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Advancing Health Disparities Science Through Social Epigenomics Research

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Abstract

IMPORTANCE Although scientific and technological discoveries have improved the health of the US population overall, racial and ethnic minority (American Indian and Alaska Native, Asian, Black or African American, Hispanic or Latino, or Native Hawaiian and Pacific Islander persons) and socioeconomically disadvantaged populations continue to experience a disproportionate burden of disease and other adverse health conditions. To better understand and address the drivers of health disparities and inform the development of effective interventions, integrative mechanistic studies examining the dynamic interplay of multiple factors across the life course and even between generations are needed. The emerging field of social epigenomics, which seeks to link social stressors and protective factors to health status through the examination of epigenomic modifications of various biological pathways, is one promising area of research contributing to this need.

OBSERVATIONS This thematic issue of *JAMA Network Open* highlights new findings from the grantees of the National Institutes of Health (NIH) Social Epigenomics Program. These findings, taken together, examine the associations of a variety of social, behavioral, and structural factors throughout the life course with epigenomic and other biological changes among populations experiencing health disparities. The studies link early-life exposures, structural inequities, and behavioral factors and interventions to epigenetic changes, and in some studies, later health outcomes. While there is still more work to be done to fully characterize the mechanistic pathways linking social exposures to epigenetic changes and health outcomes, the body of work presented in this special issue represents solid progress toward this goal.

CONCLUSIONS AND RELEVANCE The studies highlighted in this special issue demonstrate important scientific progress in the complex integration of social determinants of health and health disparities with biological pathways and health outcomes to improve understanding of the mechanisms underlying health disparities among various underserved populations. Continued progress remains important in integrating different disciplines to transform the field of health disparities research.

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Introduction

Although scientific and technological discoveries have improved the health of the US population overall, racial and ethnic minority (eg, American Indian and Alaska Native, Asian, Black or African American, Hispanic or Latino, or Native Hawaiian and Pacific Islander persons) and socioeconomically disadvantaged populations continue to experience a disproportionate burden of disease and other adverse health conditions.[1,2] As the nation's steward of biomedical and behavioral research, the National Institutes of Health (NIH) has devoted considerable resources, led by the National Institute on Minority Health and Health Disparities (NIMHD) since 2000 to characterize the root causes of health disparities, uncovering a complex web of interconnected factors, including social, biological, behavioral, environmental, and societal factors. However, to better understand and address the

drivers of health disparities and inform the development of effective interventions, integrative mechanistic studies examining the dynamic interplay of multiple factors across the life course and even between generations are needed. The emerging field of social epigenomics is one promising area of research contributing to this need.

Health disparities are health differences that adversely affect socially disadvantaged groups and are potentially preventable. Health disparities have been widely linked to social determinants of health, ie, the conditions in which people are born, grow, live, work, and age that impact health. Social determinants of health include the variations in individuals' exposure to chemical and nonchemical stressors. For example, individuals living in disadvantaged neighborhoods are exposed to a variety of stressors, both physical (eg, noise pollution, lack of green space) and social (eg, food desert, violence or threat of violence, residential segregation, and psychosocial stress).[3,4] Individuals from marginalized communities also face various forms of social stress, including racism and discrimination, early-life adversity, prenatal exposure to maternal stress, or increased rates of unhealthy behaviors (eg, substance use, unhealthy diet) and lower rates of healthy behaviors (eg, physical activity, sleep). Health disparities therefore may arise because of the synergistic effects of exposure to multiple environmental hazards and social stressors among certain populations—that is, the social environment may, in a literal and figurative sense, get under the skin to affect biology and health outcomes. However, the specific mechanisms through which these combined stressors affect biology, and which of these pathways ultimately cause observed health disparities in these populations, have remained relatively unknown.

Recent studies suggest that social stressors and/or protective factors may affect health status through epigenomic modifications of various biological pathways.[5,6] The epigenome includes histone modifications, noncoding micro RNAs, chromatin remodeling, and, most notably, DNA methylation, all of which affect gene expression and cellular phenotypes. Unlike the underlying genome, which is largely static within an individual, the epigenome can be dynamically altered by social and environmental conditions. Epigenetics is one of the currently active topics in biomedical research that may serve as a functional read-out of disease risk and health-related phenotype. Epigenomic studies of social influences hold great promise to identify classes of genes and specific biological pathways through which social factors might act and mechanisms through which social environments might affect minority health and health disparities. Operating through epigenomic changes, adverse social and environmental experiences early in life may predispose an individual to dysfunctional physiological responses and to future stressors in adulthood, which in turn might influence risk of obesity, cancer, stroke, mental illness, and other adverse health outcomes. Exposure to protective or resiliency factors may also buffer some of these adversities; however, the mechanisms through which these factors operate are not clear.

The study of epigenetic variations within and between populations offers a unique opportunity to understand how exposures from the social environment, diet, lifestyle, and other factors interact with genes to influence health and disease across the lifespan. Research now shows how diverse social and environmental factors, such as maternal health and education, healthy nutrition, exposure to environmental toxins, housing conditions, poverty, and child rearing practices, can affect how our genetic building blocks (DNA) are expressed. These differences in gene expression contribute to individual differences in health, development, and behavior. Social epigenetics is the process by which early-life experiences influence chemical reactions that in turn alter the ways our genes function or are expressed, and these differences in expression may influence lifelong health and well-being. Research that enhances our understanding of the effects of various social experiences (both positive and negative) on epigenomic changes presents an opportunity to illuminate the underlying mechanisms of health disparities, which can ultimately lead to the development of innovative strategies in disease diagnosis, prevention, and clinical improvements in personalized care and reduction of health disparities.

NIMHD Social Epigenomics Initiative

Previously, the NIH made significant investments in epigenomics research through the Common Fund,[7] an effort which focused mainly on the development of epigenomic technologies, creation of standard reagents for quantitative measurements, analytical tools, and the construction of epigenome maps. However, genomic and epigenomic data from US racial and ethnic minority populations and other populations experiencing health disparities remained limited, and advancements had not been applied toward understanding the basis for unequal burden of disease in these populations. In the past, the science of health disparities research has been siloed in various disciplines, eg, social sciences or molecular biology, with limited efforts in integrating them. Since social determinants of health are known to influence health disparities, NIMHD initiated efforts to stimulate interdisciplinary research that advances our understanding of the effects of the social environment on epigenomic changes as a potential set of underlying mechanisms of health disparities.

In 2016, the NIH, led by NIMHD, developed funding opportunities to support Social Epigenomics Research Focused on Minority Health and Health Disparities.[8-10] The overarching objectives of this initiative were to advance understanding of mechanisms by which social factors lead to epigenetic changes that affect minority health and/or health disparities and promote epigenetics research to better predict disease risk or resiliency among populations experiencing health disparities. This initiative was also intended to promote multidisciplinary collaborations combining the knowledge and scientific expertise of social scientists, public health researchers, and molecular biologists. A particular focus of this initiative was integrating the study of social determinants of health with the study of epigenetic mechanisms of health disparities, with the goal of enhancing the field's understanding about how both protective and adverse social determinants may affect human biology through the epigenome and possible mechanisms driving health disparities.

Ultimately, 38 projects were awarded funding because of these opportunities, funded by NIMHD, the National Cancer Institute, the National Institute on Aging, and the National Human Genome Research Institute. Funded projects focused on a range of priority populations with health disparities (eg, African American or Black, American Indian or Alaska Native, Hispanic or Latino, and Native Hawaiian and Pacific Islander individuals and individuals of low socioeconomic status [SES]). The projects covered a full range of life-course stages (prenatal, infancy, childhood, adolescence, young adulthood, adulthood, parenthood, midlife, and older adulthood), a multitude of health conditions (eg, cardiovascular disease, systemic lupus, cancer, asthma, obesity, chronic obstructive pulmonary disease, diabetes, blood pressure, posttraumatic stress disorder, mental health, substance use), and a variety of social context exposures (eg, childhood adversity, trauma, violence, discrimination, neighborhood factors, environmental hazards, economic hardship, psychosocial stress, food insecurity, social support, positive parenting, enculturation- or biculturalism-induced resilience). Projects also used a range of epigenomic approaches, including examination of epigenomewide DNA methylation, microRNA, histone modification, changes in gene expression, epigenetic aging, and telomere length as mechanisms linking social context exposures to health outcomes. Recently, data have emerged from research groups funded by this initiative that demonstrates how measurable epigenetic dysregulation has been observed in association with psychosocial processes across the lifespan in different populations with health disparities.

For example, a study by Yan et al[11] identified preliminary links between nasal epithelial methylation markers associated with measures of exposure to violence and chronic stress to atopic asthma in children and adolescents in Puerto Rico. Another study by Lussier et al[12] found that exposure to financial hardship and physical or sexual abuse in childhood were associated with time-varying differences in DNA methylation, which might link exposure to adversity to potential adverse health outcomes in children and adolescents.[12] Sullivan et al[13] examined childhood adversity and epigenetic aging in the context of improved parenting and found that children with developmental

delays exposed to more adversity showed lower epigenetic age acceleration when parents had more positive and fewer negative parenting practices,[13] suggesting that these epigenetic changes are reversible.

The Thematic Issue on Social Epigenomics

The thematic issue of *JAMA Network Open* highlights new findings from the grantees of NIH's social epigenomics initiative.[14-24] These findings, taken together, clearly link a variety of social, behavioral, and structural factors throughout the life course to epigenomic and other biological changes among populations experiencing health disparities and, in some cases, to downstream health outcomes and disparities.

Some of these findings elucidate how early-life exposures get under the skin to influence epigenetics and, potentially, downstream health outcomes. Brown and colleagues[15] found that lower parental education and higher perceived stress in girls at a median age of 11 years were associated with epigenetic aging and insulin resistance at ages 36 to 43 years, illuminating mechanisms through which low childhood SES can contribute to adult health disparities. The cohort study by Daredia et al[18] found that the children of women who engaged in agricultural fieldwork while pregnant in the Salinas valley in California had accelerated epigenetic aging. This study by Daredia et al[18] provides novel evidence regarding how maternal occupation, with associated environmental and social exposures, may affect the health of children long-term.

On a positive note, findings highlighted in this issue also point toward how interventions may mitigate the negative impacts of early-life challenges on epigenomic markers. A study by Merrill and colleagues[22] found that a 20-week internet-based parent-child interaction training intervention delivered to parents of mostly Black or Latino children with developmental delays led to slower epigenetic aging relative to those in a control condition 12 months after the intervention. There were also lower levels of a DNA-methylation–derived C-reactive protein but not interleukin-6.

Other findings in this special issue illuminate epigenomic pathways through which structural racism and economic deprivation may impact health. The study by Krieger and colleagues[20] found that epigenetic aging was associated with exposure to racialized, economic, and environmental injustice, finding that being born in a Jim Crow state (ie, US states that enforced racial segregation before 1965) was associated with epigenetic age acceleration for Black individuals, and low parental education and adult impoverishment were similarly associated with epigenetic aging for both Black and White participants. A study by Maunakea et al[21] also found associations of low neighborhood SES with a higher rate of epigenetic aging in a cohort primarily composed of Japanese American, Native Hawaiian, and White adults, with the highest rate of accelerated aging among Native Hawaiian participants. Maunakea et al[21] also identified potential protective factors against the adverse associations of neighborhood SES with biological aging, including education and physical activity.

Chiu and colleagues[16] further illuminated behavioral factors that may be health protective via epigenetic mechanisms through their study of dietary quality and epigenetic age. In a cohort of Black and White women at midlife, higher diet quality scores were associated with decelerated epigenetic age, whereas increased added sugar intake was associated with accelerated epigenetic age.[16]

Ultimately, to establish epigenomics as a link between social determinants of health and health disparities in specific populations, it is important to link epigenetic mechanisms to ultimate health outcomes. Smith and colleagues[23] do so with their findings from a prospective cohort study of 864 women from the Gulf Coast who were living in areas affected by the Deepwater Horizon oil spill. Smith et al[23] found that epigenetic age acceleration, which was higher among Black and Native American participants relative to White participants, was associated with PTSD symptoms at a later wave of the study. While there is still more work to be done to fully characterize the mechanistic pathways linking social exposures to epigenetic changes and finally to health outcomes, this study by Smith et al,[23] and the body of work presented in this special issue as a whole,[14-22,24] represent solid progress toward this goal.

These and other findings from the studies highlighted in this special issue[7,14-24] demonstrate important scientific progress in the complex integration of social determinants of health and health disparities with biological pathways and health outcomes to improve our understanding of the mechanisms underlying health disparities among various underserved populations.

Conclusions

Biomedical research has been focused on describing and understanding the biological mechanisms involved in disease causation. Comparatively less attention has been paid to the biological interplay of the social and behavioral factors that are known to impact health disparities. It is very likely that epigenetic processes are at least 1 component that explicates how social context and adverse experiences in an individual's life can alter stress-related inflammatory responses over the lifespan, which, in turn, contribute to social inequalities in risk for certain diseases.

We are excited to present this series of articles in *JAMA Network Open*[14-24] that represent progress in the field of social epigenomics through the NIMHD-led program and demonstrate how integrating social historical context, social determinants of health, and life-course perspectives with molecular mechanisms through epigenomics in research studies have helped elucidate how health disparities emerge among disadvantaged populations. We look forward to continued progress in integrating different disciplines to transform the field of health disparities research.

ARTICLE INFORMATION

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