We read with interest the review by Erickson on Southwestern Athabaskan genetic diseases.[1] We would like to point out that it is not only rare autosomal recessive disorders that may be clinically important heritable diseases in this group. More specifically, a significant proportion of colorectal cancer in the Navajo is due to a type of autosomal dominantly inherited colorectal cancer susceptibility known as hereditary non-polyposis colorectal cancer (HNPCC). A family that had been followed by Lynch and colleagues since 1983 was found to carry a specific MLH1 mismatch gene founder mutation known to cause HNPCC.[2,3] During a 2-day visit in 1995, the family was offered genetic education in small groups about HNPCC, followed by individualized genetic counseling regarding the risks and benefits of genetic testing. DNA testing was performed on 51 family members. Twenty-three individuals underwent genetic counseling and received test results. Seven were positive for MLH1.[4]

Why study cancer in the Navajo, or for that matter, other Native American groups? The practical clinical answer focuses upon the potential for cancer control through the identification of individuals who are at inordinately high risk for cancer of multiple anatomic sites with the most common being colorectal cancer in the Lynch syndrome II variant. However, in our experience, cancer detection services are often unavailable or under-utilized by the Navajo.[4]

From the research perspective, the answer relates to characterization of the Navajo people who are a subgroup of the Athabaskan linguistic group who migrated to the Southwest U.S. from Eastern Alaska and Canada in about 1000–1200 BCE. It is estimated that approximately 150,000 Navajo reside in New Mexico and Arizona, most of whom live on reservation lands, where they have undergone relatively little genetic mixing with other groups. "This racial homogeneity and the generally common environment exposures of reservation life make it likely that the evaluation of cancer family history and lifestyle among the Navajo, could elicit important epidemiologic clues about host and environmental interactions in cancer etiology. Prospective studies used to identify MLH1 or MSH2 mutations could facilitate such genetic-epidemiologic research. This would allow the identification of environmental exposures in concert with knowledge of who is versus who is not inordinately predisposed to cancer."[3]

Lynch et al.[4] noted the importance of offering culturally sensitive genetic counseling with specific attention to perceived cross-cultural, economic, and social barriers to the use of genetic and other medical services. We agree with Erickson, that "as more Native Americans move off the Reservation, the awareness of susceptibility to particular genetic diseases needs to be more widely disseminated." The key to recognizing such a possible genetic susceptibility is the taking of a thorough family history, which includes ethnic background along with history of both common and rare disorders. In the case of HNPCC, identification of specific mutations remains a long, tedious, and expensive process for families. Knowledge of a specific founder mutation segregating in a Navajo family would make single site MLH1 mutational analysis possible for diagnosis of HNPCC, much as has been accomplished with BRCA1/2 testing among those of Ashkenazi Jewish background.[5] Presumably there would be founder mutations to account for significant proportions of other common diseases as well. Collectively, these may constitute an important public health issue for Native American people and a challenge for healthcare providers.

June A. Peters, MS
Assistant Professor of Human Genetics &
Genetic Counselor, Cancer Genetics Program
Graduate School of Public Health
Pittsburgh, Pennsylvania

Henry T. Lynch, MD
Hereditary Cancer Institute
Professor & Chairman, Department of Preventive Medicine
and Public health
Professor, Department of Medicine
Creighton University
Omaha, Nebraska

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