinical feasibility and acceptability of implementing pharmacogenetic tests in tribal healthcare settings, which emphasized that precision medicine agendas must include research in diverse practice settings outside large metropolitan areas. The trusted research partnerships that have been built provide a foundation for exploration of the broader potential of precision medicine research with AIAN communities and lay the groundwork for implementation of precision medicine in these communities. Our approach to establish community-academic partnerships may be a model for engaging other underserved populations in precision medicine research.