Cancer Disparities: Disentangling the Effects of Race and Genetics

By Vicki Brower

For certain cancers, African American patients have higher incidence and mortality rates than white Americans, but the reasons for this are not fully understood. Many recent studies have looked to genetics for an explanation, but, taken in isolation, these studies can raise more questions, and controversy, than they answer.

Recently, two sets of researchers both found that two genes, known as PSPHL and CRYBB2, that were not previously associated with cancer, are expressed at extremely high levels in African American breast and prostate cancer patients but not white patients. “We could tell with high accuracy by looking at the expression of those two genes which race the patients were. These differences may help explain the poorer prognoses seen among black and white patients with those diseases and may eventually help find better, more effective treatments for black patients with cancer, according to their tumor types,” said Tiffany Wallace, Ph.D., lead investigator of the study in Atlanta, dismiss gene profiling studies performed in isolation and their conclusions. “Such genetic research is well meaning, but the conclusions that these diseases are different in African Americans is simply untrue. Race is a social variable, not an inherent biological variable. It is overly simplistic to think of race as a genetic or biological construct, even though there are genetic or biologic correlates of race. Let’s deal with logistics [access and quality of care] first; genetics, second,” he said.

Conducting genetic research without controlling for other factors and drawing conclusions about race and biology without keeping larger issues in mind “is like the elephant and the blind man in the room,” said University of Chicago geneticist Funmi Olopade, M.D., who is conducting transdisciplinary research on breast cancer in black women. “What you see depends on what you are looking at and where you are standing,” she said. “For a long time, researchers in different disciplines did not talk to each other, but now we are looking at multiple layers, using new tools, and sharing perspectives across disciplines.”

Olopade and Rebbeck are two of a growing number of disparities researchers trying to take a broader approach, examining not one or two variables but instead looking at the many intertwined factors influencing health and disease to understand who is at risk and determine how to reduce or eliminate disparities.

A spirited debate exists among disparities researchers about whether the differences in health outcomes are caused by differences in biology that correspond to race or by a range of other interacting factors, such as poverty and SES, for which race is merely a surrogate. Although each side seeks to understand and remedy these disparities, research priorities differ between the two sides, as do policy recommendations.

Although most researchers agree that health disparities are deeply rooted in society and are influenced by a range of variables, including race-based discrimination, SES, sex, and geography, they disagree on the importance and meaning of genetic studies. Underlying the critique of standalone genetic studies is an impassioned rejection of the idea that race is biologically based. The belief that diseases differ along racial lines led to the practice of “race medicine” in the U.S. in the 19th and 20th centuries, Brawley said. “Even the medical community has not always understood that observations of disease in one race are also true for others.”

Harold Freeman, M.D., medical director of the Ralph Lauren Center for Cancer
Care and Prevention in New York and former director of the NCI Center to Reduce Health Disparities summed up a consensus among geneticists: “Racial classifications are not based on science or anthropology … Races, in the sense of genetically homogeneous populations, do not exist in the human species today, nor is there any evidence that they have ever existed in the past. Therefore, the biological concept of race is untenable and has no legitimate place in biologic science. Instead, a better understanding of population genetics and the effects of poverty, culture, and social injustice and racism is needed to evaluate the use of race as a variable in scientific research.”

Genetics research can be used to delineate the complex origins of traits and close biological affinities between groups to help dispel stereotypes or to promote stereotypes, argued Vence Bonham, J.D., a member of the National Human Genome Research Institute’s Race, Ethnicity, and Genetics Working Group. “Because of the history of misuse of ideas about genetics, geneticists have a special responsibility to examine carefully their use of racial and ethnic categories in their research,” he wrote in 2005 in the American Journal of Human Genetics.

Citing a 2002 study by Cathy Bradley, Ph.D., of East Michigan University in Lansing (JNCI 2002;94:490–6), Brawley noted that this and other studies discredit the hypothesis that race is an inherent determinant of biological behavior of breast cancer. In that study, before controlling for Medicaid and poverty, black women had worse survival rates than white women, but after accounting for these variables, the authors found that race was not a statistically significant factor, except in the decision to undergo surgery. Poverty, however, was the determinant of poorer outcome regardless of race.

**Biology or Poverty?**

Research of disparities has often produced conflicting results, even when factors such as SES are controlled for, as illustrated by two recent epidemiological studies. The first, published in the August issue of Cancer, included more than 13,500 patients with breast, prostate, and colon cancer in seven states and found that those with lower SES had more advanced cancer at diagnosis, received less aggressive treatment, and were more likely to die in the 5 years after diagnosis than patients in higher-SES neighborhoods. Although blacks and Hispanics were more likely than non-Hispanic whites to live in areas of lower SES, the low SES effect was true across all racial and ethnic groups.

In contrast, a forthcoming study of nearly 20,000 black and white patients in phase III trials for leukemia, lymphoma, myeloma, breast, lung, ovarian, prostate, and colon cancers found disparities according to race only in patients with ovarian, prostate, and breast cancer.

Investigator Kathy Albain, M.D., of Chicago’s Loyola University School of Medicine said that the results raise the question of whether interactions between genetics and hormonal factors in these sex-specific cancers explain the results. Genetic polymorphisms relating to endogenous hormones or drug metabolism enzymes could underlie these differences and will be investigated next, she said.

Besides genetics, access to care and equal treatment, along with poverty and discrimination, are crucial factors in health disparities. Before 1980, breast cancer mortality rates were about equal for blacks and whites, said Ismail Jatoi, M.D., Ph.D., head of the breast care center at the National Naval Medical Center in Bethesda, Md. “It is likely that the widening gulf between black and white patients is due to the widespread use of mammography by white women, which began around 1980, and adjuvant therapies, including tamoxifen.” Over the past 25 years, death rates among white women began falling as they gained access to screening and new treatments, whereas rates for black women did so to a lesser degree. “White women are also more likely to have estrogen-positive breast tumors, which respond to tamoxifen, and they are more likely to be diagnosed sooner,” he said.

The problem of limited access to cancer screening has not improved much over the past three decades for many minorities. A new study in the June 23 issue of Archives of Internal Medicine suggested that blacks and Hispanics are less likely to undergo colorectal cancer screening than whites because of SES, access to health care, and language barriers.

But the problem may be more complicated than just access to care. In a meta-analysis of breast cancer survival rates published in 2006 in the Journal of Clinical Oncology, Jatoi described a more complex picture: For men and women with Medicaid, an indicator of equal access, 5-year survival rates for all cancers were lower among the poorer patients. Even with adjustment for SES, blacks and other minorities still had lower 5-year survival rates. “We see that even in an equal-access situation, disparities remain,” Jatoi said. “Is the problem biology or access? I think it is both.”

A more recent study by Arden Morris, M.D., of the University of Michigan (JNCI 2008;100:738–44) also found that equal access did not result in equal treatment. Among anal cancer patients with Medicare, blacks were still less likely to receive post-surgical treatment for their disease (54%) than were white patients (70%), even with adjustments for stage, age, and income. “We hypothesized that different rates of referral would explain this, but that was not the case,” Morris said. Among black
patients, younger ones—those who would have had a 20% survival gain with treatment—were less likely to be treated. Black patients were also more likely to be single, divorced, or separated. Reasons for these disparities are unclear, she said. “I am concerned that patients are not getting good explanations and making fully informed decisions about receiving treatment.” In a follow-up study, she will conduct separate focus groups to help understand what is responsible for this disparity.

Successful Interventions
Nina Bickell, M.D., of Mount Sinai School of Medicine in New York found that many inner-city patients were less likely to get adjuvant care after surgery for breast cancer. Black patients were referred to oncologists as often as white patients, but they were less than half as likely as whites to receive adjuvant treatment.

Bickell designed a subsequent study and reported her results in April at the annual meeting of the American Association for Cancer Research. She designed a tracking and feedback registry aimed at closing the “referral loop” for minority patients. This registry resulted in greater use of adjuvant treatment and eliminated race as a risk factor for underuse of adjuvant therapy. “Closing the gap between surgeon and oncologist is crucial to helping reduce underuse of adjuvant treatment,” she said. “There are different reasons for underuse; if a patient thinks the treatment is worse than the disease, this intervention would not work.”

Another new study, published online in June in the journal Cancer, shows that community education and outreach initiatives, such as the use of patient navigators—specialty trained personnel who help cancer patients navigate the health care system from diagnosis through treatment and follow-up—has been associated with an increase in the number of women diagnosed with earlier-stage disease, as opposed to late-stage disease, and the number receiving adjuvant treatment.

Transdisciplinary Research
With contradictory data and the possibility that ethnic or racial disparities cannot be fully explained by inequities in SES or access to and use of health care, attention returns to biology and how it plays out in the context of these other factors. Social environment, including culture, is increasingly viewed as having an important influence on the biology of cancer development and progression. Environmental stressors such as life stress, racism, and discrimination may negatively affect physiological (e.g., immune function, cardiovascular reactivity) and behavioral (e.g., coping efforts, dietary behaviors, smoking) responses to prostate cancer, according to a February 2008 study of prostate cancer by Rebbeck on the genetics of the disease in African and African American men.

Bringing together multiple perspectives and getting such research funded has not always been easy. “When I first started speaking about taking a biopsychosocial approach to disparity research over 20 years ago, people thought it was heresy,” said Lovell Jones, Ph.D., a molecular biologist and director of the Center for Research on Minority Health at the University of Texas M. D. Anderson Cancer Center in Houston. Jones said that bridging three academic disciplines and obtaining funding for the work was extremely challenging in the field’s early days. “The idea of one research
group doing both science and service did not fit into established funding categories and institutions.”

In broad terms, the center examines the relationship between gene–environment interactions and disparities. In one study, researchers are examining the genetics of breast cancer in African American and African women and tracing patients’ paths of migration from Africa to three main areas of settlement: the Chesapeake Bay, the Carolina coast, and the Mississippi delta. They seek to isolate environmental, cultural, and social factors, that might have influenced African American women’s high rates of early-onset breast cancer and to relate the prevalence of the cancer back to similar incidence in Africa.

NCI, through its Centers for Population Health and Health Disparities, funds a network of eight transdisciplinary teams that are examining cancers in racial/ethnic minorities and other underserved populations. Examples include Appalachian women, who have extremely high rates of cervical cancer incidence and death, and African American women with triple-negative breast cancer, a form of the disease in which tumor cells lack receptors for estrogen, progesterone, and HER2 and that often has an unfavorable prognosis. Team members at each site collaborate with experts in a range of disciplines to investigate disparities from multiple vantage points, and the research encompasses basic, clinical, and population research.

Olopade’s group is working to identify not only the correlates but also the causal links between genetic mechanisms and social, environmental, and geographic factors in triple-negative breast cancer patients on the south side of Chicago. By putting genetic research in a wider context, Olopade hopes to discover new targets for drugs to treat this type of breast cancer, which is considered the most difficult to cure. Taking a top-down approach, the group is examining how an individual’s reaction to her physical environment can affect endocrine, immune, and neurological function to inhibit apoptosis and normal gene regulation in cancer. They have developed an animal model of environmental stress and social isolation to study why breast cancer is so aggressive in black women on Chicago’s south side who are newly diagnosed with the disease.

No matter what approach scientists take, disparities research is highly charged and filled with strong feelings, Morris said. Ferreting out causes and coming up with solutions may be best done not in isolation but rather with the help of the convergence of many minds and disciplines. “The concern of many, which is not unfounded, is that by continuing to use ‘race,’ some of the biases that have caused so much trouble to some groups will [continue to] be perpetrated,” Rebbeck said, “and the real causes of these problems can be ignored or not dealt with in a meaningful way.”