Conquering Cancer Disparities: New Opportunities for Cancer Epidemiology, Biomarker, and Prevention Research

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Cancer disparities represent a significant public health problem in the United States. Inequity in cancer screening, incidence, treatment, prognosis, and mortality is a hallmark of many common cancers (1). These disparities exist across groups defined by race, ethnicity, gender, age, and socioeconomic status. For example, African American men have a 34% greater prostate cancer-specific incidence and 123% greater prostate cancer-specific mortality than European American men (2). The greater disparity in mortality relative to the disparity in incidence suggests that factors related to biology, behavior, social circumstances, access to care, and other postdiagnosis factors influence clinical outcomes beyond those that contribute to disease etiology. Elimination of cancer disparities is also a critical public health need: Woolf et al. (3) estimated that the complete elimination of health disparities (including but not limited to cancer disparities) during the 1990s would have saved five times more lives than were saved by technological innovations in health care over the same period.

The kind of disparities observed for prostate and other cancers probably involves the complex interaction of many factors acting less favorably in specific groups over the lifetime of the individual. To illustrate this hypothesis, Table 1 presents information about the continuum of disease from preneoplastic to preclinical to clinical prostate cancer. Data obtained from autopsy studies (4-6) indicate that rates of high-grade prostatic intraepithelial neoplasia and prostate cancer are slightly higher in African American men compared with European American men, and this disparity is greatest in the age range 40 to 60 years. This is consistent with the observation that prostate cancer occurs at a slightly earlier age in African American men compared with European American men (7). This disparity persists when measured by Surveillance, Epidemiology, and End Results incidence and mortality rates (Table 1). The disparity in diagnosed prostate cancer again peaks in the age range 40 to 60 years, and shows a much greater disparity in mortality than in incidence. These data suggest that African Americans are at greater risk and have poorer outcomes for prostate cancer at most ages, and that this disparity increases across the continuum of disease from latent high-grade prostatic intraepithelial neoplasia to subclinical disease to clinically apparent disease to mortality.

One interpretation of the example cited above is that prostate cancer disparities are caused by innate biological susceptibility in conjunction with environmental exposures that accumulate over time to confer prostate cancer risk. Furthermore, unfavorable social influences, physical environ-

Not Just Genes . . . Not the Same Old Environment

Cancer etiology and outcome research typically involves evaluation of individual-level biomarkers and/or environmental exposures. However, to fully understand the causes of cancer disparities, a more comprehensive approach to the study of cancer causation and prevention may be required. Although cancer disparities have been described in the epidemiology and public health literature, there are significant gaps in our knowledge of the social, environmental, and biological factors that explain disparities in cancer etiology or outcomes. Our lack of understanding of the biological events that cause cancer disparities is a limitation in our ability to ameliorate these disparities. Thus, studies of cancer disparities represent an important opportunity for cancer epidemiology, biomarker, and prevention research. Advances in molecular biology, genome sciences, and biomarker technology provide an unprecedented opportunity to apply knowledge of carcinogenic mechanisms to the problem of cancer disparities. The incorporation of biomarkers in cancer disparities research provides new opportunities for clinical and public health research and practice and has the potential to catalyze needed improvements in the prevention and management of cancer to eliminate cancer disparities.

In addition to biomarkers, a complete understanding of disparity in cancer etiology or outcome may require a more comprehensive definition of environmental exposure. For example, expanded definitions of “the environment” could be developed to include social environment (e.g., socioeconomic status, access to health care, social isolation, cultural beliefs, and values); physical environment (e.g., location or type of residence, access to computer and internet resources, or medical care); and behavioral factors (e.g., attitudes, beliefs, and practices associated with cancer screening). In addition to these individual-level environments, neighborhood- or community-level factors could also be considered using a multilevel approach (11). Neighborhood-level factors could
include housing density, measures of social capital such as cultural/civic participation or neighborhood cohesiveness, neighborhood stability such as the percent of rental housing, measures of deprivation such as the violent crime rate, and social conditions such as percent of individuals in the neighborhood who live below the poverty level or have below average educational attainment. Similarly, institutional factors such as health care patterns, access to care, insurance, and type and quality of health care that has been accessed could also be considered. In general, cancer epidemiology, biomarker, and prevention research has focused on individual-level variables, and therefore has not been able to address the larger context in which genes, biological factors, or individual environmental exposures are acting. A multilevel approach would represent a more holistic view of the complex multifactorial nature of cancer etiology, treatment, and outcomes. Similarly, studies of genotype by environment interaction could be extended by considering the interaction of genes and other biomarkers with individual- and neighborhood-level environments.

What Can Cancer Epidemiologists, Biomarker Researchers, and Prevention Scientists Do?

Long et al. (12) have proposed three phases of disparities research: defining, explaining, and eliminating the disparity. Cancer epidemiologists, biomarker researchers, and prevention scientists have the opportunity to contribute to each of these areas.

Define Disparities. Race, sex, age, and other demographic characteristics are commonly used as surrogate measures of exposures, risk factors, or other life events that are usually difficult or impossible to measure or analyze. However, demographic surrogates such as age or race are relatively crude and may not adequately define groups who are most likely to suffer disproportionately from cancer. Use of these surrogate measures inevitably leads to misclassification of individuals with respect to the disparities they may suffer. Thus, researchers need to develop improved definitions of groups experiencing cancer disparities. For example, rather than use U.S. Census definitions of race, it may be useful to identify correlates of race-based education, income, home ownership, or other individual or neighborhood variables that are more meaningful in defining groups for disparity studies. These new definitions may then guide future studies aimed at explaining or eliminating disparities by more accurately identifying the target group(s) of interest.

Explain Disparities. Both cancer epidemiology and prevention research contribute valuable approaches that can be used to explain health disparities. These methods include the ability to design and power studies of representative and relevant populations. Molecular epidemiology has traditionally considered a wide range of risk factors, including biomarkers that measure exposure, biological effect, and phenotypic changes associated with carcinogenesis (13). These approaches can be translated to multilevel studies of cancer disparities. For example, biomarkers of stress in the individual level may be correlated with neighborhood stress. Numerous biomarkers associated with stress exist, including serum or urinary cortisol levels, plasma, urine, or serum catecholamine levels, chronic EBV infection, markers of oxidative stress, C-reactive protein levels, activation of nuclear factor κB, and others. Neighborhood stress may be measured by high neighborhood poverty, low socioeconomic status, low education level, housing stability, or measures of gentrification. Molecular epidemiologists are in a unique position to link biomarkers with individual-level factors and with neighborhood-level factors to better understand disparities in cancer etiology and outcomes. Standard approaches and methods have also been developed to define, measure, and assess changes in health disparities (14). The integration of methods from molecular epidemiology and health disparities research suggests that novel transdisciplinary analytic approaches can be developed to explain cancer disparities.

Valid approaches to the study of cancer disparities should also draw on methods and concepts from other fields as well. First, health disparities research activities may be most appropriately carried out in the context of community-based participatory research (15). Integration of community-based participatory research and traditional epidemiologic methods provides an opportunity to better define relevant research questions by involving the community in the development of this research, and provides opportunities for improved translation of research results back to the community. This translation can focus interventions, prevention strategies, screening, and other activities to groups that are disproportionately affected by cancer. Second, identification of populations or specific groups as having disparate cancer risks, treatment responses, or prognoses could raise potential human subject concerns. These issues identify research on the ethical, legal, and social implications of identifying biological (particularly genetic) causes of these disparities as an important area of focus and opportunity for cancer disparities researchers.

Eliminate Disparities. The molecular epidemiology and cancer prevention communities are uniquely positioned to develop and apply interventions that can specifically ameliorate disparity disparities in cancer risk and outcome. Approaches have been proposed to reduce or eliminate health disparities that involve improved health care training, health care delivery, and public policy activities (16). Often, these activities are not

Table 1. Prostate cancer disparities at all stages of the etiologic continuum in African American and European American men

<table>
<thead>
<tr>
<th>Decade</th>
<th>Men with autopsy-identified high-grade prostatic intraepithelial neoplasia* (%)</th>
<th>Men with autopsy-identified prostate cancer* (%)</th>
<th>Age-adjusted SEER prostate cancer incidence rates (per 100,000)</th>
<th>Age-adjusted prostate cancer mortality rates (per 100,000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-29</td>
<td>7 8 0.88</td>
<td>8 8 1.00</td>
<td>0.0 0.0</td>
<td>—</td>
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<tr>
<td>30-39</td>
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<td>31 31 1.00</td>
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<td>46 29 1.59</td>
<td>43 37 1.16</td>
<td>55.1 19.7</td>
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<tr>
<td>50-59</td>
<td>72 49 1.47</td>
<td>46 44 1.05</td>
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<tr>
<td>60-69</td>
<td>75 53 1.42</td>
<td>70 65 1.08</td>
<td>1,210.6 751.9</td>
<td>1.61</td>
</tr>
<tr>
<td>70-79</td>
<td>91 67 1.36</td>
<td>81 83 0.98</td>
<td>1,595.6 1,072.9</td>
<td>1.49</td>
</tr>
</tbody>
</table>

Abbreviations: AA, African American; EA, European American; SEER, Surveillance, Epidemiology, and End Results.

*References 4-6.
integrated with biomarker research. Knowledge of biomarkers that are correlated with cancer disparities could identify modifiable exposures or circumstances that could result in improved cancer detection, prevention, or treatment. In particular, identification of biomarkers of early disease may lead to new or improved screening strategies in disadvantaged populations. As suggested above, success in the elimination of health disparities may depend on knowledge of biomarkers, individual-level exposures, and neighborhood level context. These approaches provide opportunities to identify specific biomarkers, risk factors, and populations in which reduction of excess risk and mortality is possible. Finally, studies of cancer disparities may elucidate etiologic differences or prevention opportunities to eliminate disparities, but an understanding of the causes of cancer disparities may also lead to a better understanding of cancer etiology, treatment, and prevention in the broader population.

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References
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