Response to Conner et al. Re: “Cigarette Smoking and Breast Cancer Risk in Hispanic and Non-Hispanic White Women: The Breast Cancer Health Disparities Study”

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THANK YOU FOR THE OPPORTUNITY to respond to Ms. Heather Platter's letter and to address her concerns pertaining to our publication, “Cigarette smoking and breast cancer risk in Hispanic and non-Hispanic white women: the Breast Cancer Health Disparities Study.”¹

In her letter to the Editor, Ms. Platter states that it could be problematic to analyze U.S. Hispanics and Native Americans as one racial/ethnic group given variations in health outcomes, social distinctions, and differences in environmental factors that might modify behaviors. She points out that combining these two racial/ethnic groups is a major limitation to our analysis. In response to this concern, we would like to provide additional information on the rationale for the pooled analyses of the Breast Cancer Health Disparities Study.

In the pooled analysis, the small number of breast cancer cases and controls from the 4-Corners Breast Cancer Study who reported their race/ethnicity as Native American (either as a sole racial category or in combination with non-Hispanic white or with Hispanic race/ethnicity) were grouped with Hispanic women because of genetic factors potentially shared with U.S. Hispanic women.² These unidentified and uncontrolled genetic factors could influence various risk factors associated with breast cancer, including smoking. It has been shown that *NAT2* may interact with smoking in some populations and that the frequency of the *NAT2* genotypes differs by race/ethnicity.³ This finding provides support that genetic factors are important in modifying associations between lifestyle factors such as cigarette smoking and other behavioral risk factors and breast cancer risk.

We certainly agree that unique cultural factors exist for Hispanic and Native American women. Similarly, the non-Hispanic white population is characterized by a wide array of cultural beliefs, behaviors, religious practices, and other

factors. Although we believe the non-Hispanic white population to be extremely diverse in its cultural, social, religious, and behavioral factors, they most likely have a more shared European genetic ancestry. In an effort to address differences in cultural factors that translate to differences in behaviors in both the non-Hispanic white and Hispanic and Native American populations, we have adjusted the analyses for differences in lifestyle factors stemming from differences in beliefs and behaviors that could confound the association between smoking and breast cancer risk, such as parity, body mass index, and alcohol consumption. However, we also acknowledge there could certainly be other unidentified factors for which we have not adjusted.

Since the formation of the Breast Cancer Health Disparities Study consortium, our group has published numerous research articles that examined associations of various genetic variants and nongenetic factors with breast cancer risk and mortality, stratifying the study population by percentage of Native American ancestry.^{4–11} We agree that perhaps Native American women should be excluded from analyses that focus on lifestyle rather than genetic factors, although it can be argued that the stratifying populations with more similar genetic ancestry can help control for unidentified genetic factors that could modify associations. It is important to note that the percentage of Native American ancestry present in the Hispanic and the Native American race/ethnicity groups is not significantly different in our study population. In addition, in a study by Bryc et al., Hispanics in the southwest were found to have more Native American ancestry than Hispanics in the south and northeast, where the proportions of both European ancestry and African ancestry are higher.¹² There were only 42 self-reported Native American cases and controls included in this publication; the exclusion of this group in a sensitivity analysis had no

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impact on the findings. Ms. Platter also noted that the African American women from the San Francisco Bay Area Breast Cancer Study (SFBCS) were excluded in our analyses. The focus of the Breast Cancer Health Disparities Study was to examine differences between U.S. Hispanic, Native American, non-Hispanic white, and Mexican women for breast cancer risk and prognosis by Native American ancestry. Thus, the African American women from the SFBCS were not included in the pooled analysis.

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