TRANSFORMING ANTHROPOLOGY

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Race, Rare Genetic Variants, and the Science of Human Difference in the Post-Genomic Age

Abstract

Understanding of human genetic variation has grown significantly in the twenty-first century but has not been adequately incorporated into anti-racist anthropological perspectives. Research into the underlying structure of human disease suggests that common diseases may be caused by rare genetic variants. These variants tend to be specific to populations that are oftentimes racially defined. Consequently, genetic studies that seek to identify disease-causing rare variants rely upon racialized frameworks. Despite social scientific perspectives that endorse a nonbiological basis to race, within biomedicine, biological uses of race remain entrenched due to their utility for identifying the causes of the disease. Anthropologists must be responsive to these utilizations of race or risk irrelevance in shaping how researchers understand and use human variation. Through critique and careful incorporation of new knowledge about the nature of human genetic variation into anthropological perspectives, anthropologists can continue to make meaningful contributions to understanding the relationship between biology and race. [*race, anti-racism, human genetic variation, rare genetic variants*]

INTRODUCTION

Social and biological scientists have developed theories and methodologies to delineate how humans vary and to understand the factors that shape cultural ideas about difference (Berg and Wendt 2011; Duster 2006; Lee 2009; Mullings 2005; Smedley 1999). Despite advances in analytical tools for exploring human variation, consensus on the meaning or value of human biological difference has proved elusive (Ifekwunigwe et al. 2017; Kaszycka et al. 2009; Keita and Boyce 2001). Conceptual divides about the meaning of human variation remain especially relevant in the Post-Genomic Age because the new findings emerging from biomedicine have important implications about the relationship between race and genetics. These new biomedical findings have been instructive about the nature and distribution of genetic variation in relation to disease. Post-Genomic Age is used here to refer to the current time period in which researchers focus their efforts on genomic data in order to learn how the genome interacts with itself to produce and maintain complex phenotypes at molecular, cellular, and organismic levels (Evans 2000; Wynne 2005).

Biological anthropologists generally agree that contemporary human genetic variation is the result of an evolutionary history marked by a single common origin within Africa, introgression with other hominins, and serial founder effects as humans dispersed across the continents (Deschamps et al. 2016; Hsieh et al. 2016; Jobling, Hurles, and Tyler-Smith 2013; Ramachandran et al. 2005). However, among social scientific and biomedical researchers there are fundamental intellectual disagreements as to how to appropriately describe, incorporate, and give meaning to genetic variation in relation to group and individual identity. These dynamics have ramifications beyond the academy related to the way researchers utilize variation in their research, as well as how laypeople engage, interact, and interpret genetic and genomic data in relation to self and community identity (Benn Torres 2018; Hunt and Megyesi 2008; Nelson 2016; Outram and Ellison 2006; Wade et al. 2014). The ambiguous relationship between genetics and collective identity, specifically racial identity, is further amplified by discoveries of new types of human genetic variation. Given new findings about the distribution of human genetic variation across global populations as well as the use of racial categories within biomedical contexts, the question of how to best describe and utilize human genetic variation that is attentive to both environmental context and evolutionary processes remains problematic.

In what follows, I consider the contradictions of the utility of race within biomedical and social

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science contexts, and I argue three main points. First, despite contemporary social scientific understandings regarding the fallacy of biological races (American Anthropological Association 1999; American Association of Physical Anthropologists 1996), new discoveries about human genetic variation foster an intense focus within biomedicine on racial differences in disease. This particular operationalization of race in biomedicine persists, in part, due to a changing disease paradigm in which common diseases are the result of rare genetic variants (Gorlov et al. 2008). Rare genetic variants are nucleotides within a genetic sequence that are infrequent within populations. They are formally defined as variants that have a minor allele frequency of 0.1%.[1] In addition, rare genetic variants are often population-specific, meaning that these variants are found primarily in some populations and not in others. This unequal distribution of rare variants may be the result of genetic drift, mutation, or localized selection effects (Tishkoff and Williams 2002). Of relevance to understanding genetic etiologies of disease, rare variants also appear to have some role in shaping phenotype or physical attributes of an individual.[2] Under this paradigm, the rare variants that underlie common disease are not uniformly distributed across human groups but rather tend to be concentrated within groups—groups that roughly correspond to "folk theories" about race (Gelman and Legare 2011; Hill 2009). Accordingly, biological concepts of race remain firmly embedded in the scientific understanding and study of human disease, creating a gap between how social and biomedical sciences conceive of, report on, and utilize race.

Second, in response to the persistence of biological notions of race within biomedicine, anthropologists must keep pace with new findings about human genetic variation or, as a discipline, risk losing credibility as a relevant source for understanding meaningful human difference. Thinking broadly yet critically about how and why race is utilized in the ways that it is across disciplines will be crucial for anthropologists in order to avoid undermining anthropological critiques about the fallacy of race as biology. Third, I argue that through continuous revision of anthropological perspectives on the relationship between race and biology in light of emerging genetic technologies, as a discipline, anthropology can contribute to more meaningful understandings of how race becomes biology.

RACE IN THE CONTEXT OF SOCIAL SCIENCE AND BIOMEDICINE

From transcontinental expeditions recorded as early as the eighth century, travelers noted that humans varied both culturally and phenotypically; these differences, as some historians argue, were fodder for modern-day notions of race and racism (Goldberg 1993; Ralph 2015; Robinson and Kelley 2000). Since then, the ways in which humans varied captured the imagination of travelers and naturalists alike, especially with improved maritime transportation and expansions of economic networks that occurred in the sixteenth and seventeenth centuries (Berg and Wendt 2011). As illustrated in the work of François Bernier (1684), the earliest efforts to categorize humans into races or varieties emerged. This endeavor to make sense of human difference continued and was refined by eighteenth-century naturalists such as Carolus Linnaeus and his student Johann Friedrich Blumenbach (Brace 2005). In these writings, the authors went beyond simply categorizing human variation, but also probed the nature and ultimately the value of such difference by applying judgments regarding the mental and or physical characterizations of each variety or race (Marks 2001). It was Blumenbach's categorization, or rather hierarchy of human racial types—Ethiopian (African), Malay, Mongolian, and American Indian as degenerates of the ideal-type European—that proved to be very influential in shaping how science was used to justify existing economic and political inequalities (Gould 1994). Throughout the nineteenth and into the twentieth centuries, the work of scientific racists such as Arthur Gobineau, Samuel Morton, Josiah Nott, George Gliddon, and Louis Agassiz upheld racist notions of difference that proved useful in shaping exclusionary immigration and eugenic policies of the early twentieth century (Marks 2009). As detailed by Amos Morris-Reich in his book *Race and Photography* (2016), many of the ideas espoused by these scientific racists were purportedly substantiated through the application of photography within biological studies of racial difference. Not all late nineteenth and early twentieth century scholars agreed with the inclinations of the aforementioned; Anténor Firmin, Franz Boas, and W.E.B. Du Bois, for example, while not denying the existence of racial difference, challenged hierarchical notions of race (Boas 1912; Du Bois 2004; Firmin 2002). During the times that Firmin, Boas, and Du Bois were active, the scientific evidence to support the nonbiological basis to race did not yet exist. As a

consequence, and as evidenced by the writings of these scholars, biological concepts of race were both implied and explicit. Using the available data, the goals of these scholars was not to displace biological race concepts, but instead to deconstruct notions of inherent inequality among human races (Torres Colón and Hobbs 2016). Concurrent with the development of analytical tools to examine human variation from molecular perspectives, scholars working in the mid- to late twentieth century began to assert the lack of support for biological notions of race (Barbujani et al. 1997; Lewontin 1972; Montagu 1962).

For contemporary anthropologists, these early anti-racist works became cornerstones in shaping modern ideas about human difference. Accordingly, most contemporary North American anthropologists take their cue from the American Anthropological Association in suggesting that "differentiating species into biologically defined 'races' has proven meaningless and unscientific as a way of explaining variation" (American Anthropological Association 1995, 3). In this context, race is defined as comprising of fixed, discrete clusters of human groups based on a series of phenotypic characteristics. Rather than a biological reality, race becomes a conception of difference that is built, maintained, and structured by social dynamics itself. In this constructivist perspective, race is reflective of factors including, but not limited to, socioeconomic status, psychosocial/sociopolitical environment, education, discrimination, or access to resources (Cooper 1994; Jackson 1992; Smedley and Smedley 2005). All of these factors, in turn, mediate health-related outcomes in a variety of ways (Berger and Sarnyai 2015; Braveman, Egerter, and Williams 2011; Goodman 2000; Kawachi, Daniels, and Robinson 2005; Lewis, Cogburn, and Williams 2015). For example, as argued by Jones (2000), the negative psychosocial effects of racism can be internalized causing poor decision making with regard to health-seeking behaviors. Similarly, Paradies et al. (2015) found significant associations between racism and physical and mental health where ethnicity (referenced as Asian American, Latino(a) American, and African American) moderated the effects of racism. Finally, there is also research outside of the United States that highlights how psychosocial/sociopolitical factors influence health outcomes. Within Cuba, though racism remains salient, there is less racial disparity with regard to socioeconomic status relative to other regions of the Americas (Paradies et al. 2015; Roland 2011). Ordúñez et al. (2005; 2013) report that, unlike other places throughout the Americas, where individuals of recent African descent experience higher incidences of hypertension, Black Cuban men residing in Cuba have a lower or comparable incidence of hypertension relative to their White peers. Cooper et al. (2005) report similar results for three African-descended populations in a cross-cultural study. The work of Ordúñez, Cooper, and those cited above illustrate that both psychosocial and sociopolitical environments, and not race presumably acting as a proxy for some undetermined biological factor, are potent factors that influence health outcomes.

Accordingly, from the constructivist perspective, employing biological notions of race can preclude the ability to fully understand disparity between groups (Caulfield et al. 2009). Some scholars have cautioned against research efforts that focus solely on genetic or biological factors as causative explanations for racial disparities, noting that such efforts may divert resources away from efforts to understand how psychosocial and sociopolitical factors shape disparity (Braun 2002; Duster 1984, 2015; Williams and Sternthal 2010). Despite the critiques of biological race concepts in medical discussions of disease disparities, the notion that human difference can be codified into racial groups persists and is most apparent in biomedical contexts.

With the discovery of the structure of DNA in 1952 and the subsequent incorporation of molecular biology methodologies into questions of human variation, improved technologies seemingly helped to acquire support for nonbiological explanations of race. Richard Lewontin's seminal paper, "The Apportionment of Human Diversity" (1972), showed that the distribution of human genetic variation does not adequately conform to constructs of race. Since that paper, a number of additional genetic studies, some concurring and others critiquing Lewontin's conclusions, have fueled the debate about human variation as it pertains to the biology of race (Edwards 2003; Jorde et al. 2000; Shiao et al. 2012; Witherspoon et al. 2007).

Despite Lewontin's work and four decades of corroborating research indicating a lack of support for biological races, a 2009 survey by Kaszycka et al. revealed that there remains variability in the perspectives on race; variability that is shaped by sociopolitical factors as well as education. In this survey, Kaszycka et al. asked European anthropologists and scientists from a variety of fields about the existence of biological race. They found

that, "Respondents educated in Western Europe and middle-aged persons reject race more frequently than respondents educated in Eastern Europe and those from both younger and older generations" (Kaszycka et al. 2009, 43). In addition, they noted that biological anthropologists were more likely to reject biological notions of race more often than scientists in other fields. These findings suggest that a biological race concept remains ever present within the sciences and that there is no unifying consensus on the value of human difference across scientific fields.

A series of recent studies by Wagner et al. (2017) and Ifekwunigwe et al. (2017) examined contemporary ideas about the relationship between race, ancestry, and genetics. These new studies, based on survey responses from over three thousand people associated with the American Anthropological Association, appear to challenge Kaszycka et al.'s (2009) findings. Wagner et al. focused on the quantitative aspects of the survey, while Ifekwunigwe et al. analyzed the qualitative aspects of the survey, generally concluding that, among anthropologists, there is consensus on the biological fallacy of race as well as the acknowledgment that the social realities of race as lived experience can have significant impacts on other aspects of life including health. Like Kaszycka et al.'s study, both studies recognized that sociopolitical factors, operationalized as privilege groups, shaped sentiments about race and genetics.[3] While the studies by Wagner et al. and Ifekwunigwe et al. indicate a growing acceptance of the nonbiological basis to race among anthropologists, their results must be tempered against their sample size and participant characteristics. Of the 3,286 survey participants, 82% (n = 1918) were professional anthropologists, and of this amount, only 10% (n = 201) of the respondents were biological anthropologists. This is an important factor because, presumably professional biological anthropologists shape scholarly narratives on biological aspects of human variation which are then disseminated to other academics and eventually the lay public. Accordingly, based on the paucity of responses from biological anthropologists, it may be difficult to accurately gauge consensus on race specifically among this group of anthropologists. Regarding the nuance gained by considering sociopolitical factors, the distribution of participants representing each privilege group were unequal, where only about one-quarter of the participants identified as non-White women or men and about 75% of the respondents identified as White women or men. In the most general terms, this aspect of the study is informative about how sociopolitical factors shape ideas about the relationship between race, ancestry, and genetics. However, the disparity in representation between privilege groups makes it difficult to appreciate variation across and within each group and the reasons behind why such differences in understanding exist. This is particularly important because, as noted by Wagner et al., a nuanced understanding of how privilege groups shape ideas about race is critical due to differences in how privilege groups interpret human variation, and this has implications on how science is done and disseminated to the public (e.g., public policies, appropriate study questions, funding, etc.). Despite evidence of a growing acceptance of a nonbiological bases to race among anthropologists, using available data, there remains some debate about appropriate ways to rectify relationships between race, biology, and genetics.

As I have argued previously (Benn Torres and Kittles 2007), despite an increasing acknowledgment of the limits of the concept of race to explain biological differences, some biomedical scientists continue to employ the "race as biology" paradigm for a variety of reasons (Burchard et al. 2003; Risch et al. 2002; Winker 2006). Though generalizing, in studies that rely on purported biological race, there is usually no clarification of how key terms are being deployed. These types of studies rely on the presumption that the reader knows what or who constitutes each racial group, and this presumption illustrates a lack of scientific holism (Winker 2006). In the absence of an explanation for perceived racial differences, researchers often fall back to using cultural categories about race that are loaded with biological meaning. This approach is reductive and allows for the attribution of group characteristics, biological and otherwise, to a particular health outcome (Bamshad et al. 2004; Kaplan and Bennett 2003).

Additionally, confounding usages of race have become institutionalized in the most influential US scientific establishments (Banks 2011; Kaplan and Bennett 2003; Lee, Nelson, and Wailoo 2012). In grant applications to the largest US public research-funding agency, the National Institutes of Health, investigators are compelled to represent individuals of all races in their proposed study. If a particular group is excluded, investigators must provide a justification. In meeting this obligation, each investigator must estimate the number of people they will attempt to enroll, categorized by

race, where racial categories are defined by the federal Office of Management and Budget or the OMB (Banks 2011; Gabriel 2012). The OMB sets the standard of racial categories to be used in all federal data including the census (Kaplan and Bennett 2003). As evidenced in the social science literature, racial categories change and are often revised with every census even when—as in 2000—individuals were permitted to choose multiple races (Hirschman, Alba, and Farley 2000). Though the upcoming 2020 census will continue to query census takers about their race and ethnicity, academics have developed critiques about how the OMB asks about race and ethnicity. These academics cite problems with how the data are used and interpreted with regard to how majority/minority status is (mis)represented. Additionally, they note that these problematic census data can potentially change policy and rhetoric about the affected populations. (Strmic-Pawl, Jackson, and Garner 2018).[4] While the requirement to adhere to racial categorizations in federal research grants is an attempt to rectify past abuses, such as those that occurred within the Tuskegee Syphilis study (see Washington [2006] for details about this study) and mitigate the possibility of ignoring understudied/underrepresented groups, it, in effect, encourages researchers to impose a racialized study design sometimes without thoughtful regard to the role or meaning of race within the study. While the ethical motivations for this requirement cannot be ignored and have been discussed elsewhere by biologists and social scientists, the imposition of racial categories within biomedical research can aid in reifying racial groups as naturally occurring and biologically distinct groups (Banks 2011; Hahn and Stroup 1994). Thus, many scientists find themselves in a seemingly contradictory position in which they must employ biologized racial constructs yet disregard these purported differences due to the lack of an empirically supported biological basis to race (Banks 2011). In other words, investigators acknowledge difference between human groups and consequently use race as a proxy for these differences, but they are in no way compelled to investigate the nature of relevant differences that may or may not play some role in the health outcomes the research is designed to measure. This federal mandate, while attempting to uphold ethical tenets, can hinder the ability to think about or value human difference in innovative and meaningful ways. Furthermore, according to several meta-analyses, the mandate has not mitigated the lack of minority representation in research (Chen et al. 2014; Geller, Adams, and Carnes 2006; Geller et al. 2011; Knerr, Wayman, and Bonham 2011) and by extension, has not encouraged researchers to shift toward a more critical understanding of how race shapes disease susceptibility. The investigator's paradox, it seems, reflects the larger issue of how to think about and utilize race and human variation as meaningful categories in biomedical research.

While both social science and biomedical researchers agree that humans exhibit variation, as illustrated above, there are fundamental disagreements about how to incorporate and give meaning to difference (Hunt and Megyesi 2008; Outram and Ellison 2006). In the years surrounding the Human Genome Project (1990–2003), scientists and politicians alike projected a future in which genomics held new answers to old problems (Altman 2000; Collins et al. 1998; Guyer and Collins 1995; Lander 1996).[5] Yet, as illustrated in a series of publications between Shiao et al. (2012) and Fujimura et al. (2014), improved understandings of the nature and distribution of human genetic variation have not provided solutions but instead have further heightened tensions about how race is operationalized in the biomedical sciences. Correspondingly, robust responses to these newer findings within genetics have not yet been fully incorporated into anti-racist anthropological perspectives.

THE UNCERTAINTY OF RACE IN THE POST-GENOMIC AGE

Genetic information of the Post-Genomic Age has complicated the debate of how best to employ human genetic variation within research. As referenced here, the Genomic Age refers to both the time period during the Human Genome Project and also the aftermath of the project in which researchers annotated the sequence (Guttmacher and Collins 2003). Increasingly, the term Post-Genomic Age is used to refer to complex investigations into how the different components and products of the sequence work. This includes many types of "-omic" areas of study such as proteomics, which examines the ways that genes are expressed as proteins, or metabolomics, which examines how DNA sequence influences the chemicals that control cellular biochemistry and metabolism (Benner, Trabesinger, and Schreiber 1998; Brower 2001; Jones 2001).

Shortly before the formal end of the Human Genome Project, in the much cited 2002

publication, Rosenberg et al. (2002) used genetic data from fifty-two worldwide populations to examine global patterns of genetic variation. Their analyses suggested that 93%–95% genetic variations can be found within populations, while only 3%–5% was attributed to between-group variation. They also found the most statistical support when the data were portioned into five geographic clusters: Africa, Americas, East Asia, Europe, and Oceania. While the authors did not outwardly promote these clusters as racial groups, these five geographic groups generally correspond to the five varieties identified by Blumenbach some two centuries earlier. This correspondence between nineteenth- and twenty-first-century scientific notions was not missed among the popular press (Wade 2002).[6] Thus, Rosenberg et al.'s publication was perceived as a "scientific" method to determine race because the researchers presumably used biological data to establish differences between groups.

At the time of Rosenberg et al.'s 2002 publication, the statistical estimation of genetic ancestry was not at all a new technique. Several decades before, researchers used a variety of allelic systems based on various genetic markers derived from blood groups, plasma proteins, red cell enzymes, or immunological polymorphisms to estimate proportions of ancestry from global populations (Chakraborty 1975; Mielke, Konigsberg, and Relethford 2010; Pollitzer 1972). However, Rosenberg et al.'s publication was one of the first to use molecular markers derived directly from observing DNA sequences, as opposed to classic or protein genetic markers, to examine human population structure on a global scale.

The use of molecular markers represented a technological advancement. Rather than examining the products of the genetic sequences, researchers could now consider specific locations throughout the genome as well as directly examine forces of evolution (mutation, gene drift, gene flow, and natural selection) in a more refined fashion (Rubicz, Melton, and Crawford 2007). Consequently, this use of molecular markers represented the most up-to-date method of examining global patterns of human genetic variation with the bonus of a precision that had not been available in previous studies.

In addition to examining population substructure at a global scale, researchers have also leveraged human genetic variation to understand the genetic etiologies of disease through the use of genome-wide association studies (GWAS). The primary goal of GWAS is to identify genetic variants that have some role in altering disease risk (Donnelly 2008). While GWAS have had some successes in implicating genetic contributors to disease (MacArthur et al. 2017; McCarthy and MacArthur 2017), they have added to the uncertainty of race as it relates to genetics (Clark et al. 2005; Clarke and Cooper 2010). Of most relevance to human variation and GWAS is the problem of non-replication of significant associations across human groups. With non-replication, genetic variants that confer disease risk within one population do not hold the same significant risk in other populations (Huang et al. 2016; Marigorta et al. 2011; Moonesinghe et al. 2012). Non-replication can be attributed to an uneven distribution of alleles within subpopulations or population substructure (Falush, Stephens, and Pritchard 2003). Population substructure can lead to false positive results in GWAS and diminished statistical power. The problems created by population substructure can be statistically adjusted for in GWAS studies by using genetic ancestry estimates as a corrective factor (McCarthy et al. 2008). Alternatively, researchers may opt to use homogenous populations in GWAS in order to minimize the effects of population substructure (Tian, Gregersen, and Seldin 2008). These analytical issues caused by population substructure and resulting in inconsistent associations across populations can be conflated with biological race concepts. In this line of reasoning, the inconsistent associations between different populations serve as evidence of meaningful biological difference between these populations. Accordingly, the notion of biological race is reified where differences between predetermined groups serve as evidence that the predetermined groups are indeed real and biologically distinct. This stance potentially reinforces the errant conclusion that humans can be divided into biologically meaningful racial groups and, by extension, that genetic etiologies of disease may differ between these groups. This idea of biological race differences is pervasive throughout biomedicine and most evident in study designs that partition by race (Burchard et al. 2003; Caulfield et al. 2009). As a result, both anthropologists and sociologists have critiqued in detail the inconsistent uses of race to describe human genetic variation and the use of race as a biologically meaningful variable (Benn Torres and Kittles 2007; Bolnick et al. 2007; Hatch 2016; Kahn 2012; Roberts 2012; Tall-Bear 2013). As described in these sources, when racialized paradigms become integrated into

biomedical research, the findings of such work can potentially create and reinforce racism as results permeate into health initiatives and policy.

As discussed in the preceding sections, the meanings and value of race within social scientific and biomedical perspectives remains contested, and this issue is highlighted with GWAS. Correspondingly, in response to the problems associated with GWAS, some researchers have called for a change in the underlying disease models used to study the genetics of complex disease (Adeyemo and Rotimi 2010; Katsanis 2016; Rosenberg et al. 2010). These proposed changes to disease models also have relevance to questions of race and human genetic variation.

HUMAN VARIATION AND MODELING HUMAN DISEASE

With the advent of sophisticated bioinformatics analyses, population geneticists and pathobiologists have debated the most appropriate way to model human disease (Gibson 2012; Pritchard and Cox 2002; Zuk et al. 2014). Several competing models have been proposed, among them is the Common Disease Common Variant hypothesis, or CDCV (Bomba, Walter, and Soranzo 2017; Gibson 2012; Peng and Kimmel 2007; Schork et al. 2009). Briefly, the CDCV model proposes that a small number of moderately frequent (in greater than 5% of the population) genetic variants with moderate effects on disease risk underlie common complex diseases such as hypertension or diabetes. In other words, the genetic factors that are associated with common disease are relatively common among affected individuals. According to the CDCV model, one might expect that comparisons of the entire genomes of affected and unaffected groups would reveal genetic factors contributing to the disease because the responsible variants would be found in higher frequencies within the affected group relative to the unaffected group. As mentioned above, this is the idea behind GWAS. While the CDCV model, and by extension, GWAS have been successful in identifying genetic risk factors underlying some inherited diseases, there are significant methodological and statistical challenges in elucidating genetic risk variants in complex disease, especially identifying causal variants across human groups. These challenges include, but are not limited to, developing the appropriate statistical tools to analyze different types of genetic variation such as copy number variants (CNVs), accounting for error in genotype calls that have been imputed (calls that are based on reference data rather than directly genotyped), determining the roles of variants in disease risk, as well as figuring out which and how genes interact with each other to influence disease susceptibility (McCarthy et al. 2008; Moore, Asselbergs, and Williams 2010; Rosenberg et al. 2010). As mentioned, one commonly cited critique of GWAS is lack of replication between populations (Kraft, Zeggini, and Ioannidis 2009). In addition to a lack of replication, another commonly cited limitation of GWAS and its underlying disease model is that for the vast majority of common diseases, the identified risk variants only explain a small amount, about 5%–30%, of the heritable component of a disease (Hirschhorn and Gajdos 2011; Schork et al. 2009). This effectively means that the majority, 70%–95%, of the underlying heritable causes of disease are unknown. Researchers have put forward several ideas to explain why GWAS studies only detect small amounts of the heritable components of a disease: these ideas include epigenetic factors, gene interactions, and discounting the effects of the microbiome as well as population genetic parameters (Sandoval-Motta et al. 2017; Simons et al. 2018). One increasingly accepted idea involves the use of alternative disease models (Manolio et al. 2009; Marian 2012; Zuk et al. 2014).

Though there have been some successes using the CDCV model and GWAS, one alternative model that holds some potential for understanding the genetic architecture of common disease is known as the Common Disease Rare Variant model (CDRV). Under the CDRV model, a large number of rare variants, where rare variants are nucleotide substitutions that occur in less than 1% of the population, have large effects that underlie a common disease (McCarthy et al. 2008).

In a genetic survey published in *Science*, Tennessen et al. (2012) examined the frequency and distribution of rare variants within the protein-coding region of the genome in about twenty-four thousand North Americans. Of the study participants, roughly half were of European descent and the other half of recent African descent. By sequencing the entire protein-coding regions of the genome in each of the participants, the authors identified over five hundred thousand variants, some of which were predicted to influence disease risk. Of the total number of variants observed in the entire sample, approximately 86% were rare and, in evolutionary terms, recent. Tennessen et al. also found that the vast majority, 91%, of the identified rare variants were private or population-specific variants. Of these rare variants, roughly

50% were found only among African Americans, and 41% were found only among European Americans. The remaining 9% of the rare variants were shared between both African American and European American populations. The distribution pattern of rare variants was unlike the pattern observed for common variants, in which 76% of the identified common variants were shared between African American and European American populations. The private alleles are thought to have arisen within their respective populations as a result of demographic histories, namely differences in population growth and in selective pressures.

As explained by the Tennessen et al. findings, because many of these rare variants are private, replication of significant associations in GWAS across different human groups may be unlikely to occur. As some rare variants are predicted to have an impact on disease risk and susceptibility, these private rare variants will, out of necessity, be the focus of biomedical research (Kosmicki et al. 2016). Consequently, as the search to identify disease-causing, population-specific rare genetic variants disseminates through biomedicine, this research will likely be done using a framework that is responsive to the population-specific nature of rare genetic variants. In other words, as the search for causative genetic elements increasingly incorporates rare variants, study designs will have frameworks that are consistent with biological notions of difference, namely, race. Already, some researchers have suggested that racial/ethnic groups should be analyzed independent of one another in attempt to find disease risk alleles in association studies (Ntzani et al. 2012; Wise et al. 2012). Other researchers, however, have begun to make attempts to statistically adjust for confounding that can occur as a result of including multiple ethnic groups in association analyses (Hoffmann and Witte 2015; Lee et al. 2013; Liu et al. 2013). Considering these types of studies, it becomes apparent that due to an expanding understanding of genetic variation in combination with the ease of using race/ethnicity as a categorical variable, where such categorical variables can work to erroneously substantiate invalid notions of biological race, racialized frameworks will persist within biomedicine. This difference between how social scientific and biomedical researchers make use of race will therefore remain distinct and problematic. Accordingly, anthropologists need to critically think about how to reconcile these distinctive applications of race between social and biomedical contexts.

ANTHROPOLOGICAL PERSPECTIVES ON GENETICS AND RACE IN THE POST-GENOMICS AGE

As a discipline, anthropologists espouse the use of holistic approaches to understand human experience; this includes elucidating the nature of what makes humans similar and simultaneously different from each other. While many anthropologists have set aside notions that rely on biology to categorize humans into racial groups, the idea that there is a biological basis to race remains pertinent within some of the broader fields in which anthropological knowledge is produced, as discussed in previous sections. As scholars of human variation, anthropologists must be prepared to engage in and respond to biological ideas about the nature of human difference or risk becoming irrelevant in discussions of meaningful human variation. Given new findings about human variation, such as rare genetic variants and the potential role of rare variants in disease, the overly simplistic idea that race is only a social construct is no longer sufficient. The idea that race can simply be deconstructed into social factors fails to explain underlying elements that shape human difference and potentially falls short in explaining meaningful biological difference between populations that potentially contribute to disease disparity as understood in epidemiological and biomedical literature. Consequently, anthropologists must lead efforts that both critique biological notions of race yet explain the distribution of genetic difference within and across populations. While there is no standard approach to this endeavor, such efforts should be context dependent and consider specific histories, politics, as well as demographic and environmental factors. Constructivist approaches to race, as discussed in previous sections, are attentive to how race and racism shape variation in disease outcomes. These approaches can serve as useful paradigms that may be incorporated into biomedical models, which simultaneously reject biological notions of race yet acknowledge the roles that race may play in shaping biological outcomes.

Inter- and intradisciplinary dialogues between scholars will be necessary to implement new ideas and innovate existing models that allow for the reconciliation of the broader meanings of race, such as social constructions and their interactions with biology. Implementing approaches that promote a critical usage of race across both social and biomedical contexts requires a willingness to seriously consider how and why race is utilized within respective fields. One interesting approach

to this issue was considered by Maglo (2010). In this paper, Maglo proposes that race potentially can be utilized as a "problem-solving tool rather than a concept with an objective referent in nature." Accordingly, the utilization of a biological concept of race may provide a rudimentary means of considering variables such as environment or population structure that are biologically salient. According to Maglo, race becomes a "validity-indifferent utility," meaning that it is not necessary for race itself to be a real biological or evolutionary factor; rather, race is valued on its ability to address research problems (Maglo 2010, 361). Noting this, uses of race in biological frameworks must be done in a critical manner. Researchers must provide some justification explaining the criteria for establishing each group it defines as distinct in an investigation. With a more critical approach to operationalizing race, the constructivist nature of race is acknowledged, and race is valued as a concept in terms of its ability to make sense of biological data. While the inherent danger of typological thinking remains even with this formulaic, this more critical deployment of a race concept has the potential to help bring racialized factors to the forefront of research and to elucidate how race becomes biology. It is through subtle shifts in perspective that race, in a variety of contexts, can be more fully understood and utilized to produce more holistic insights into the factors that modify human experience.

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NOTES

1. See also: "Rare Variants." *Nature* website. Accessed April 22, 2013. https://www.nature.com/subjects/rare-variants.

2. See also: Hayden, Erika. 2012. "Humans Riddled with Rare Genetic Variants." *Nature* website. May 17, 2012. Accessed April 23, 2013. http://dx.doi.org/10.1038/nature.2012.10655.

3. In these studies, sociopolitical factors were approximated by categorizing participants into one of four "privilege categories": non-White woman, White woman, non-White man, and White man.

4. See also: Alba, Richard. 2018. "Analysis | There's a Big Problem with How the Census Measures Race." *Washington Post* website, February 6, 2018, sec. Monkey Cage Analysis. Accessed May 24, 2018. https://www.washingtonpost.com/news/monkey-cage/wp/2018/02/06/theres-a-big-problem-with-how-the-census-measures-race
Autry, Robyn. 2017. "How Racial Data Gets 'Cleaned' in the U.S. Census." *The Atlantic* website, November 5. Accessed May 24, 2018. https://www.theatlantic.com/technology/archive/2017/11/how-racial-data-gets-cleaned/541575/.

5. See also: Clinton, Bill. 2000. "Announcing the Completion of the First Survey of the Entire Human Genome." The White House at Work website. June 26. Accessed April 25, 2018. https://clintonwhitehouse4.archives.gov/WH/Work/062600.html.
Watson, James, and Norton Zinder. 1990. "Genome Project Maps Paths of Diseases and Drugs." *The New York Times* website, October 13, 1990, sec. Opinion. Accessed April 25, 2018. https://www.nytimes.com/1990/10/13/opinion/l-genome-project-maps-paths-of-diseases-and-drugs-239090.html

6. See also: Wade, Nicholas. 2003. "2 Scholarly Articles Diverge On Role of Race in Medicine." *The New York Times* website, March 20, sec. U.S. Accessed May 22, 2018. https://www.nytimes.com/2003/03/20/us/2-scholarly-articles-diverge-on-role-of-race-in-medicine.html

REFERENCES CITED

Adeyemo, Adebowale, and Charles Rotimi. 2010. "Genetic Variants Associated with Complex Human Diseases Show Wide Variation across Multiple Populations." *Public Health Genomics* 13: 72–9. doi.org/10.1159/000218711.

Altman, Lawrence K. 2000. "Genomic Chief Has High Hopes, and Great Fears, for Genetic Testing." The New York Times, June 27.

American Anthropological Association. 1995. "AAA Resolution on 'Race' and Intelligence." *Anthropology News* 36(1): 3.

American Anthropological Association. 1999. "AAA Statement on Race." *American Anthropologist* 100(3): 712–13.

American Association of Physical Anthropologists. 1996. "AAPA Statement on Biological Aspects of Race." *American Journal of Physical Anthropology* 101: 569.

Bamshad, Michael, Stephen Wooding, Benjamin A. Salisbury, and J. Claiborne Stephens. 2004. "Deconstructing the Relationship between Genetics and Race." *Nature Reviews Genetics* 5(8): 598–609. doi.org/10.1038/nrg1401.

Banks, Taunya Lovell. 2011. "Funding Race as Biology: The Relevance of Race in Medical Research." *Minnesota Journal of Law, Science & Technology* 12: 571.

Barbujani, Guido, Arianna Magagni, Eric Minch, and L. Luca Cavalli-Sforza. 1997. "An Apportionment of Human DNA Diversity." *Proceedings of the National Academy of Sciences* 94(9): 4516–19. doi.org/10.1073/pnas.94.9.4516

Benn Torres, Jada. 2018. "'Reparational' Genetics: Genomic Data and the Case for Reparations in the Caribbean." *Genealogy* 2 (1): 7. doi: 10.3390/genealogy2010007

Benn Torres, Jada, and Rick Kittles. 2007. "The Relationship between 'Race' and Genetics in Biomedical Research." *Current Hypertension Reports* 9: 196–201.

Benner, Steven A., Nathalie Trabesinger, and David Schreiber. 1998. "Post-Genomic Science: Converting Primary Structure into Physiological Function." *Advances in Enzyme Regulation* 38: 155–80. doi.org/10.1016/S0065-2571(97)00019-8

Berg, Manfred, and Simon Wendt, eds. 2011. *Racism in the Modern World: Historical Perspectives on Cultural Transfer and Adaptation*. New York: Berghahn Books.

Berger, Maximus, and Zoltán Sarnyai. 2015. "'More than Skin Deep': Stress Neurobiology and Mental Health Consequences of Racial Discrimination." *Stress* 18: 1–10.

Bernier, François. 1684. "Nouvelle Division de La Terre, Par Les Differentes Especes Ou Races d'hommes Qu Habitent, Envoyée Par Un Fameux Voyageur à Monsieur . . . a Peu Pres En Ces Termes." *Journal Des Sçavans* 12: 148–55.

Boas, Franz. 1912. *The Real Race Problem from the Point of View of Anthropology*. National Association for the Advancement of Colored People. Publications, 3. New York: The National Association for the Advancement of Colored People.

Bolnick, Deborah A., Duana Fullwiley, Troy Duster, Richard S. Cooper, Joan H. Fujimura, Jonathan Kahn, Jay S. Kaufman, et al. 2007. "The Science and Business of Genetic Ancestry Testing." *Science* 318(5849): 399–400. doi.org/10.1126/science.1150098.

Bomba, Lorenzo, Klaudia Walter, and Nicole Soranzo. 2017. "The Impact of Rare and Low-Frequency Genetic Variants in Common Disease." *Genome Biology* 18: 77. doi.org/10.1186/s13059-017-1212-4.

Brace, C. Loring. 2005. *"Race" Is a Four-Letter Word: The Genesis of the Concept*. New York: Oxford University Press.

Braun, Lundy. 2002. "Race, Ethnicity, and Health: Can Genetics Explain Disparities?" *Perspectives in Biology and Medicine* 45: 159–74.

Braveman, Paula, Susan Egerter, and David R. Williams. 2011. "The Social Determinants of Health: Coming of Age." *Annual Review of Public Health* 32(1): 381–98. doi.org/10.1146/annurev-publhealth-031210-101218

Brower, Vicki. 2001. "Proteomics: Biology in the Post-Genomic Era: Companies All over the World Rush to Lead the Way in the New Post-Genomics Race." *EMBO Reports* 2(7): 558–60. doi: 10.1093/embo-reports/kve144

Burchard, Esteban González, Elad Ziv, Natasha Coyle, Scarlett Lin Gomez, Hua Tang, Andrew J. Karter, Joanna L. Mountain, Eliseo J. Pérez-Stable, Dean Sheppard, and Neil Risch. 2003. "The Importance of Race and Ethnic Background in Biomedical Research and Clinical Practice." *New England Journal of Medicine* 348(12): 1170–5. doi.org/10.1056/NEJMsb025007.

Caulfield, Timothy, Stephanie M. Fullerton, Sarah E. Ali-Khan, Laura Arbour, Esteban G. Burchard, Richard S. Cooper, Billie-Jo Hardy, Simrat Harry, Robyn Hyde-Lay, and Jonathan Kahn. 2009. "Race and Ancestry in Biomedical Research: Exploring the Challenges." *Genome Medicine* 1: 1–8.

Chakraborty, Ranajit. 1975. "Estimation of Race Admixture–a New Method." *American Journal of Physical Anthropology* 42 (3): 507–11. doi.org/10.1002/ajpa.1330420319

Chen, Moon S., Primo N. Lara, Julie H. T. Dang, Debora A. Paterniti, and Karen Kelly. 2014. "Twenty Years Post-NIH Revitalization Act: Enhancing Minority Participation in Clinical Trials (EMPaCT): Laying the Groundwork for Improving Minority Clinical Trial Accrual." *Cancer* 120(S7): 1091–6. doi.org/10.1002/cncr.28575

Clark, Andrew G., Eric Boerwinkle, James Hixson, and Charles F. Sing. 2005. "Determinants of the Success of Whole-Genome Association Testing." *Genome Research* 15(11): 1463–7. doi.org/10.1101/gr.4244005

Clarke, Angus J., and David N. Cooper. 2010. "GWAS: Heritability Missing in Action?" *European Journal of Human Genetics* 18(8): 859–61. doi.org/10.1038/ejhg.2010.35

Collins, Francis S., Ari, Patrinos, Elke, Jordan, the members of the DOE and NIH Planning Groups. 1998. "New Goals for the U.S. Human Genome Project: 1998-2003." *Science* 282(5389): 682–9. doi.org/10.1126/science.282.5389.682.

Cooper, Richard S. 1994. "A Case Study in the Use of Race and Ethnicity in Public Health Surveillance." *Public Health Reports* 109(1): 46–52.

Cooper, Richard S., Katharina Wolf-Maier, Amy Luke, Adebowale Adeyemo, José R. Banegas, Terrence Forrester, Simona Giampaoli, et al. 2005. "An International Comparative Study of Blood Pressure in Populations of European vs. African Descent." *BMC Medicine* 3: 2.

Deschamps, Matthieu, Guillaume Laval, Maud Fagny, Yuval Itan, Laurent Abel, Jean-Laurent Casanova, Etienne Patin, et al. 2016. "Genomic Signatures of Selective Pressures and Introgression from Archaic Hominins at Human Innate Immunity Genes." *The American Journal of Human Genetics* 98: 5–21.

Donnelly, Peter. 2008. "Progress and Challenges in Genome-Wide Association Studies in Humans." *Nature* 456: 728–31.

Du Bois, W.E.B. 2004. "*Illustrated Souls of Black Folk*." In *Provenzo*, edited by Eugene F. Provenzo. London: Routledge.

Duster, Troy. 1984. "A Social Frame for Biological Knowledge." In *Cultural Perspectives on Biological Knowledge*, edited by Troy Duster and Karen Garrett, 1–40. Norwood: ABLEX Pub. Corp.

Duster, Troy. 2006. "Lessons from History: Why Race and Ethnicity Have Played a Major Role in Biomedical Research." *The Journal of Law, Medicine & Ethics* 34: 487–96. doi.org/10.1111/j.1748-720X.2006.00060.x.

Duster, Troy. 2015. "A Post-Genomic Surprise. The Molecular Reinscription of Race in Science, Law and Medicine." *The British Journal of Sociology* 66: 1–27.

Edwards, A.W. 2003. "Human Genetic Diversity: Lewontin's Fallacy." *BioEssays : News and Reviews in Molecular, Cellular and Developmental Biology* 25: 798–801. doi.org/10.1002/bies.10315

Evans, Glen A. 2000. "Designer Science and the 'Omic' Revolution." *Nature Biotechnology* 18(2): 127–127. doi.org/10.1038/72480

Falush, Daniel, Matthew Stephens, and Jonathan K. Pritchard. 2003. "Inference of Population Structure Using Multilocus Genotype Data: Linked Loci and Correlated Allele Frequencies." *Genetics* 164(4): 1567–87.

Firmin, Anténor. 2002. "*The Equality of the Human Races: Positivist Anthropology*, Translated by Asselin Charles. Urbana and Chicago: University of Illinois Press.

Fujimura, Joan H., Deborah A. Bolnick, Ramya Rajagopalan, Jay S. Kaufman, Richard C. Lewontin, Troy Duster, Pilar Ossorio, et al. 2014. "Clines Without Classes How to Make Sense of Human Variation." *Sociological Theory* 32: 208–27.

Gabriel, Abram. 2012. "A Biologist's Perspective on DNA and Race." In *Genetics and the Unsettled Past: The Collision of DNA, Race, and History*, edited by Keith Wailoo, Alondra Nelson, and Catherine Lee, 43–66. New Brunswick: Rutgers University Press.

Geller, Stacie E., Marci Goldstein Adams, and Molly Carnes. 2006. "Adherence to Federal Guidelines for Reporting of Sex and Race/Ethnicity in Clinical Trials." *Journal of Women's Health* 15(10): 1123–31. doi.org/10.1089/jwh.2006.15.1123.

Geller, Stacie E., Abby Koch, Beth Pellettieri, and Molly Carnes. 2011. "Inclusion, Analysis, and Reporting of Sex and Race/

Ethnicity in Clinical Trials: Have We Made Progress?" *Journal of Women's Health* 20(3): 315–20. doi.org/10.1089/jwh.2010.2469.

Gelman, Susan A., and Cristine H. Legare. 2011. "Concepts and Folk Theories." *Annual Review of Anthropology* 40: 379–98.

Gibson, Greg. 2012. "Rare and Common Variants: Twenty Arguments." *Nature Reviews Genetics* 13(2): 135–45. doi.org/10.1038/nrg3118.

Goldberg, David Theo. 1993. *Racist Culture: Philosophy and the Politics of Meaning*. Cambridge, MA: Blackwell.

Goodman, Alan H. 2000. "Why Genes Don't Count (for Racial Differences in Health)." *American Journal of Public Health* 90: 1699–702.

Gorlov, Ivan P., Olga Y. Gorlova, Shamil R. Sunyaev, Margaret R. Spitz, and Christopher I. Amos. 2008. "Shifting Paradigm of Association Studies: Value of Rare Single-Nucleotide Polymorphisms." *The American Journal of Human Genetics* 82: 100–12. doi.org/10.1016/j.ajhg.2007.09.006.

Gould, Stephen Jay. 1994. "The Geometer of Race." *Discover* 15: 65–9.

Guttmacher, Alan E., and Francis S. Collins. 2003. "Welcome to the Genomic Era." *New England Journal of Medicine* 349: 996–8. doi.org/10.1056/NEJMe038132.

Guyer, Mark S., and Francis S. Collins. 1995. "How Is the Human Genome Project Doing, and What Have We Learned so Far?" *Proceedings of the National Academy of Sciences of the United States of America* 92(24): 10841–8.

Hahn, Robert A., and Donna F. Stroup. 1994. "Race and Ethnicity in Public Health Surveillance: Criteria for the Scientific Use of Social Categories." *Public Health Reports* 109(1): 7–15.

Hatch, Anthony Ryan. 2016. *Blood Sugar: Racial Pharmacology and Food Justice in Black America*. Minneapolis: University of Minnesota Press.

Hill, Jane H. 2009. *The Everyday Language of White Racism*. Malden, MA: John Wiley & Sons.

Hirschhorn, Joel N., and Zofia K. Z. Gajdos. 2011. "Genome-Wide Association Studies: Results from the First Few Years and Potential Implications for Clinical Medicine." *Annual Review of Medicine* 62(1): 11–24. doi.org/10.1146/annurev.med.091708.162036.

Hirschman, Charles, Richard Alba, and Reynolds Farley. 2000. "The Meaning and Measurement of Race in the U.S. Census: Glimpses into the Future." *Demography* 37: 381. doi: 10.2307/2648049

Hoffmann, Thomas J., and John S. Witte. 2015. "Strategies for Imputing and Analyzing Rare Variants in Association Studies." *Trends in Genetics* 31: 556–63. doi.org/10.1016/j.tig.2015.07.006.

Hsieh, PingHsun, August E. Woerner, Jeffrey D. Wall, Joseph Lachance, Sarah A. Tishkoff, Ryan N. Gutenkunst, and Michael F. Hammer. 2016. "Model-Based Analyses of Whole-Genome Data Reveal a Complex Evolutionary History Involving Archaic Introgression in Central African Pygmies." *Genome Research* 26: 291–300. doi.org/10.1101/gr.196634.115.

Huang, Minjun, Britney E. Graham, Ge Zhang, Reed Harder, Nuri Kodaman, Jason H. Moore, Louis Muglia, et al. 2016. "Evolutionary Triangulation: Informing Genetic Association Studies with Evolutionary Evidence." *BioData Mining* 9: 12. doi.org/10.1186/s13040-016-0091-7.

Hunt, Linda M., and Mary S. Megyesi. 2008. "The Ambiguous Meanings of the Racial/Ethnic Categories Routinely Used in Human Genetics Research." *Social Science & Medicine* 66: 349–61.

Ifekwunigwe, Jayne O., Jennifer K. Wagner, Yu Joon-Ho, Tanya M. Harrell, Michael J. Bamshad, and Charmaine D. Royal. 2017. "A Qualitative Analysis of How Anthropologists Interpret the Race Construct." *American Anthropologist* 119(3): 422–34. doi.org/10.1111/aman.12890.

Jackson, Fatimah L. C. 1992. "Race and Ethnicity as Biological Constructs." *Ethnicity & Disease* 2(2): 120–5.

Jobling, Mark, Matthew Hurles, and Chris Tyler-Smith. 2013. *Human Evolutionary Genetics: Origins, Peoples & Disease*. New York: Garland Science.

Jones, Camara P. 2000. "Levels of Racism: A Theoretic Framework and a Gardener's Tale." *American Journal of Public Health* 90 (8): 1212–15.

Jones, Patricia. 2001. "Bioinformatics in the Post-Genomic Age." *World Patent Information* 23: 349–54. doi.org/10.1016/S0172-2190(01)00043-6

Jorde, Lynn B., W. Scott Watkins, Michael J. Bamshad, M.E. Dixon, C.E. Ricker, M. Seielstad, and Mark A. Batzer. 2000. "The Distribution of Human Genetic Diversity: A Comparison of Mitochondrial, Autosomal, and Y-Chromosome Data." *American Journal of Human Genetics* 66: 979–88.

Kahn, Jonathan. 2012. *Race in a Bottle: The Story of BiDil and Racialized Medicine in a Post-Genomic Age*. New York: Columbia University Press.

Kaplan, Judith B., and Trude Bennett. 2003. "Use of Race and Ethnicity in Biomedical Publication." *JAMA : The Journal of the American Medical Association* 289(20): 2709–16. doi.org/10.1001/jama.289.20.2709

Kaszycka, Katarzyna A., Goran Štrkalj, and Jan Strzałko. 2009. "Current Views of European Anthropologists on Race: Influence of Educational and Ideological Background." *American Anthropologist* 111: 43–56. doi.org/10.1111/j.1548-1433.2009.01076.x

Katsanis, Nicholas. 2016. "The Continuum of Causality in Human Genetic Disorders." *Genome Biology* 17: 233. doi.org/10.1186/s13059-016-1107-9

Kawachi, Ichiro, Norman Daniels, and Dean E. Robinson. 2005. "Health Disparities By Race and Class: Why Both Matter." *Health Affairs* 24(2): 343–52. doi.org/10.1377/hlthaff.24.2.343

Keita, Shomarka O. Y., and A.J. Boyce. 2001. "'Race': Confusion about Zoological and Social Taxonomies, and Their Places in Science." *American Journal of Human Biology* 13: 569–75. doi.org/10.1002/ajhb.1095.

Knerr, Sarah, Dawn Wayman, and Vence L. Bonham. 2011. "Inclusion of Racial and Ethnic Minorities in Genetic Research: Advance the Spirit by Changing the Rules?" *The Journal of Law, Medicine & Ethics* 39(3): 502–12. doi.org/10.1111/j.1748-720X.2011.00617.x.

Kosmicki, Jack A., Claire L. Churchhouse, Manuel A. Rivas, and Benjamin M. Neale. 2016. "Discovery of Rare Variants for Complex Phenotypes." *Human Genetics* 135(6): 625–34. doi.org/10.1007/s00439-016-1679-1.

Kraft, Peter, Eleftheria Zeggini, and John P. A. Ioannidis. 2009. "Replication in Genome-Wide Association Studies." *Statistical Science : A Review Journal of the Institute of Mathematical Statistics* 24(4): 561–73. doi.org/10.1214/09-STS290.

Lander, Eric S. 1996. "The New Genomics: Global Views of Biology." *Science* 274(5287): 536–9. doi.org/10.1126/science.274.5287.536.

Lee, Catherine. 2009. "'Race' and 'Ethnicity' in Biomedical Research: How Do Scientists Construct and Explain Differences in Health?" *Social Science & Medicine* 68: 1183–90.

Lee, Catherine, Alondra Nelson, and Keith Wailoo. 2012. *Genetics and the Unsettled Past the Collision of DNA, Race, and History*. New Brunswick, NJ: Rutgers University Press.

Lee, Seunggeun, Tanya M. Teslovich, Michael Boehnke, and Xihong Lin. 2013. "General Framework for Meta-Analysis of Rare Variants in Sequencing Association Studies." *The American Journal of Human Genetics* 93: 42–53. doi.org/10.1016/j.ajhg.2013.05.010.

Lewis, Tené T., Courtney D. Cogburn, and David R. Williams. 2015. "Self-Reported Experiences of Discrimination and Health: Scientific Advances, Ongoing Controversies, and Emerging Issues." *Annual Review of Clinical Psychology* 11: 407–40.

Lewontin, Richard C. 1972. "The Apportionment of Human Diversity." *Evolutionary Biology* 6: 381–98.

Liu, Jinghua, Juan Pablo Lewinger, Frank D. Gilliland, W. James Gauderman, and David V. Conti. 2013. "Confounding and Heterogeneity in Genetic Association Studies with Admixed Populations." *American Journal of Epidemiology* 177: 351–60. doi.org/10.1093/aje/kws234.

MacArthur, Jacqueline, Emily Bowler, Maria Cerezo, Laurent Gil, Peggy Hall, Emma Hastings, Heather Junkins, et al. 2017. "The New NHGRI-EBI Catalog of Published Genome-Wide Association Studies (GWAS Catalog)." *Nucleic Acids Research* 45(D1): D896–901. doi.org/10.1093/nar/gkw1133.

Maglo, Koffi N. 2010. "Genomics and the Conundrum of Race: Some Epistemic and Ethical Considerations." *Perspectives in Biology and Medicine* 53(3): 357–72. doi.org/10.1353/pbm.0.0171.

Manolio, Teri A., Francis S. Collins, Nancy J. Cox, David B. Goldstein, Lucia A. Hindorff, David J. Hunter, Mark I. McCarthy, et al. 2009. "Finding the Missing Heritability of Complex Diseases." *Nature* 461(7265): 747–53. doi.org/10.1038/nature08494.

Marian, Ali J. 2012. "Elements of 'Missing Heritability'." *Current Opinion in Cardiology* 27(3): 197–201. doi.org/10.1097/HCO.0b013e328352707d.

Marigorta, Urko M., Oscar Lao, Ferran Casals, Francesc Calafell, Carlos Morcillo-Suárez, Rui Faria, Elena Bosch, et al. 2011. "Recent Human Evolution Has Shaped Geographical Differences in Susceptibility to Disease." *BMC Genomics* 12(1): 55–69. doi.org/10.1186/1471-2164-12-55.

Marks, Jonathan M. 2001. *Human Biodiversity: Genes, Race, and History*. New Brunswick, NJ: Transaction Publishers.

Marks, Jonathan. 2009. *Why I Am Not a Scientist: Anthropology and Modern Knowledge*. Berkeley: University of California Press.

McCarthy, Mark I., Gonçalo R. Abecasis, Lon R. Cardon, David B. Goldstein, Julian Little, John P. A. Ioannidis, and Joel N. Hirschhorn. 2008. "Genome-Wide Association Studies for Complex Traits: Consensus, Uncertainty and Challenges." *Nature Reviews Genetics* 9(5): 356–69. doi.org/org/10.1038/nrg2344.

McCarthy, Mark I., and Daniel G. MacArthur. 2017. "Human Disease Genomics: From Variants to Biology." *Genome Biology* 18: 20. doi.org/10.1186/s13059-017-1160-z.

Mielke, James H., Lyle W. Konigsberg, and John H. Relethford. 2010. *Human Biological Variation*, Vol. 2, USA: Oxford University Press.

Montagu, Ashley. 1962. "The Concept of Race." *American Anthropologist* 64: 919–28.

Moonesinghe, Ramal, John P.A. Ioannidis, W. Dana Flanders, Quanhe Yang, Benedict I. Truman, and Muin J. Khoury. 2012. "Estimating the Contribution of Genetic Variants to Difference in Incidence of Disease between Population Groups." *European Journal of Human Genetics* 20(8): 831–6. doi.org/10.1038/ejhg.2012.15.

Moore, Jason H., Folkert W. Asselbergs, and Scott M. Williams. 2010. "Bioinformatics Challenges for Genome-Wide Association Studies." *Bioinformatics* 26(4): 445–55. doi.org/10.1093/bioinformatics/btp713.

Morris-Reich, Amos. 2016. *Race and Photography: Racial Photography as Scientific Evidence, 1876–1980*. Chicago, IL: University of Chicago Press.

Mullings, Leith. 2005. "Interrogating Racism: Toward an Antiracist Anthropology." *Annual Review of Anthropology* 34: 667–93. doi.org/10.1146/annurev.anthro.32.061002.093435.

Nelson, Alondra. 2016. *The Social Life of DNA : Race, Reparations, and Reconciliation after the Genome*. Boston: Beacon Press.

Ntzani, Evangelia E., George Liberopoulos, Teri A. Manolio, and John P. A. Ioannidis. 2012. "Consistency of Genome-Wide Associations across Major Ancestral Groups." *Human Genetics* 131: 1057–71. doi.org/10.1007/s00439-011-1124-4.

Ordúñez, Pedro, Jay S. Kaufman, Mikhail Benet, Alain Morejon, Luis C. Silva, David A. Shoham, and Richard S. Cooper. 2013. "Blacks and Whites in Cuba Have Equal Prevalence of Hypertension: Confirmation from a New Population Survey." *BMC Public Health* 13(1): 169. doi.org/10.1186/1471-2458-13-169.

Ordunez, Pedro, Jose Luis Bernal Munoz, Alfredo Espinosa-Brito, Luis Carlos Silva, and Richard S. Cooper. 2005. "Ethnicity, Education, and Blood Pressure in Cuba." *American Journal of Epidemiology* 162(1): 49–56. doi.org/10.1093/aje/kwi163.

Outram, Simon M., and George T. H. Ellison. 2006. "Anthropological Insights into the Use of Race/Ethnicity to Explore Genetic Contributions to Disparities in Health." *Journal of Biosocial Science* 38: 83.

Paradies, Yin, Jehonathan Ben, Nida Denson, Amanuel Elias, Naomi Priest, Alex Pieterse, Arpana Gupta, Margaret Kelaher, et al. 2015. "Racism as a Determinant of Health: A Systematic Review and Meta-Analysis." *PLoS ONE* 10: e0138511.

Peng, Bo, and Marek Kimmel. 2007. "Simulations Provide Support for the Common Disease-Common Variant Hypothesis." *Genetics* 175: 763.

Pollitzer, William S. 1972. "Problems in Admixture Estimates from Different Genetic Loci." *Haematologia* 6: 193–8.

Pritchard, Jonathan K., and Nancy J. Cox. 2002. "The Allelic Architecture of Human Disease Genes: Common Disease-Common Variant… or Not?" *Human Molecular Genetics* 11: 2417–23. doi.org/10.1093/hmg/11.20.2417.

Ralph, Michael. 2015. *Forensics of Capital*. Chicago: University of Chicago Press.

Ramachandran, Sohini, Omkar Deshpande, Charles C. Roseman, Noah A. Rosenberg, Marcus W. Feldman, and L. Luca Cavalli-Sforza. 2005. "Support from the Relationship of Genetic and Geographic Distance in Human Populations for a Serial Founder Effect Originating in Africa." *Proceedings of the National Academy of Sciences* 102(44): 15942–7. doi.org/10.1073/pnas.0507611102.

Risch, Neil, Esteban Burchard, Elad Ziv, and Hua Tang. 2002. "Categorization of Humans in Biomedical Research: Genes, Race and Disease." *Genome Biology* 3(7): comment2007.1–2007.12.

Roberts, Dorothy. 2012. *Fatal Invention: How Science, Politics, and Big Business Re-Create Race in the Twenty-First Century*. New York: The New Press.

Robinson, Cedric J., and Robin D. G. Kelley. 2000. *Black Marxism: The Making of the Black Radical Tradition*. Chapel Hill: The University of North Carolina Press.

Roland, Lorecia Kaifa. 2011. *Cuban Color in Tourism and La Lucha: An Ethnography of Racial Meanings*. New York: Oxford University Press.

Rosenberg, Noah A., Lucy Huang, Ethan M. Jewett, Zachary A. Szpiech, Ivana Jankovic, and Michael Boehnke. 2010. "Genome-Wide Association Studies in Diverse Populations." *Nature Review Genetics* 11: 356–66.

Rosenberg, Noah A., Jonathan K. Pritchard, James L. Weber, Howard M. Cann, Kenneth K. Kidd, Lev A. Zhivotovsky, and Marcus W. Feldman. 2002. "Genetic Structure of Human Populations." *Science* 298(5602): 2381–5. doi.org/10.1126/science.1078311.

Rubicz, Rohina, Phillip E. Melton, and Michael H. Crawford. 2007. "Molecular Markers in Anthropological Genetic Studies." In *Anthropological Genetics: Theory, Methods and Applications*, edited by Michael H. Crawford, 141–86. New York: Cambridge University Press.

Sandoval-Motta, Santiago, Maximino Aldana, Esperanza Martínez-Romero, and Alejandro Frank. 2017. "The Human Microbiome and the Missing Heritability Problem." *Frontiers in Genetics* 8: 80. doi: 10.3389/fgene.2017.00080

Schork, Nicholas J., Sarah S. Murray, Kelly A. Frazer, and Eric J. Topol. 2009. "Common vs. Rare Allele Hypotheses for Complex Diseases." *Current Opinion in Genetics & Development* 19: 212–19. doi.org/10.1016/j.gde.2009.04.010.

Shiao, Jiannbin Lee, Thomas Bode, Amber Beyer, and Daniel Selvig. 2012. "The Genomic Challenge to the Social Construction of Race." *Sociological Theory* 30(2): 67–88.

Simons, Yuval B., Kevin Bullaughey, Richard R. Hudson, and Guy Sella. 2018. "A Population Genetic Interpretation of GWAS Findings for Human Quantitative Traits." *PLoS Biology* 16 (3): e2002985. doi: 10.1371/journal.pbio.2002985

Smedley, Audrey. 1999. *Race in North America: Origin and Evolution of a Worldview*. Boulder, CO: Westview Press.

Smedley, Audrey, and Brian D. Smedley. 2005. "Race as Biology Is Fiction, Racism as a Social Problem Is Real: Anthropological and Historical Perspectives on the Social Construction of Race." *American Psychologist* 60(1): 16–26. doi.org/10.1037/0003-066X.60.1.16.

Strmic-Pawl, Hephzibah V., Brandon A. Jackson, and Steve Garner. 2018. "Race Counts: Racial and Ethnic Data on the U.S. Census and the Implications for Tracking Inequality." *Sociology of Race and Ethnicity* 4(1): 1–13. doi.org/10.1177/2332649217742869.

TallBear, Kimberly. 2013. *Native American DNA: Tribal Belonging and the False Promise of Genetic Science*. Minneapolis: University of Minnesota Press.

Tennessen, Jacob A., Abigail W. Bigham, Timothy D. O'Connor, Wenqing Fu, E. E. Kenny, Simon Gravel, S. McGee, et al. 2012. "Evolution and Functional Impact of Rare Coding Variation from Deep Sequencing of Human Exomes." *Science* 337: 64–9. doi: 10.1126/science.1219240

Tian, Chao, Peter K. Gregersen, and Michael F. Seldin. 2008. "Accounting for Ancestry: Population Substructure and Genome-Wide Association Studies." *Human Molecular Genetics* 17: R143–50. doi: 10.1093/hmg/ddn268

Tishkoff, Sarah A., and Scott M. Williams. 2002. "Genetic Analysis of African Populations: Human Evolution and Complex Disease." *Nature Review Genetics* 3: 611–21.

Torres Colón, Gabriel Alejandro, and Charles A. Hobbs. 2016. "Toward a Pragmatist Anthropology of Race." *The Pluralist* 11(1): 126–35. doi.org/10.5406/pluralist.11.1.0126.

Wade, Nicholas. 2002. "Gene Study Identifies 5 Main Human Populations, Linking Them to Geography." *New York Times*, December 12.

Wade, Peter, Carlos López López Beltrán, Eduardo Restrepo, and Ricardo Ventura Santos. 2014. *Mestizo Genomics: Race Mixture, Nation, and Science in Latin America*. Durham, NC: Duke University Press.

Wagner, Jennifer K., Yu Joon-Ho, Jayne O. Ifekwunigwe, Tanya M. Harrell, Michael J. Bamshad, and Charmaine D. Royal. 2017. "Anthropologists' Views on Race, Ancestry, and Genetics." *American Journal of Physical Anthropology* 162(2): 318–27. doi.org/10.1002/ajpa.23120.

Washington, Harriet. 2006. *Medical Apartheid*. New York: Double Day.

Williams, David R., and Michelle Sternthal. 2010. "Understanding Racial-Ethnic Disparities in Health: Sociological Contributions." *Journal of Health and Social Behavior* 51 Suppl: S15–27. doi: 10.1177/0022146510383838

Winker, Margaret A. 2006. "Race and Ethnicity in Medical Research: Requirements Meet Reality." *The Journal of Law, Medicine & Ethics* 34(3): 520–5. doi.org/10.1111/j.1748-720X.2006.00065.x.

Wise, Lauren A., Edward A. Ruiz-Narvaez, Julie R. Palmer, Yvette C. Cozier, Arti Tandon, Nick Patterson, Rose G. Radin, et al. 2012. "African Ancestry and Genetic Risk for Uterine Leiomyomata." *American Journal of Epidemiology* 176(12): 1159–68. doi.org/10.1093/aje/kws276.

Witherspoon, David J., Stephen Wooding, Alan R. Rogers, Elizabeth E. Marchani, W. Scott Watkins, Mark A. Batzer, and Lynn B. Jorde. 2007. "Genetic Similarities Within and Between Human Populations." *Genetics* 176: 351–9. doi.org/10.1534/genetics.106.067355.

Wynne, Brian. 2005. "Reflexing Complexity: Post-Genomic Knowledge and Reductionist Returns in Public Science." *Theory, Culture & Society* 22(5): 67–94. doi.org/10.1177/0263276405057192

Zuk, Or, Stephen F. Schaffner, Kaitlin Samocha, Ron Do, Eliana Hechter, Sekar Kathiresan, Mark J. Daly, et al. 2014. "Searching for Missing Heritability: Designing Rare Variant Association Studies." *Proceedings of the National Academy of Sciences* 111(4): E455–64. doi.org/10.1073/pnas.1322563111