Racial Meanings and Scientific Methods: Changing Policies for NIH-Sponsored Publications Reporting Human Variation

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Abstract Conventional wisdom holds that race is socially constructed and not based on genetic differences. Cutting-edge genetic research threatens this view and hence also endangers the pursuit of racial equality and useful public health research. The most recent incarnation of racial genetics is not due to scientific discoveries about population differences per se, but follows from how the United States and other governments have organized racial categories. This article explains tensions in U.S. government guidelines and publications on the study of human genetic diversity, points out the absence of any compelling public health benefits that might justify this research, introduces conceptual tools for addressing the complicated heuristic and policy problems posed by medical population genetics, and offers two policy proposals to remedy the current problems.

Background to Current Debates on Human Genetic Variation Research

Most of the research on human genetics, and the attendant hopes and fears, pertain to predicting individual-level risks of diseases associated with particular genes.[1] Long-standing anxieties about unintended conse-

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1. As of 26 September 2002, the Online Mendelian Inheritance in Man (OMIM) database maintained by the U.S. National Center for Biotechnology Information (NCBI) listed 10,339 possible genetic associations with diseases (see the U.S. NCBI Web site at www.nlm.nih.gov/omim). However, another Web page also maintained by NCBI states that, as of 26 September 2002, the human genome map had "assisted directly in identifying about 100 disease-causing genes" (www.ncbi.nlm.gov/disease). Yet another Web page (maintained by the Oak Ridge National Laboratory) put the figure, as of 26 September 2002, at "about 60." (www.ornl.gov/hgmis/posters/chromosome/diseaseindex.html). On the rarity of single mutation diseases, see Collins et al. 1998 and the National Human Genome Research Institute (NHGRI) Web pages.

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quences tend to concern eugenics, including cloning (Duster 1990; Cowan 1992); genetic discrimination in employment and health insurance (Greely 1992; Murray 1997; Roche, Glantz, and Annas 1997); genetic fingerprinting (Lander 1992); and deoxyribonucleic acid (DNA) sequence patenting (Marshall 1999).

Social scientists, especially medical anthropologists and sociologists of science and health, have written rather extensively on these matters, referred to by the National Human Genome Research Institute (NHGRI) as ELSI (Ethical, Legal, and Social Implications).[2] Among the emerging areas of ELSI research that have tremendous political implications and that are only beginning to be widely discussed is inquiry into genetic differentiation among subpopulations of human beings divided into categories of race or ethnicity.[3] Disguised in the alphabet soup of acronyms characterizing the cutting-edge technical developments that only a handful of highly specialized scientists understand (e.g., SNPs [single-nucleotide polymorphisms], ESTs [expressed sequence tags], STSs [sequenced tagged sites]), the unsettled heuristics of population genetics have the potential to alter the political landscape of this country and elsewhere with no less force than the Jim Crow laws implemented just about one century ago.

Consider one bioethicist's worries about what may happen in places in the Americas as a result of research attempting to trace the migratory movements of so-called indigenous peoples[4] by inferences based on alleles supposedly unique to a particular population: "to the extent that anti-indigenous prejudice still animates the policies of some countries in this hemisphere, a detectable genetic hallmark . . . could serve as an indelible 'yellow star' marking for oppression those with indigenous ancestry" (Juengst 1998). Another essay worries that genetic research on Ashkenazi Jews will have "dual consequences: stigmatizing the population through

2. Currently ELSI research is incorporated into virtually all aspects of the U.S. genomic research programs, though it is also housed in the ELSI Research Program, founded in 1990; the ELSI Office of Policy Coordination, founded in 1995 with an explicit public relations component; and the Office of Genome Ethics in the NHGRI, established in 1996.

3. By *race* I mean a subpopulation of human beings with observed or imagined physical characteristics associated with a geographical territory of origin. By *ethnicity* I mean an intergenerational group that exists by reference to a past, present, or future political society that is often in a location other than where putative members of the group currently reside. For a further elaboration of these terms, see Stevens 1999.

4. All human beings have ancestors from Africa (Cann, Stoneking, and Wilson 1987). Only those residing in a very small portion of Africa are actually indigenous. We all arrived here, wherever that here may be, from elsewhere. *Indigeneity* falsely prehistoricizes in particular non-Europeans and deprives them, misleadingly, of a role in the developing cosmopolitanism of the species.

the creation of a new racialized disease, while at the same time contributing to the idea that this population is somehow biologically distinct, that it constitutes a separate 'race'" (Lee, Mountain, and Koenig 2001: 65).

This essay reviews the current government practices regarding genetic variation, describes their inconsistencies, and offers new approaches to conceptualizing the kinds of dangers posed by this new scientized politics of racial and ethnic difference.[5] In light of the current evidence on the relevance of genetic research for public health in general, the centrality of government funding for this research, and the expectation that the government protect and not harm its citizens, this article proposes that the National Institutes for Health (NIH) issue a regulation prohibiting its staff or grantees from publishing in any form—including internal documents and citations to other studies—claims about genetics associated with variables of race, ethnicity, nationality, or any other category of population observed or imagined as heritable, unless statistically significant disparities between groups exist and description of these will yield clear benefits for public health, as deemed by a standing committee to which these claims must be submitted and authorized prior to their circulation in any form beyond the committee. The feasibility of this approach is discussed in the final section. For a discussion of the methods used below, see Stevens 2002.

While restricting the use of race in genetic studies, the NIH needs to articulate and operationalize a new method for using race variables in other studies. The conclusion explains why and how health researchers should characterize race and ethnicity as synchronic variables—attributes to be studied in their immediate contexts—and not as hereditary traits.[6] Studying the effects of race or ethnicity in the manner that one might research the effects of occupation, residential location, or education, for instance, would allow useful research on health differences to proceed, but without the underlying and overbearing message that race is a genetic and not social attribute. Just as lung cancer rates of coal miners can be

5. The most important book-length study on this is Troy Duster's *Backdoor to Eugenics* (Routledge, 1990). A useful collection of essays addressing a range of practical, political, and ethical questions prompted by the HGP is Edward Smith and Walter Sapp's *Plain Talk about the Human Genome Project* (Tuskegee University Press, 1997).

6. *Hereditary* refers here to alleles that individually or in identifiable units are solely responsible for large variations in biological functions among humans. Anything broader than this confuses being human with having a genetic predisposition (Sarkar 1998). Amoebae do not catch colds, and my genes differ from those of amoebae, but that does not mean that a cold is caused by inherited genes, except in a very trivial and uninteresting way no more medically helpful than observing colds are caused by having noses and breathing.

compared with those of stockbrokers without implying a genetic etiology for occupation, race or ethnic differences can be characterized also as demographic variables. Restricting publication of genetic taxonomies for disease can preclude hereditary inferences without limiting studies of intergenerational causal patterns: one can study the effects of, say, being born to parents residing near a toxic waste dump without conveying the sense that some people are genetically predisposed to living near pollution. Here intergenerational effects are neither racialized nor geneticized.

To study race as a strictly synchronic variable seems counterintuitive because we are so accustomed to believing in a genetic basis for this classification. The popular misunderstandings of kinship in general and race in particular resemble those regarding the hereditable status of serfs in feudal periods. Race is no more produced by genes today than was the ancestral condition of being a lord or serf an expression of a lord or serf gene five hundred years ago, even though one would have been able to locate statistically significant differences of particular DNA fragments between serfs and lords. Resistance to claims about the lack of a hereditary basis to feudal status would have been as widespread during the medieval period as is the current naïveté about population heuristics among many contemporary medical researchers. Whereas the documents of social class then were legal expressions of beliefs in God-given differences, today the legal distinctions of race and ethnicity are legitimated through publicly funded scientific publications. When scientists receive government aid, it is perfectly legitimate for that government to hold these scientists accountable for the use of census classifications that, by virtue of being used by scientists, gain the imprimatur of objective knowledge, even when unwarranted by the actual research.

The sections below document how current genetic studies of disease mislead the public about the importance of genetic etiologies for prevalent diseases in general, and their racial variations in particular; reveal weaknesses in current NIH policies for documenting racialized disease rates; and commend new criteria for the NIH to regulate its grantees in this area. The NIH is the major agency supporting genetic research and hence is the appropriate target for these evaluations. Just as public dollars used for cloning research invite regulatory scrutiny to ensure that scientists' immediate agendas do not conflict with those of the public funding them, racialized genetic research with public money invites similar caution.

Assessing the Risks and Benefits in Racial Classifications of Genetic Variation

That racial and ethnic classifications may be a harmful business, and the NIH a perpetrator of these risks, seems insufficient grounds for instituting oversight of racial and ethnic genetic taxonomies. The statistical significance of some correlations of genetic variables with deadly diseases has encouraged the intuition among the research community and broader public, including even some health advocates for ethnic and racial minorities, that such work is not wrong and harmful, but correct and beneficial. Until critics can address claims about the potential utility of these taxonomies and provide alternative approaches, complaints about ethnic and racial categories in genetic research will be as compelling to those pursuing such research as complaints about the rainy season, and it would be as ludicrous to blame scientists for discovering correlations of racial groups with genetic diseases as it would be to blame the meteorologist for a nasty storm. The question is, are reports on, say, the Ashkenazi Jewish gene for breast cancer like the bad weather report—in which case we need to develop even more precise instruments for measuring the disease for this population—or is there something else going on?[7] Are geneticists providing useful alerts about racialized diseases or false alarms that cause harmful panic?

Benefits of Diversity Research by Race Are Limited or Illusory

With the strong hunch that work passing as objective was actually offering the public some very misleading cues, the U. S. National Research Council (NRC) in 1997 proactively issued a challenge to the population genetics research community: show us that your approach will improve health or stop making claims about populations being genetically discrete. Suspicious of whether racial categories could be used to alleviate widespread and pernicious diseases, and aware of the harms from such typologies, the NRC Committee on Human Genome Diversity advocated a cost-benefit approach:

> For any specific goal-oriented protocol, it should be possible to anticipate the risks and benefits to the subjects and to pursue informed con-

7. Actually, pediatricians have been cautioned for several years to be on the lookout for sickle cell symptoms among their White patients, as they also suffer from this disease (Caruso-Nicoletti et al. 1992).

> sent accordingly. For projects that are not able to specify goals in sufficient detail to quantify risks and benefits reasonably, the worst-case scenario should be assumed: the benefits will be at the lowest anticipated level and the risks at the highest. That means that the burden of proof for any DNA-sampling project that does not have a well-defined hypothesis will be high. *It also underlines the most basic starting point for all ethical analyses of genetic variation research, regardless of which model is pursued: defining a hypothesis and determining the benefit of whether it is true* (U.S. NRC 1997: 7; emphasis added).

If they could contemplate that association studies of breast cancer among Ashkenazi Jews, for instance, would lead to a significant breakthrough for health benefits from this knowledge—not just association information about a miniscule portion of disease etiology—then those studies would receive their imprimatur.

Although one would not have guessed it from the barrage of racialized genetic disease disparities discussed in the mainstream media, the NRC committee was pointedly pessimistic about such research advancing under those conditions. The reason was simple: the only way to prove that a genetic disease is not confined to one group is to perform large-scale studies of DNA differences among subpopulations and compare outcomes—something that has occurred relatively infrequently and with no clear results. The committee wrote: "most biomedical investigations will require considerably larger samples and substantially more information on each person sampled than the committee deems practical on a global scale" (U.S. NRC 1997: 22). For instance, each test for breast cancer genes costs about $2,000 (Newman 2002). Even if costs go down, achieving statistical significance in comparing populations will remain a costly proposition. Although such an obstacle would seem to condemn racial population studies to ignominy, this was not the sole conclusion.

Instead, the committee offered a second, contradictory, assessment. The penultimate section of the "Scientific and Medical Value of Research on Human Genetic Variation" chapter states: "In summary, although biomedical applications are clearly important goals of population-based surveys of genomic variability, *it appears more realistic at this stage of planning for biomedical investigations to be viewed as secondary targets*. The committee appreciates that this view will be controversial and that it could have some negative consequences, such as a lesser willingness to participate in a study that has no immediate health benefits for participants" (U.S. NRC 1997: 22, 59; emphasis added). The passage is quite interest-

ing because, while emphasizing the lack of any health benefits from studying population variations in DNA, it nonetheless seems to authorize such studies. Not only is the committee's claim that this research is unlikely to assist medicine potentially "controversial," it also contradicts the criterion quoted earlier that the "most basic starting point" for such research is "defining a hypothesis and determining the benefit of whether it is true." Biomedical utility in the first section is not a "secondary target," but the only legitimate basis for proceeding with this research.

If one focused on the committee stating it is not "realistic" to envision benefits from biomedical research programs using sequence diversity "at this stage," and that the "worst case scenario" should be contemplated before proceeding, one might infer that the committee would seek to discourage any such research at this time. But then one sentence later they conclude: "Careful variability sampling in conjunction with the Human Genome Project could contribute fundamentally to a new era of modern molecular medicine" (U.S. NRC 1997: 23). The report, with many serious caveats and even complaints that their committee is not quite clear on their assignment, then goes on to offer ambiguous guidelines as to how sequence diversity research might proceed.

The reason for the ambivalence within that committee, and for the more general difficulty in criticizing this research program, is that, like much of the genetics research being pursued today, its allure depends not on overwhelming benefits to date but on its *potential*, what variation research "could contribute" even if it is not doing that at present. While this should prompt a normally skeptical intellectual community to raise serious questions about the merits of the work, the "potential" mantra has taken the form of a new religion. For what other scientific discussion would a potential result trump the findings of present discoveries? If a community of population geneticists, including medical researchers, has decided that there are minimal biomedical benefits today from population research, then this seems the only reasonable empirical basis for allocating the funds and attention of the national scientific research community. In making this determination about the medical benefits from the research, as we'll see below, the committee is not making an observation that might be made for any research program, that one does not know its impact. Instead, they are closely examining the current work in this field and inferring that from a public health perspective it appears to be rather unimpressive. Still, they seem unable to bring themselves to disrupt such expectations, immersed as they are in today's genetically obsessed culture.

Scientists are aware of the potential for the messiah to come, for the sky

to fall, for extraterrestrials to take over the White House—all of which would affect us dramatically—and yet still no one funds research with these possibilities in mind. Perhaps not yesterday, or today, but one day soon, our expectations for this human genetic variation research will pay off, the thinking goes, and since the potential rewards are so enormous—increased life expectancy, no more cancer, few diseases—they suspend suspicion, even if this should conflict with every antireligious bone in a scientist's body. In truth, it is as impossible to quantify the potential of genetic variation research contributing to a "new era of modern molecular medicine"—that is, research that does not simply identify proteins but prevents, treats, and cures disease—as it is to quantify the chance of Jesus being resurrected. Scientists dismiss the relevance of claims about a potential resurrection for future planning because to date the actual empirical evidence supporting this scenario is scant. The situation for genetic research is similar.

Potential cures hyped one year are next year's failed experiment: "On June 1, 1999, a 50-year-old man with hemophilia A received the first *in vivo* gene therapy for this disease as part of a phase I clinical trial performed at the University of Pittsburgh Medical Center. . . . The therapy offers promise for the tens of thousands of men affected with this disease worldwide" (University of Pittsburgh Medical Center 1999). This is one of the hundreds of dated press releases issued by biotech companies, many of which have soured on gene therapy endeavors. Reports such as this filter into the press, creating the impression that gene therapy research is a fait accompli. When the virus vector in the Chiron study showed up in a patient's semen, not only did the University of Pittsburgh Medical Center and Chiron fail to alert the media, but the U.S. Food and Drug Administration (FDA), dismayed by the late reporting of that result to the government, shut down the study. The research briefly resumed but ended after failing to yield any promising results, again with no public fanfare.

If there were widespread success stories from this research, such an example would be meaningless, but in over a decade of basic and clinical research there have been no drugs approved that change gene function and only one based on molecular genetics that directly targets the protein causing a disease: Gleevec, a drug for a rare form of leukemia.

While publicists from the pharmaceutical industry to the NIH to desperate patient advocacy groups pitch the promise of gene therapy, only a handful of the hundreds of studies begun over the past decade have proceeded through all the stages of the clinical trails, and these produced no

marketable treatments. The results were overwhelmingly negative, and some experiments caused cancer or killed the patients (Thomas, Ehrhardt, and Kay 2003; Borger 2000). Some in the government recognize the weak prognosis for gene therapy and genetic research more generally. According to Muin Khoury, director of the Centers for Disease Control and Prevention (CDC) Washington, D.C., Office of Genetics and Disease Prevention, "As human gene discoveries continue, the usefulness of the resulting information in the practice of medicine remains in question." Writing in *GeneLetter*, Khoury endorses an article in the *New England Journal of Medicine*, maintaining that "genetics has limited value in predicting, preventing, or treating common diseases such as cancer, diabetes, and other diseases with multifactorial causation" (Khoury and Thornburg 2001, citing Holtzman and Marteau 2000), in other words, exactly the opposite of what NHGRI Director Frances Collins promised (Collins et al. 1998).

While biotech hype led venture capitalists and the wider public to grab shares of companies trading on the potential to cure cancer and so forth, the bubble is beginning to burst. Financial analysts now substitute caution for exuberance, as some associated with the field proclaim it the next dotcom phenomenon, with chief executive officers (CEOs) walking off with insider profits before failing companies announce dashed hopes: "[R]evelations that ImClone Executives hyped the heck out of their experimental drug Eritux—while keeping mum about serious concerns expressed by U.S. drug regulators—do not exactly engender a lot of trust in the biotech sector" one analyst writes. After pointing out that the ImClone CEO and his brother sold more than $150 million in that stock before its price plummeted, this same analyst quotes a biotech fund manager: "[W]e've seen a series of clinical trial disappointments from other companies. With this kind of pessimistic outlook, biotech valuations are only going to contract" (Feuerstein 2002).

These setbacks might dim hopes in the marketplace, but unlike dotcoms, government scientists are not dependent on venture capital. Their fervor means public relations victories even absent empirical success stories. "Potential" has an infinitely long shelf life: Jesus still hasn't risen and yet Christian Evangelicals know he will. A similar scenario for genetics research means the invigoration of racial and other hereditary schemas that lead to inequality alongside the failure to address substantial health problems rooted in politics and not genes.

Risks of Racial Framing

Misapprehensions about racial and ethnic groups. To press the point about the disparity between empirical evidence on disease research and the general impression about this among an educated public, I will explore the well-publicized research on breast cancer mutations among Ashkenazi Jews. Despite the low expectations of a genomic revolution among public health officials and now among traders on Wall Street, the average informed reader deluged with reports about ancestry and breast cancer may be surprised to learn that only 5 to 10 percent of breast cancer is due to inherited autosomal mutations.[8] That such a low rate would occasion an intensive focus on hereditary etiologies seems so implausible that one thinks this figure must be wrong. Yet not only is this range widely quoted, according to the scholar whose 1988 study is frequently cited, it has not even been challenged in the scientific literature (Newman 2002). For a sense of the ubiquity of this fact in the breast cancer literature, consider the following excerpts from articles by leading researchers on breast cancer and BRCA genes:[9]

- "About 5% to 10% of breast cancer patients carry germ line mutations that predispose them to inherited disease" (Malone et al. 1998, citing Newman et al. 1988 and Claus, Risch, and Thompson 1991).
- "5%–10% of all breast cancers diagnosed among women <40 years of age occur in carriers of germ-line mutations" (Whittemore, Gong, and Itnyre 1996).
- "It is estimated that 5–10% of breast cancer may be due to inherited autosomal dominant susceptibility genes" (Durocher et al. 1996, citing Claus, Risch, and Thompson 1991 and Hoskins et al. 1995 [both citing Newman et al. 1988]).
- "The rarity of the susceptibility allele is small. . . . [T]he majority of women diagnosed with breast cancer can probably be defined as nongenetic. . . . These results concur with those of Newman et al. (1988)" (Claus, Risch, and Thompson 1991: 231).
- "The low prevalence of 1 in 30 cases attributable to BRCA is consistent with statistical projections from other population based stud-

8. Indeed, based on the anonymous readers' responses to this point (provided to the author in 2001 and available from the author), it would be more accurate to say that this audience would be entirely disbelieving. If public health policy scholars in the social sciences are confused on this matter, then it is not surprising that the general public would be even more mystified by the genetic icon.

9. BRCA is the acronym for breast cancer mutation sites.

ies of the proportion of breast cancer due to all susceptibility genes combined" (Newman et al. 1998, citing Newman et al. 1988 and Claus, Risch, and Thompson 1991).

Even a study claiming that "family history is an important risk factor for female breast cancer" offers the same citations to Newman et al. 1988 and Claus, Risch, and Thompson 1991, as well as to Colditz et al. 1993, Slattery and Kerber 1993, and McCreddie et al. 1998. These studies, including the Boston nurses study showing only 6 percent of breast cancer among those subjects was inherited (Colditz et al. 1993), are cited to suggest the promise for genetic research because the rare BRCA mutations appeared to confer a substantially higher risk for breast cancer. This attracted research interest and funding—academic interest that has confused the media, the public, and even many scientists into believing most breast cancer has a heritable etiology.

Among major articles on the BRCA gene research, the highest range given for inherited propensities is "5–20%," with a caveat that the higher end comes from a study including distant relatives (Slattery and Kerber 1993). In light of the prevalence of breast cancer in the general population of the United States—a lifetime risk of 1/9 for all women (Feuer et al. 1993)—it is likely that some of these cases result from nonhereditary causes. Because of the focus on studying the genes associated with breast cancer among Ashkenazi Jews, this community and others now mistakenly think Jews are at an especially high risk of breast cancer. The truth is that Ashkenazi Jews are affected at a slightly lower rate (11.3 percent) (Moshlehi et al. 2000: 1267, Table 5) than the rest of U.S. women (12.7 percent), the only difference being that a gene alteration associated with a higher than average risk of breast cancer has been found in Ashkenazi Jews (and later, among women in Iceland) at a slightly higher rate than in the general population, while similar kinds of mutations are not as well characterized for the general population (Egan et al. 1996).

Finally, the U.S. National Cancer Institute (NCI), on its CancerNet Fact Sheet, says BRCA mutations account for 7 percent of breast cancer among Ashkenazi Jews (U.S. NCI 2000, citing Oddoux et al. 1996; Struewing et al. 1995), explaining that Ashkenazi Jews and the general public have the same risk of inheriting genes predisposing one to breast cancer (U.S. NCI 2000). Exemplary of the public health confusion on the significance of these hereditary mutations, the same question and answer sheet with this information states: "family history is the strongest single predictor of a woman's chances of developing breast cancer" (ibid.), a point that con-

flates statistical significance with causal importance. A more accurate statement would be that a research community focused on genetics has found that a relatively small but statistically significant amount of breast cancer is associated with inherited mutations and that to understand the causes of most breast cancer would require research that looks far beyond genetic associations, say, to behavior, nutrition, or environmental exposures. As Bernadine Healy (1997), former director of the NIH, writes, "Without facts about these other variables, the fortunetellers [authors of BRCA studies] are reading a pretty cloudy crystal ball."

Another reason the publicized findings on the associations of subpopulations and disease present a muddled picture is that the early studies tested only on the dependent variable of people of a specific ethnic or racial group afflicted with a disease. Instead of controlled studies following the health status of all BRCA carriers in the general public, they studied Ashkenazi Jews with breast cancer and looked to see how many had certain BRCA mutations. Studies following up on claims that BRCA genes explained up to 87 percent of breast cancer among its carriers (Easton et al. 1993; Ford et al. 1994) have shown this figure is off by a factor of about two or even more (Ford et al. 1998; Struewing et al. 1997). More recent findings, at odds with the earlier dramatic emphasis on BRCA1 and BRCA2 mutations, have not received the same press attention as the original announcements of their linkages.

While the studies that mention the rate of inherited breast cancer overwhelmingly use the 5–10 percent range, many omit this information altogether (Moshlehi et al. 2000; Ford et al. 1998, 1994; Fodor et al. 1998; Struewing et al. 1997), which means that readers do not have a clear sense of the public health relevance of the findings. Among Ashkenazi Jews with breast cancer, about 7 percent have one of the three major BRCA mutations (Fodor et al. 1998; Struewing et al. 1995; Struewing et al. 1997). These genes were thought to be carried by about 2 percent of the general population of Ashkenazi Jews (Struewing et al. 1995; Ford et al. 1998), though that number has been reduced to about 1 percent now (Easton 2002). The risk of breast cancer among Ashkenazi Jewish "carriers of one of three BRCA1 and BRCA2 mutations is about 33% by age 50 and 56% by age 70" (Fodor et al. 1998).

The impression of breast cancer's hereditable etiology occurs when findings testing on the dependent variable are highlighted, for instance, when a study points out that "BRCA1 gene carriers have a lifetime risk of either breast or ovarian cancer of close to 100%" (Ford et al. 1994: 694). These numbers diminish radically, however, in a study of prenatal DNA

samples from the general Ashkenazi Jewish population, which Fodor et al. (1998) believe accounts for the dramatically lower rate of cancer associations than found in earlier studies, in which participants with sisters or mothers with breast cancer self-selected for observation. In a letter referring to work by Hartge et al. (1999), Hopper and Jenkins (1999: 1775) write that "population-based data on mutation carriers" and not just populations with breast cancer "are challenging previous beliefs and language based on monogenic diseases." Ford, Easton, and Peto (1995) report that "1.7% of all breast cancer cases diagnosed before age 70 years are due to BRCA1," the most common site of mutations associated with breast cancer in current research. In the Fodor et al. (1998) study, among Ashkenazi Jews with breast cancer only about 6.7 percent had any of the BRCA mutations. In studies of the general population of breast cancer patients, only between 2.6–16 percent of patients had any recognized BRCA mutations (Peto et al. 1999; Malone et al. 1998; Newman et al. 1998). Approximately 1.5–2.3 percent of Ashkenazi women were thought to have this genetic susceptibility, compared to about .12–.7 percent of those in the general U.S. population (Ford et al. 1998; Whittemore, Gong, and Itnyre 1996; Claus, Risch, and Thompson 1991).

Sandra Soo-Jin Lee, Joanna Mountain, and Barbara Koenig (2001: 34), who are worried about such population studies, state that only 1/1,666 people or .0006 in the general population have the BRCA1 mutation (and cite Ford, Easton, and Peto 1995), a difference from Jews that seems to legitimate the inquiry. But the rate given by Ford, Easton, and Peto is 1/833 people, based on work by Easton et al. (1993), who, in response to an inquiry, explained the confusion as follows: "The estimate from the paper is that the population allele frequency of BRCA1 mutations (i.e. per copy of BRCA1) is .0006, or 1/1666. But everyone has two copies of BRCA1, so the carrier frequency is double that, i.e. an estimated 1 in every 833 women carries a BRCA1 mutation. Recent studies also appear to support an estimate of around this magnitude. The corresponding carrier frequency in Ashkenazis is around 1%, or about 8 times higher" (Easton 2002). One way to state the difference is that U.S. Jews (over 90 percent of U.S. Jews are Ashkenazi) are at eight times greater risk for these particular gene alterations. Unmentioned by Lee, Mountain, and Koenig (2001), but also accurate, and from a public health perspective much more relevant, is that Jews are only about 1 percent more likely than anyone else to have even these genetic alterations. The rate of disease conferral by this mutation is quite low and so is the absolute difference in its presence between subpopulations.

False genetic rationales for population misconceptions. Just as the hereditary component of breast cancer is misrepresented and misunderstood, the public and scientists who do not specialize in population genetics are likely to misinterpret the current findings in genetic diversity research. Knowledge that Jews are at higher risk for Tay-Sachs and that African Americans and those from certain Mediterranean areas of North Africa, Greece, and Italy are at higher risk than others for sickle cell anemia is fairly widespread (although Caucasians too are susceptible [Caruso-Nicoletti et al. 1992; Noronha 1979]). Nonetheless, although current research has discovered inherited diseases that are more strongly associated with particular races and ethnic groups, new research on human genetic diversity does something else. In non-SNP research, deviations from the norm at the level of individuals — such as hereditary blindness — and even those deviations overrepresented among certain stereotypical races or ethnicities — such as Tay-Sachs mutations — yielded no evidence of any underlying genetic distinctiveness beyond the association with the mutation. Instead, such genetic defects reveal what Ernst Mayr (1942) called the "founder effect," which is when a particular mutation appears long after a kinship group has been established.[10] Endogamy, not long-standing genetic features of this group, leads to a particular mutation being overassociated with breast cancer in this group (ibid.).

This earlier approach to understanding mutation transmission can be analogized to detecting differences between characteristics of people sorted into two rooms by the criteria of the first initial of the last name, A–Ls in one and M–Zs in another. Imagine that three people in the A–L room are each given a marble and no one in the M–Z room is given a marble, similar to a mutation randomly occurring in an individual who happens to be in a politically recognized racial or ethnic group (as well as a variety of other groups that would confer a higher chance of being close to someone with the gene, even if these other groups, like occupation, are not studied as hereditary). Based on that information, one knows that there is a chance of picking a few people at random in the A–L room and finding a marble, which one cannot do in the second room. This renders

10. Kinship relations should not be confused with genetic ties, as the two frequently do not coincide. In a country with a divorce rate hovering around 50 percent, this point should not need to be stressed, but because the nuclear family ideology persists even as almost 50 percent of children will be raised in a single- or nongenetic-parented household at some point, this bears mention (U.S. Census Bureau 2000). Since Jewish people are most likely to marry other people who consider themselves Jewish, for instance, finding a mutation when the founder is Jewish will be easier if one looks among Jews.

a statistically significant difference between the members of the two rooms, if one is looking at their chances of marble possession. Still, such a statistical difference does not indicate a genetic (or any other) link among the members of either room. In a situation where a mutation is found among several members in the room, that still only indicates genetic matter shared among those with the mutation and does not in itself indicate a genetic link among others in the room, although any individual in that room can be distinguished from an individual in another room who has a lower statistical likelihood of being found with the mutation.

To state the point slightly differently, if someone from California happens to have a mutation leading her to grow three heads and no one else has this mutation, one would be accurate in saying that Californians are more likely than people anywhere else to have three heads, but that would not mean that "Californian" was either hereditary or causal of mutations, even though it would be a fair inference that because of tendencies of Californians to stay put, the gene for this would be more likely to be passed down in California than elsewhere.

Interestingly, the popular and incorrect inference from family studies of disease—that there is a genetic basis to ethnic and racial categories (if Tay-Sachs is inherited and predominantly afflicts Jews, therefore Jewishness is genetic)—is one that will be tautologically correct if population-based studies of SNPs adopt current population taxonomies from the U.S. Census and other political definitions. In SNP research, scientists assign particular DNA fragments to a definition of a population, thereby constituting the group as genetic. When individuals who may otherwise be identified as members of a certain group lack the selected markers, these individuals are considered not to belong to that group and are excluded from study. Here it is not the higher than average rate of possessing marbles, but rather the genetic sorting of people into the different rooms in the first place, that creates a genetically based group difference. If the denominator for sorting people is genetic (SNPs) rather than arbitrary (initial of last name/identity from census category), then findings about statistical differences are logically amenable to idiomatic racial or ethnic inferences about an array of inherited difference among subpopulations.

In SNP-based medical studies distinguishing by race, individuals may walk in and self-identify as White, Black, and so forth but then have their data discarded or shifted to another group if it turns out they do not possess the particular alleles scientists assign as the respective markers for membership. Exclusions or reclassifications are reported as side comments that do not question the heuristics of assigning racial attributes to

particular alleles. For instance, a study comparing "164 Caucasian women and 59 African-American women with primary invasive breast cancer" states that "[t]wo Caucasian controls were removed from the study after the *Msp1*-AA analysis suggested a discrepancy in race" (Bailey et al. 1998: 66). The authors had already described this fragment as the "race-specific *m3* allele" (ibid.: 65). Discovering the Caucasian who also had an *m3* allele, rather than undermining the researchers' conviction that this mutation indicated race, led the researchers to invalidate the self-identification of two subjects. Clearly the researchers are using this allele as an independent variable to assign weight to the dependent variable of not only disease prevalence, but also race. This brings the research community back full circle to the genetic equivalent of a "one drop" rule. Whereas earlier this drop was inferred based on legal kinship, today's molecular biological racial assignation is made even more concrete by the researchers claiming to actually see a race allele, in this case, *m3* (*MspI*-AA, with AA signifying African American).

The intellectual conundrum of taxonomies tied to population differences is not new to race. Charles Darwin recognized it in the very founding of evolutionary theory. He begins the chapter on "Variation" in *On the Origin of Species* (1859) by acknowledging the difficulty of distinguishing a species from a variety: "No one definition has as yet satisfied all naturalists; yet every naturalist knows vaguely what he means when he speaks of a species. Generally the term includes the unknown element of a distinct act of creation. The term 'variety' is almost equally difficult to define; but here community of descent is almost universally implied, though it can rarely be proved" (Darwin 1964: 44). Elaborating on the problem, Darwin (ibid.: 48) explains:

> Amongst animals that unite for each birth, and are highly locomotive, doubtful forms, ranked by one zoologist as a species and by another as a variety, can rarely be found within the same country, but are common in separated areas. How many of those birds and insects in North America and Europe, which differ very slightly from each other, have been ranked by one eminent naturalist as undoubted species, and by another as varieties, or, as they are often called, as geographical races! Many years ago [in the Galapagos], I was much struck how entirely vague and arbitrary is the distinction between species and varieties.

And, he (ibid.: 49) writes: "to discuss whether [certain insects] are rightly called species or varieties, before any definition of these terms has been generally accepted, is vainly to beat air," a comment directing scientists to notice

that such classificatory systems reflect the interests of the researchers and not to encourage them to land on truthful, correct definitions.

Those vaguely familiar with species criteria may retort that Darwin's problem has been solved by Ernst Mayr (1942), who stated that the ability to produce fertile offspring distinguished members of the same species and that within this group those with differing morphologies and functions are subspecies. While this has been the rule of thumb for the past half century, it has not been entirely hegemonic, and it is now under attack by molecular biologists. They point to animals currently classified as separate species that can reproduce fertile offspring (e.g., the fin and blue whales) and that have the same number of mitochondrial DNA (mtDNA) differences as those not classified as different species. These whales are classified as separate species because of differences in morphology and function that approximate those differences between species that cannot produce viable offspring. Rather than look at these visible, functional differences in organisms, many biologists are now using mtDNA, which has no known biological function, as the phenotype for species differentiation. There is a lively debate over whether Bornean and Sumatran orangutan are different varieties of the same species (their current classification, as they mate in captivity and produce viable offspring) or whether they are different species (because the average differences in their mtDNA are as large as those between other mammals currently classified as being in different species) (Xu and Arnason 1996: 435). Once mtDNA differences replace fertile offspring as the criterion of a species, then it is plausible that certain research and political communities will begin to apply such criteria to characterizing differences among humans as well—indeed this is already occurring—using new taxonomies to perform categorical differences, classifications that may or may not reflect traditional racial or ethnic groups.

One response to the above might be that this is all fine. Now that scientists can discern genetic details that previously escaped detection, it is possible to arrive at more precise taxonomies. However, there is no observational basis for using mtDNA to define species or subspecies or for a priori selecting particular DNA fragments as definitive of a population (Hey 2001). A leading textbook on the topic announces the limits of molecular genetics in this area: "Questions of molecular evolution are far trickier [than Mendelian observations], because it is usually harder, and sometimes even impossible, to do the right experiments. If we want to know, for example, whether humans are more closely related to chimpanzees or gorillas, we would really like to examine the missing link between the species. But

these transitional organisms have not survived, and we must instead compare DNA sequences in the surviving species" (Watson 1987: 1160). This is the same problem posed to the analysis of mtDNA within the human population, whereby theoretical population geneticists assume parsimony and then model the rate of sequence diversification but empirically do not, because they cannot, associate their current information with actual DNA from thousands of years ago, which they do not possess.

There are two difficulties with SNP-based population inferences. First, their accuracy depends on computational models using probability formulas or arbitrarily selected markers, not self-evident break points indicating the differences relevant to defining one group as a species (or a race). The statistically significant allele differences between idiomatic racial or ethnic groups can only exist after one has markers defining a group preordained as genetic. The embarrassing problem of data-mining that occurs among so many scientists—natural and otherwise—using high-powered computers with huge data sets, changes the meaning of statistical significance. With so many possible variables being crunched in these large data sets it is inevitable that enough hunting around will lead to correlations within the old-fashioned 5 percent range of standard error. If a researcher finds one out of the twenty markers studied in a group has a prevalence reaching a level of supposed statistical significance, it is not obvious that this indicates something distinctive to the putative population or is in the range of standard error, a problem confounded when researchers compare hundreds of such sites. Indeed some of the statistical techniques used by population geneticists have been employed by Christian statisticians to prove that the Bible conceals a code for each human individual that statistical analysis can decipher, foretelling major events and events for each individual's life.[11]

The current method of inferring variation among earlier genetic groups based on present variation (including the famous "out of Africa" hypothesis [Cann, Stoneking, and Wilson 1987]) depends on assumptions about rates of migration and mutation that come from observations of fruit fly populations in laboratory settings as well as picking among various probability formulas. Hey (2001: 79) writes of the same techniques for inferring species differentiation with this method: "As simple and reasonable

11. Numerous best-selling books and active Web sites advocate this position, including Michael Drosnin's *The Bible Code* (Simon and Schuster, 1997), which contains a reprint from the journal *Statistical Science* supporting the notion that scanning the Bible diagonally and vertically will yield hidden codes.

as the theory of evolutionary groups might seem, it flows entirely from the idea of molecular replicators and draws not at all from information on variation among real world organisms or DNA." Hey believes there is a good chance populations of organisms have fractal characteristics, making it almost impossible to distinguish among nested groups because of the overlap of peaks from one group with valleys of another, a point that seems to be the case for human populations as well, further compounded by migration and the far more subtle differences between putative races as opposed to species.

All this is to say that if there were genetically distinct human populations nested in a broader world of genetically distinct organisms, such as species, these populations would be difficult to discern: "What we can see readily with hypothetical evolutionary groups are the ways those groups may not be distinct. Because of hierarchical structure within them, and partial boundaries between them, we would expect evolutionary groups to sometimes be uncountable" (ibid.: 87). What Hey writes of species holds true for races also modeled on ideas of evolutionary, genetic drift. However, if mtDNA becomes a prevalent object of taxonomic inquiry, this will itself redefine the science and in this way manufacture mtDNA differences as empirically sound indications of speciation and racial differences, every bit as solid and observable as the fertile offspring that Mayr used for his criterion, and indeed this seems to be well underway already in studies of functional genes (Wilson et al. 2001), a topic discussed below.

Current Federal Practices on Human Sequence Diversity Research and Their Weaknesses

The U.S. Human Genome Project (HGP) is run through the Department of Energy (DOE) and NIH, the latter of which supervises the NHGRI. The HGP coordinates the efforts of various laboratories that are mapping portions of the human genome. This also entails supporting research on the genome maps of other organisms, ranging from single-cell bacteria to dogs. Laboratories around the world—most significantly those funded through the European Human Genome Organization (HUGO) and in Japan, as well as the Wellcome Institute in England—are also mapping various portions of chromosomes for the HGP.[12] The chromosomal ref-

12. For an overview of various programs, see Zilinskas 1997. The DOE and NIH Web site on the Human Genome Project, with links to many others, is www.ornl.gov/hgmis.

erence sample for the HGP is from blood donated by sixty-seven Northern Americans and Northern Europeans (Jackson 1997), though at the Human Evolution Conference at Cold Spring Harbor in April 1999, Mark Stoneking, director of HUGO (the reference sample repository), said that only forty of these samples were actually being analyzed—twenty-nine from individuals from Utah and eleven from France (Stoneking 1999). The private company Celera's genome, formerly run by Craig Ventner, is based on DNA from two Caucasian men, one Black woman, one Hispanic woman, and one Chinese woman. A year into the collaboration between the NIH and Celera a report stated that "most of the consortium's DNA comes from a single man" (Wade 2000), and we now know that man to be Ventner himself (Wade 2002).

Coincidental with the HGP are hundreds if not thousands of laboratories—some university-run, many private—doing isolated functional coding for diseases in particular regions of chromosomes, with large amounts of resources devoted to research on putatively homogeneous groups, such as Ashkenazi Jews or small isolated villages in South America. When a particular chromosome contains only a few allele differences from the same chromosome in someone else, it is easier to spot the relevant mutations than when chromosomes differ in many places.[13]

Until the mid-1990s, NHGRI was able to skirt questions about the implications of its research for race and ethnic categories by stressing that the HGP was interested in the human genome map and aspired to represent the genetic sequences humans have in common. On its Internet sites and in other publications, the HGP highlighted the refrain that "all humans still share the same basic set of genes and genomic regulatory regions that control the development and maintenance of their biological structures and processes" (U.S. DOE 1998), a sentiment echoed in the HGP's goal of determining the "DNA sequence for a complete 'reference' human genome that will help orient researchers and provide them with tools for further studies of fundamental human biology" (ibid.). A reference human genome is feasible only if other genomes are largely the same; otherwise it is the map of one particular genome. Until the 1998 NHGRI statement of goals for the next six years, obtaining information on DNA sequence variation was not an HGP objective (Collins et al. 1998). That changed, and by 2003 Collins aspired to map 100,000 SNPs

13. For a critique of all human genetic research from a public health perspective, see especially Sarkar 1998: 175–190 and Duster 1990.

that will characterize genetic differences among humans (Collins, Brooks, and Chakravarti 1998; Pennisi 1997).[14]

The major health goal of genetic variation research by the government is certainly not that of taxonomizing the U.S. population by race or ethnicity, but rather of finding individual-level risks and potential therapies. However, science policy makers overseeing the research recognize its imminent divisive political implications, not simply among those who turn out to have different genetic risks, but also for those belonging to a racial or ethnic group said to have a propensity for having the SNPs linked to a disease.

A Cautious Element at the HGP

Portions of the NIH and NHGRI are attempting to proceed into this new area of SNP research with methodological modesty and political caution. While many geneticists offer bold claims for the potential of their research to isolate certain genes for purposes of diagnosis and even therapy, the discourse of population genetics within some portions of the NIH lacks a similar vision and bluster. Because some in the NHGRI recognize the political bases and implications of racial and ethnic taxonomies, this field is a rare example of natural science that is characterized as political not only by fussy philosophers or grumpy activists, but by some of the researchers themselves.

The phenomenology of population genetics among some prominent population geneticists is not that scientists know how to taxonomize populations and the rest of us laypersons and social scientists ought to be self-conscious about what to do with this information, but that population genetics, far from being transparent, are beset by major heuristic puzzles.[15] Among

14. Genes are mapped by notations of the sequence of DNA's four amino acids (adenine A, guanine G, cytosine C, and thymine T) that are paired as nucleotides in the double helix form first discovered by James Watson and Bernard Crick in 1953. The sequences of these pairs are largely the same among all human individuals, but in approximately one in one thousand base pairs (bps) there is a single nucleotide difference. The biological importance of these differences is unknown; some result in a different protein being produced by the respective codon (a string of three base pairs) while others do not. At a minimum, though, the differences, many of which are fairly common, are useful for marking sites for structural analyses of the DNA, as landmarks, so to speak, that help orient the researcher to the exact site that is being studied.

15. A heuristic is a concept that its user relies on or develops to pursue a particular investigation. A heuristic can be experienced as an axiomatic and irrefutable truth, or it can be understood as provisional, ideological, or discursive. For instance, a triangle (defined as consisting of three corners totaling 180 degrees) is a heuristic for geometry just as class (defined in any of a number of ways appropriate to a particular research agenda) is a heuristic for the social sciences. Population geneticist Jody Hey's (2001) explorations of the difficulties in ascertaining criteria to define a species offer an especially clear and nuanced description of the challenges facing human population taxonomies. As scientists are unable to settle on the right definition for a species, the difficulties in establishing criteria for a race can be inferred to be especially confounding.

the goals that Collins et al. (1998) list for studying SNPs is to "Develop the intellectual foundations for studies of sequence variation," including questions of population genetics. No similar call for "intellectual foundations" exists in any of the other five major areas of research that Collins et al. list as HGP goals through 2003.

Though not a goal mentioned by Collins et al., the NIH, NHGRI, and other researchers in this field seem to prioritize as well responsiveness to political constituencies, a point emphasized also by the National Research Council's *Evaluating Human Genetic Diversity* report mentioned earlier for its cost-benefit schemes. This report, in addition, states: "*researchers will have to make sure that their participants understand both the objections of their community and the rationale for them as part of the informed-consent process and, when doing research that is opposed by a specific community, will also have to take into account the possible impact of doing such research on the likelihood that other communities will cooperate with other genetic-variation researchers in the future*" (1997: 64; emphasis in original). This recommendation to involve representatives from various racial and ethnic groups in genetic variation research was operationalized by the 1999 NHGRI Request for Applications (RFA) for grants to study the "Ethical, Legal, and Social Implications of Research into Human Genetic Variation," in which NHGRI says that this work is of "special concern to individuals from diverse communities, including those who traditionally have not been involved in genetic research, as researchers, research participants, or policy makers." The RFA continues: "Questions have already been raised concerning the inclusion of members of these populations in early genetic studies and whether the under-representation or, in some cases, the over-representation of these populations have led to an increase in stigmatization and discrimination in employment, health care, insurance, or in society more broadly. These issues may become even more acute if research into human genetic variation reveals data on the interaction between genotype, disease, and traditional, socially-constructed concepts of race, ethnicity, and culture" (U.S. NHGRI 1999). Similar RFAs were issued thereafter (www.genome.gov/Grants/).

In addition to the RFAs for ELSI analyses of sequence variation, the NHGRI has issued restrictive rules for the use of human genome chromosomes supplemental to those available for the reference map. The new database emerged after various constituencies voiced objections to the homogeneity of the Centre d'Etude du Polymorphisme Humain (CEPH) HGP samples. The NHGRI database for SNP research is based on 450 samples that are "African, Asian, European, North and South American,

with extensive samples from Native Americans," but the samples come without any individual-level phenotype information, about health histories or anything else (Marshall 1997).

Moreover, researchers were instructed that they should not offer post hoc speculation on the population taxonomies for the database, a condition met with resistance and even ridicule by those scientists using this data. One physical anthropologist familiar with these protocols told me during a conversation in April 1999, that the guidelines mean that a "high school kid will publish a *Science* article" speculatively grouping the samples. This has not occurred, and while this is certainly possible—like all NHGRI data, the SNP information from this database is available on the Internet—the potential impact of such conjecture is minute, since professional scientists wishing access to NIH funding would be prohibited from referencing a study produced by non-NIH individuals circulating such inferences.

While some were anxious about thwarting racialization, other constituencies who had objected to the homogeneity of the CEPH HGP sample favored more access to phenotype information on the samples, including ethnic and racial backgrounds. Yet there is no evidence that the SNPs collected from this extremely small sample approximate those variations in the general population. By virtue of its sheer size (ten times larger than the HGP database in use), this database is an improvement. But the current reference sample could have been usefully improved by adding 450 samples of people from Utah, too, if they were randomly selected.[16] The problem with the racial taxonomies for this SNP research is that they are neither a good means for studying population differences nor a good means for studying any random variations among SNPs in the U.S. population as a whole. John Moore, a cultural anthropologist and the director of the North American portion of the Human Genome Diversity Project (HGDP)—a controversial population genetics research group based at Stanford University—criticized the SNP groupings as "ridiculous" because there "aren't any boundaries between races" (Marshall 1998). At the same time, Moore also objected to the removal of population source data on the grounds that this information would prove the actual genetic similarity among putatively different populations. In sum, the initial classifications sustain the credibility of genetic classifications by race, for reasons explained below, and they do not reflect the variation of SNPs among

16. Even if a majority of those in Utah are Mormons who have children with other Mormons and live in Utah, there are many others residing there as well, including precolonial peoples and recent immigrants, Mormon and otherwise. A truly random sample would capture this variation.

the larger population, which would be better achieved by sampling thousands of individuals selected from telephone directories.[17]

Inconsistencies at NHGRI

Some portions of the NHGRI and the scientific community seem sensitive to the political-economic effects of genetic diversity research, but many, including Collins, ignored the concerns and caveats discussed above. According to the NHGRI document calling for sequence diversity research, "association studies should be particularly efficient for identification of genes with relatively common variants that confer a modest or small effect on disease risk—precisely the type of gene expected in most complex disorders," listed as "diabetes, hypertension, asthma, common cancers, and the major neuropsychiatric diseases" (Collins, Guyer, and Chakravarti 1997). The rubric of "association studies" refers to comparisons of suspected genetic mutation sites within particular subpopulations. Oblivious to any of the caveats and hand-wringing in the ELSI section of the NHGRI, a CDC article instructing medical researchers on the benefits and pitfalls of genetic association studies says: "First and foremost, the appropriate selection of subjects from the major racial and ethnic subgroups should always be an initial target for control selection" (Khoury and Yang 1998).

In the spirit of directives such as the one by Collins, the NIH has funded and publicized dozens if not hundreds of such association studies. Press releases issued by various NIH agencies reveal how the new racialized genetics discourse is conveyed by government officials. If government scientists instruct the public on the existence of statistically significant racialized genetic differences associated with disease, then it will seem a fair inference that such subpopulations are genetically distinct. Below are some examples:

> "Both of the African-American families included in the study showed linkage to the site of HPC-1, suggesting that the gene may eventually

17. Obtaining access to these samples was a struggle for the NHGRI: "As the cell lines [from already collected data] seemed to become less accessible by the hour, an annoyed Collins declared that, after months of discussion 'I am very troubled to learn that there still doesn't seem to be a clear answer' about whether they can be used. After a coffee break [Edward Sondik, director of the National Center for Health Statistics] announced that 600 DNA samples . . . will be made available for the SNP project." The worry was that the subjects who had agreed to participate in an earlier study had not consented to DNA research (Marshall 1997). The first use of sequence diversity research hence violated the recommendations of the National Research Council Committee on Human Sequence Diversity.

> help explain why African-American men are exceptionally vulnerable" to prostate cancer. (U.S. NHGRI 1996)
>
> "Asthma Genes Linked to Regions Unique to Different Racial and Ethnic Groups." (U.S. NHLBI 1997)
>
> Among "people of non-Ashkenazi Jewish, Armenian, Arab and Turkish background . . . as many as 1 in 5 to 1 in 7 carry a mutated FMF gene." Perhaps because the research has yielded little of public health relevance (only 1 in 200 carriers of the mutation are estimated have the disease) the release concludes with an observation of no medical value whatsoever: "Out of the three FMF gene mutations identified so far in these families, the same 2 mutations are found in ethnic populations that have been geographically separated for over 2,000 years, suggesting that most individuals with the disease are descended from a small, ancient group of individuals." (U.S. NIH 1997a)
>
> "An NIH-Funded Native American Study Finds Gene Site Associated with Scleroderma" (U.S. NIAMS 1998), even though Native Americans are a specific group that has been referenced frequently as a source of NIH anxieties about just this type of research.
>
> In 2000 the National Institute for Allergies and Infectious Diseases (NIAID) announced they will join an international consortium of geneticists creating a "searchable HLA (human leukocyte antigen) database linking multiple-interacting genes with function, ethnicity, and disease." (U.S. NIAID 2000)
>
> Even studies finding no correlation between gene mutation prevalence and population may nonetheless reinforce the genetic trope, as when the NIH announces a "lupus gene" on "chromosome 1 in Caucasians, Asians and African-Americans with lupus." (U.S. NIH 1997b)

Why no mention the gene was found on chromosome 1 in Lakers' fans, Knicks' fans, and people with lupus who hate basketball, as surely this was the case as well? In fact, the press releases above are part of a steady stream of NIH-funded research published in high-profile journals focusing on the very racial and ethnic classifications the NRC cautioned against (1997).

Two well-placed articles arguing for using racial and ethnic markers for drug research come directly out of NIH grants and ignore the NRC concerns about subject consent for research on group differences. Publication of these poorly defended claims also exemplifies why the NIH needs firm

regulations and not just periodic caveats. Phillips et al. (2001) were funded by the NIAID and the National Cancer Institute — both eager to link disease to genetic predispositions — and Risch et al. (2002) were funded by an NIH grant.

Phillips et al. (2001), in their meta-analysis of genetic predispositions for adverse drug reactions (ADRs), report on alleles suspected to be associated with the poor metabolization of drugs by populations of Whites, Chinese, Japanese, Koreans, African Americans, Egyptians, and Indians. They write that "race is correlated with many gene patterns and therefore genotyping raises issues about stereotyping and preferential treatment: As stated by one observer, 'What happens when the patient comes in and says, 'I hear there's a great new drug for asthma,' and the doctor says, 'Yeah, but it's only for whites?' " (ibid.: 2276).

Although the passage above implies that serious empirical studies have established that different racial groups have genes predisposing them to ADRs, the references provided are merely a *Washington Post* article and an unsupported claim by an interviewee in a short piece on pharmacogenomics who merely says, "Drug response might be predicted from a certain pattern of polymorphisms rather than only a single polymorphism, yet these patterns probably differ between ethnic groups" (Sadee 1999). Phillips et al. also misattribute the Sadee piece by changing the standard PubMed title to omit mention that the entire piece is an interview with Sadee, himself among the Phillips et al. authors. Not a single study on the robustness of racial and ethnic differences directly associated with actual ADRs linked to specific alleles is cited. The observation is that Caucasians, for instance, produce a certain allele that is associated with poor drug metabolism, but there is no study comparing the drug response among Caucasians to that among other groups by isolating a particular allele and comparing the reactions among those who have it with the reactions among those who do not. Instead, the article references molecular-level studies of alleles associated with enzymes associated with ADRs, not clinical studies of adverse drug reactions.

Phillips et al. (2001: 2271) imply that the matter is settled and that they are just standing on earlier work: "several studies have found a direct link between specific genetic variants and ADRs." Yet they do not cite "several studies," just two small studies of ADRs in schizophrenics, and the implications are murky. In one, subjects heterozygous for a suspect allele were represented as far more likely to have ADRs than those who had no copies of the allele in question (thirteen people with the allele had an ADR and three people without the allele had an ADR), but half of those

without the allele also had ADRs, and the study did not control for other variables known to be associated with ADRs, such as gender and smoking (Kapitany et al. 1998: 101–106). The small sample size of the study ($n = 41$) provides no grounds for sweeping claims about genetic variation underlying ADRs. The second article cited is a preliminary study of a gene associated with an enzyme associated with ADRs among schizophrenics who smoke; it too, while potentially suggestive, is, by the authors' own account, preliminary and ambiguous (Basile et al. 2000: 415). These two studies hardly warrant the strong claim made in the *Journal of the American Medical Association* that racial groups predispose for specific genes predisposing people to ADRs. Of course now that this claim has been published in the *Journal of the American Medical Association* the association has become an objective fact to be cited by others.

The article by Risch et al. (2002) is especially contentious on the health significance of genetic differences associated with races, and, interestingly, despite its frequent self-announced "objectivity and scientific perspective," it appears in *Genome Biology* under the heading of "Opinion." Risch et al. are uncharacteristically provocative: they want to use racial categories to study genetic diseases. Without dwelling on the technical disagreement Risch et al. have with another piece on the topic (Wilson et al. 2001, arguing that post hoc designations of population membership from computer models of allele distributions are more accurate than relying on race self-identification), two obvious points can be made in response to their endeavor.

The first regards an assertion Risch et al. (ibid.: 2007.1) make in their opening lines: "Clearly it is important to know whether particular individuals within the population are more susceptible to particular disease or most likely to benefit from certain therapeutic interventions." But this point is not at all clear, or at least not from a public health point of view. "Important" is a word indicating a priority. In light of the vast similarities among most people, and the very common and similar causes of most diseases afflicting us, and given known interventions for addressing these that are not currently being pursued, it is not at all "clear" that it is "important" to know more about individual-level variations in order to significantly improve the country's health. After the United States figures out how to provide access to basic health services to 45 million citizens who lack insurance; after the ballooning rate of obesity in this country has been brought down; after the pollutants that have triggered a 75 percent increase in asthma in the past twenty years have been identified and controlled (U.S. NAS 2000: 1); and after basic public health measures have been

accomplished, including community design to accommodate walking and bicycling instead of driving, decreasing poverty (a predictor for poor health far more robust and important than genes for ADRs), and after the widespread seepage of radioactive contaminants into this country's groundwater and food chain has been stopped (U.S. DOE 2000), for instance, then it might be "important" to study our differences. Until then, these genetic variations may prove a source of cocktail conversation and speculation, but they are not a "clear" public health priority.

On a conceptual level, Risch et al. (2002: 2007.5) repeat old canards, including the scientifically indefensible notion of a "one drop" rule indicating Blackness: "Gene flow from non-Caucasians into the US Caucasian population has been modest. On the other hand, gene flow from Caucasians into African Americans has been greater; several studies have estimated the proportion of Caucasian admixture in African Americans to be approximately 17%, ranging regionally from about 12% to 23%." If you have parental genes from Group A and parental genes from Group B contributing to a child, it is ridiculous to state that genes from one group have gone into genes of another group, since of course the child has genes from both (and this is assuming that these are originally "pure" groups in the first place, which is also incorrect). Risch et al.'s contention that genes are flowing in a particular direction follows not from the genes but from how this country categorizes its population. It is not the genes themselves that are drifting from Whites to Blacks, but the entirely political convention of classifying descendants of so-called mixed relations as Black. And when Risch et al. cite U.S. census figures showing people almost always self-report being of one race or another, not mixed, this is not an indication of reproductive practices, but of conventions of raising mixed-race children and their descendants. Slaves raped by owners did not raise their children as White and often not as mixed. But obviously these children are as genetically White as they are Black. And even if they have children with others categorized as Black (but who may also reflect this mixed background) there is no logical reason to regard the theoretical gene flow as coming from Whites to Blacks instead of from Blacks to Whites, since the children will, by Risch et al.'s own scheme, be White, also. Following Hey's insights about the difficulty in directly assessing sharp breaks in population models, the practice of assuming difference can only follow from the idiomatic reiteration of conventional legal categories of race and cannot objectively separate and categorize a heterogeneous population. Indeed if Cann, Stoneking, and Wilson (1987) are correct, every one of us is African.

While Wilson et al. (2001: 268) show in their data that "genetic clus-

ters" more accurately predict alleles associated with drug metabolizing enzymes than do racial groups, and observe that these can be "derived in the absence of knowledge about ethnicity (or geographic origin)," Risch et al. reread their data and claim otherwise. Ethiopian clusters for these alleles "fit" with the Norwegian, Ashkenazi Jew, Armenian group and not other Africans, according to Wilson et al. (2001). Risch et al. (2002: 2007.6) conclude that Ethiopians are not really Africans and that the other Africans are Africans, even though there is no a priori reason for inferring this and indeed the assertion contradicts their subsequent argument about the public health concerns recommending medical researchers to use race and not genetic clusters. Risch et al. imply that U.S. census categories of race can provide a good fit for distinguishing allele distributions (Ethiopians and Pacific Islanders excepted)—a point in dispute with Wilson et al.—and that, all things being equal, race should be used because race has a public health significance genetic clusters alone lack. But since only Risch et al. regard Ethiopians as Caucasian, and Pacific Islanders as not Asian, their own taxonomies are bumping up against their policy argument. If Ethiopians in the United States are regarded as Black, and if genetics predispose for disease, then the use of this Black racial designation would prevent doctors from diagnosing Ethiopians' "Caucasian" diseases.

In sum, the preoccupation of Risch et al. (ibid.: 2007: 11) with genetic diversity, in the name of serving "those afflicted," suggests a weak grasp of the public health field. If all you have is a microscope, every problem is genetic. If Phillips et al., Wilson et al., and Risch et al. were really concerned with public health, they would put away their laboratory coats and start running for public office and speaking out on behalf of health policies that we know would help tens of millions of people. It is not ignoble that they choose not to do so, or that they study genetic diversity, but their conversation does not warrant being funded by those responsible for helping us face this country's health challenges and, in keeping with the findings of the 1997 NRC report, should not receive NIH funding as though they were.

Finally, the DNA Polymorphism Discovery Resource—the repository of the additional 450 genomes the NHGRI made available for SNP research—itself provides taxonomic information about the genomes of U.S. citizens by continent and hence by race: Europe, Africa, America, and Asia (Collins, Brooks, and Chakravarti 1998). Oddly, some have claimed otherwise: "In order to avoid the creation of a database that could be mined and studied for difference by race, individual samples are not iden-

tified racially, rather, continental origin for the entire panel is presented" (Lee, Mountain, and Koenig 2001: 58). The Office of Management and Budget (OMB) defines racial groups by citing the same continents of origin (Africa, Asia, Europe, and the Americas).[18] Since the OMB defines a Black person as someone with "black ancestors who have origins in Africa," saying the samples include Africans is the same as saying they are analyzing Blacks. When the NHGRI provides the same idiomatic racial designators as those defining race, they reinforce racial inferences about genetic information. The subjects of these studies are all U.S. citizens, so these other locations refer to origins and hence, although individual differences are not identified, the Polymorphism Discovery Resource reiterates the very vocabulary of race and heredity the NHGRI is supposedly so anxious to avoid.

Weaknesses in ELSI and ELSI-funded Cautions about Sequence Diversity Research

Just as NHGRI cannot bear to break away from the genetic etiology of race, the ELSI community overseeing the research sometimes seems to reinforce the very categories they claim to challenge. For instance, in reporting on the Ashkenazi Jewish community's fears that they are being "singled out as 'mutant,' " those arguing against racial taxonomies in medical research (Lee, Mountain, and Koenig, 2001) do not mention the low rate of inherited breast cancer; they dramatically overstate, by a factor of two, the disparity between the BRCA gene mutations among Ashkenazi Jews and the general population; and they do not mention the less than 50 percent chance of contracting breast cancer among BRCA carriers reported in more recent studies (ibid.: 34). Although part of their work strives to undo the impression that racial differences can be associated with genetic ones, the clear inference from the substance of the findings is that breast cancer is more frequently inherited by some groups of descent than from others. If breast cancer is largely triggered by environmental and not hereditary factors, it makes little sense to study breast cancer by using control groups differing in phenomenologies of descent. Research emphasizing hereditary group differences should be deterred because not only might it lead to group stigma, but because the results will not prevent, treat, or cure over 90 percent of those diagnosed with breast

18. *Code of Federal Regulations* 1, chap. 1, par. 42.402. Definitions, Subpart F—Coordination of Enforcement of Nondiscrimination in Federally Assisted Programs.

cancer. As opposed to those who accept the benefits of association studies, I am suggesting that these too have been wildly overstated.

Scientists may not enjoy hearing that their research may yield discomfiting truths and they should restrain themselves, but at least this approach suggests their work will likely contribute to important medical outcomes. If one consults even the ELSI grants NHGRI has made in human SNP research, they tend to assume that substantial medical benefits will accrue.[19] For example, a Cold Spring Harbor researcher and ELSI recipient in this field concludes an article on the subject quoting James D. Watson, cofounder of the double helix, who lives on the Cold Spring campus: the "greatest future danger will not be the misuse of genetics but rather, its disuse" (Micklos and Carlson 2000: 158). The article recommends that the government "build a critical mass of scientists and citizens who understand that the interpretation of genetic data about human beings is rarely free from value judgment" (ibid.: 158). Regardless of the controversy, it is always good advice that scientists and citizens appreciate that the interpretation of all data conveys values, so the only substantive recommendation is that diversity research proceed unimpeded. To think that the mass public should be the repository for responsibility over complicated genetic representations that the authors acknowledge even their sophisticated colleagues misunderstand dooms this society to repeat the painful errors of earlier eugenics movements Micklos and Carlson review (ibid.).

Far more crucial for unsettling NHGRI complacency on population genetics is not ELSI work on the dangers of their diversity research—the ethical complaints enhance the apparent objectivity and efficacy of the results—but pointing out that their inquiries will not revolutionize medicine, that work on population sequence diversity may yield data only on the variations of DNA fragments and not information useful to treating most people with most diseases. As long as the research challenging racial taxonomies gestures vaguely to dangers without challenging the alleged benefits, it is easy for geneticists to maintain their control of this research and, in turn, public discourse around it. Lee, Mountain, and Koenig (2001: 47) write of the possibility that genetic diversity research "carried out with an isolated population will identify a biological marker for schizophrenia" They then ask (ibid.), "will the reductionist paradigm transform, and per-

19. These NHGRI projects include Sandra Lee, "The Ethics of Identifying Race in the New Genetics"; Howard Markel, "The Stigma of Disease: Implications for Testing"; and David Micklos, "Digital Image Archive on the American Eugenics Movement" (NHGRI ELSI grant recipients).

haps 'geneticize' our understanding of identity?" Framing the problem this way situates those worried about eugenics thinking as skittish naysayers, as Luddites out to stop or slow medical progress.

The public needs to be alerted not just to the risks of racial categories, but also to the hype surrounding these anxieties. For instance, rather than restate the belief that schizophrenia is largely genetic, why not highlight the research showing that studies using monozygotic and fraternal twin data to claim schizophrenia is genetic have been questioned and in some cases dismissed (Jackson 1960; Joseph 2001, 2002)? Or that the past fifteen years of linkage studies offering predictions for schizophrenia alleles have, according to a review article on the subject, been "marked with numerous inconsistent and controversial findings" (Kato et al. 2002: 296). The authors of the article, who go on to offer suggestions for improving this record, say that as yet there have been no replicated studies that have found alleles for schizophrenia: "Numerous genomic regions have been suspected to carry the genes predisposing [schizophrenia], however, such regions of putative susceptibility vary significantly from study to study, from pedigree to pedigree suggesting a large degree of genetic heterogeneity of the disease" (ibid.). They say also that most studies lack any evidence that would encourage more research for genetic susceptibility in the regions studied (ibid., citing Strachan and Read 1999).

Rethinking Racial Discourse as an Object of Federal Science Research Policy

In addition to correctly framing the state of current research, it is also important to specify the intuitions underlying instructions on the merits of restricting the use of racial or ethnic taxonomies, a task that is necessary because many natural and social scientists still find it difficult to grasp logically cogent observations about how language does things and does not just name objects that are "out there."

The Importance of Language in Shaping Thinking about Complex Social Issues

The question that has been insufficiently addressed by humanists and scientists alike is whether racial taxonomies are not just objectively wrong but, far more crucially, whether these classifications are useful. Suggesting that a concept, say, "race," should be discarded or set off by quotation

marks because it is subjective[20] misleads because few words share a one-to-one correspondence with the objects they seem to name. Words convey meanings through a host of what language philosopher Ludwig Wittgenstein (1968) called "family resemblances," and they do not need to be incontrovertibly consistent or precise to be effectively used and to do things (Austin 1962). Despite confusion at the margins about what counts as a tall person, a fat person, an attractive person, an obnoxious person, no one demands we ban concepts of height, weight, beauty, or personality from our vocabularies. Asking more for the concept of race on these grounds alone—because its use betrays some inconsistencies—seems not only unfair, but also explains why the arguments to do so may grab people abstractly without changing their idiomatic uses of racial categories.

Whereas the high-handed dismissal of using racial categories leaves some academics out of touch with daily discourse, alarmist anxiety about some medical genetic research—say, work on BRCA mutations among Ashkenazi Jews (Lee, Mountain, and Koenig 2001)—gives life to the very myth such researchers are claiming to attack. The more accurate, possibly less dramatic point that needs to be insisted on is that racial and ethnic classifications in the articles above do things they could not have done were their infelicities of meaning as fantastic as sometimes presented in the literature critical of racial classification (Appiah 1993). If one is really interested in limiting the use of race in genetic research, then it is not enough to demonstrate the concepts have objective limitations (Keller 1995; Stevens 2002). One must demonstrate that the benefits and uses of these codes are not what many think they are, including even those critical of genetic diversity research.

The performative quality of race—what it does when it is used—occurs because, like all words, race is simultaneously a symbol and something material. I am not claiming a widely made point among various philosophers of science, which is that subjective and politicized concepts and research programs yield concrete effects. Instead, I am emphasizing the fact that this word, this sentence, this paper are material, that without the carbon in the pencil, the electronic emissions of the computer, the ink that prints the words, and the neurological charges in the brain, these thoughts and symbols and all others do not exist. This observation is an extension of one made by Albert Einstein, when he noted that light pro-

20. For an example of this argument and its related references see Lee, Mountain, and Koenig 2001.

tons behave simultaneously as waves and particles, while seemingly solid things also behave as particles and waves (Stevens 2002).[21]

Although language is denigrated by some natural and social scientists as "mere words," when those words are power, when "codes" appear through the medium of DNA in cell cultures, they are regarded as substantial, primordial, or as the genome project has been dubbed, the Book of Life, the name given in 1999 to the National Center for Biotechnology Information's home page on the genome map (www.ncbi.nlm.nih.gov/omim/). However, the codes of the scientific articles discussed above—existing in the material of print, the electronic emissions of the Internet to one's monitor, or the compression of air from a scientist's lecture—are more influential in affecting variation in life outcomes than the variations in the DNA such publications claim to represent.

These final sections present the harms of racial categories in a manner that should be familiar to those accustomed to positivist discourses of risk and health policy. I also offer a framework that addresses some of the confusion about whether and how to study racial or ethnic differences in health status and disease. In light of population genetics' ambiguity, coupled with the distinct possibility that bad decisions in this area will have dire consequences, it behooves social scientists in general and political scientists in particular not only to monitor the developments in this area, but to contribute research that will assist in making the appropriate decisions on this matter, in much the same way that social scientists participated in consultations with the OMB over the collection of racial and ethnic information on the U.S. census (U.S. Census Bureau 1999).[22] Judging by pre-

21. As examples of words whose phenomenological quality as things is especially obvious, consider the contexts below where people idiomatically treat symbols and language as generating effects warranting caution:

- "Asserting that the new media's pursuit of stories has fueled acts like copycat killings and school shootings, a judge refused today to release a transcript of a hearing in a murder case" (Associated Press 1999). The case involved an American Indian student "accused of raping and murdering a white woman on Mother's Day" in an area "struggling with racial tension" (ibid.).
- The original U.S. flag, regarded as a symbol, is fraying badly. Were it not material, it would not decay, nor require restoration and preservation estimated to cost $18 million (Molotsky 1999).
- "An entire industry of namers has sprung up to coin vaguely hip terms for the new economy's companies," even though these names are not words but invented with an "emphasis on mood" (Altman 2001).

22. The methodological lacunae of political science as a discipline were evident in their general absence from these consultations. Most active in deliberations with the U.S. government on the matter of the census categories were sociologists, demographers, and anthropologists. Exemplary of the methodological omissions of political science is that leading textbooks devote no attention to the theoretical underpinnings of the basic units of their analyses, be they ethnicity, nationality, race, or gender (Achen and Shively 1995; Bates 1998; King, Keohane, and Verba

vious incursions into the arena of biology that are far more afield from the expertise of political scientists—studies of biochemicals such as serotonin in association with measurements of "power" published in the *American Political Science Review* (Madsen 1985, 1986)—political scientists have not been shy about studying the body. Perhaps cultivating talents more appropriate to the social rather than the natural sciences might complement this work.

To make clear the need and feasibility of such interventions, it seems a good idea to consult approaches taken to comparable long-standing public health concerns. Caution in the use of racial taxonomies should be seen as continuous with other policies aimed at reducing harms and not a strange ad hoc restriction. Consider how findings on the risks posed by cigarettes and guns make these the objects of political regulations. Do the risks posed by the use of race as a genetic category compare with these? Should diversity heuristics produced by the government and its grantees also be subjected to government regulations?

Race, Guns, and Cigarettes: A Policy Analogy

One rejoinder to this comparison might be that guns and cigarettes differ from race. The former are physical, material objects whereas race appears to be a concept, a label for a thing. Put more plainly, cigarettes and guns are intrinsically things amenable to risk assessment while race seems to be merely a concept whose risks are therefore difficult, if not impossible, to assess with the objectivity and rigor required of those studies that make their way into policy deliberations. However, such a dichotomy misrepresents the character of race, cigarettes, and guns, not to mention racialized genetic taxonomies. Cigarettes and guns are not part of policy debates because they simply are risky. And, to reiterate a point above, race even as a concept is also a thing, a code every bit as concrete and worthy of political scrutiny as the dangers posed by guns and cigarettes.

When comparing the social movements that prompted legislatures to regulate cigarettes and guns, Constance Nathanson (1999: 445) makes it plain that the policy on these matters did not develop simply because guns

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1994). The tendency of political scientists to believe that mastering statistical techniques and assembling large data sets will make their research more objective is especially questionable in light of the recognition by those in the natural sciences that major research questions can be solved only by heuristic inquiry. Paradoxically, political science, precisely because it is engaged with the study of government, is especially well-suited to study the intersection of science and public policy that is of such urgent importance at this particular historical juncture.

and cigarettes are intrinsically harmful objects: "Guns and cigarettes do not have essences; they have histories and cultural baggage with which social movement entrepreneurs must control." The movements to regulate guns and tobacco did not begin because guns and cigarettes are deadly. Rather, these social movements depended on the representation of widespread risks associated with these activities: "Of greatest importance to the smoking of tobacco control movements initial mobilization and to its enduring impact has been the construction of credible risks. The authority of medicine and science in the smoking of tobacco control arena was well established before the organized movement emerged" (ibid.). Nathanson's intent is not to minimize the harms of cigarettes and guns, but to emphasize that these did not result in legislation until a medical–political establishment used a statistical discourse of risk.

Like guns and cigarettes, the representation of racialized genetics in a scientific publication is a thing and it, too, poses risks. Recognizing these risks, the NHGRI is not willing to specify the definition of a race, an ethnicity, or a population. The only fact about population genetics that it will proclaim is that its heuristics are uncertain and yield risks. Some may believe that such classificatory problems are amenable to further research, but there is no empirical basis for this hope, only a blind faith in the ultimate existence of genetic differences that could be called racial.

Still, a critic might accept the above point and question whether the NHGRI is being too cautious. Rather than viewing the category of race as an intrinsic harm, one might respond that even mistakes about racial categories are benign; the harms are caused by a small fraction of people who make an improper use of the category. One might well accept the gun and cigarette analogy and emphasize that, like these, race too is politically neutral: guns need not produce deadly accidents and people could smoke without fear if they smoked one or two cigarettes daily instead of one or two packs. And yet, despite these potentials, a significant portion of the public clamors for controls over these items because of the overwhelming record showing that absent such regulation individuals will use guns and cigarettes in ways that cause harm, to themselves and to others. There is no logical argument for why people who smoke must smoke on average one to two packs each day, rather than a few cigarettes (thereby minimizing the association of cigarettes with lung cancer). Nor is there a necessary reason for why human beings could not be trained never to leave their handguns accessible to children or never to make a mistake using a handgun. But just as these patterns of smoking and gun behavior have never been observed at levels necessary to mitigate their respective harms,

a population overlooking claims about genetically based racial differences in the allocation of resources would be also a public policy novelty, a fact about which NHGRI is well aware. Just as we know guns and cigarettes alone are harmless and still associated with harms to humans, we know that the racial taxonomies alone may be harmless and still responsible for deep and far-reaching health and other problems.

To extend or operationalize these insights about the materiality of racial taxonomies to genetics research we need to recognize that the codes of DNA are no more or less metaphorical than the codes outside DNA. Both are part of the environment that shapes various events, including the political and economic forces of "environmental racism"—only possible because of residential segregation by racial taxonomies (Bullard 1983). The results of this racial coding are higher incidences of asthma, blood pressure, infant mortality, and cancer among African Americans than among European Americans in urban areas (U.S. NAS 1999, 2000). According to the CDC (1997), although the disparity between Black and White rates of asthma is only 1 percent, Blacks are hospitalized and die from asthma at three times the rates of Whites. In East Harlem, the rate of hospitalization for asthma is 223 per 10,000 residents, while in the rest of Manhattan that number is 46 per 10,000 (Luz 1999). These disease rate differences are of an entirely different magnitude from those associated with potential genetic differences between the two populations, suggesting etiologies due to environmental differences of toxic exposures, housing quality, and access to health care (U.S. NAS 1999; Noah 1998)—all of which are determined by racism, not racial genetic differences. Yet, the U.S. government continues to devote substantial efforts to the latter.

The role of taxonomies in perpetuating such inequalities can be seen more vividly if one sees discussions of geneticized racial taxonomies not as statements about observable facts, but as themselves a series of codes that instruct the social organism of human (and other) life. When, if ever, are the words *Caucasian*, *Negroid*, and *Asian* harmless labels, and when are they like the signs "Whites Only" or "Coloreds Use Rear Entrance" or "Black Drinking Fountain"—used effectively not as mere words, but to institutionalize racial segregation? Just as DNA replication sometimes results in mutations that scientists seek to change, we might ask about the ways that publications on population genetics—also present in material media—manifest mistakes that the body politic might seek to fix. When scientists observe harmful genetic mutations they do not say the code exists as such and should not be altered, but that when the organism's own

processes do not detect or eliminate the error, the ensuing problems may call for intervention.

Genetic diversity studies classifying people by race and ethnicity have the effect of harming those segregated by a rigid grid that has provided a rationale for invidious discrimination. First, SNP designations of race in the United States mean each individual thought to be "Black" has his or her Blackness objectified, while those discriminating based on race have their prejudices legitimized and entitlements reinforced. Second, the information directs attention to genetic components of disease at a point when known environmental contributions to illness remain unaddressed. For the NHGRI in particular to stress medical applications of the research is for them to potentially violate the Hippocratic Oath, "first do no harm," since the harms of racial typologies are known while their benefits, indeed the benefits of genetic research in toto, remain remote for all but a few highly privileged elites in a very few countries. According to the World Health Organization, approximately 4 percent of the world's population may even potentially benefit from potential benefits (Mao 1998: 688).

Genetic research by the NIH draws attention away from the environmental sources of and treatments for disease, inviting us to overlook the manipulation of group differences that allows those with power to concentrate toxic chemicals and emissions in places populated by those who are "not us." There is a host of community groups organized to fight for environmental justice based on observation of strong associations between toxic exposures and poor health outcomes in areas with high concentrations of people of color (U.S. NAS 1999). A belief in an immutable difference allows groups to treat strangers in ways they would not treat members of their own putative family or kind. Finally, population geneticists who do not explicitly question the terms they use obscure the significance of their roles as agents in social change, making it difficult to subject their pronouncements to the political processes of responsible evaluation.

If we return to the example of guns and focus on the benefits and costs of gun registration and ownership, we see that policy makers engage comparatively in the rhetoric of risk. In addition to invoking the Bill of Rights, National Rifle Association lobbyists and their supporters recall anecdotes about innocent victims able to defend themselves against burglars or carjackers because their handguns were easily accessible (Nathanson 1999). That some may cite instances of gun accessibility as useful does not cause their opponents to wilt. In light of even more robust data on the public health irrelevance of genetic research, that genetic diversity research *may* prove beneficial seems an even less persuasive retort.

As discussed above, the medical arguments for gene therapy in general, and for population-based genetic research in particular, seem offset by the current state of the evidence in this regard. For many of the diseases listed by Collins, Brooks, and Chakravarti (1998), the epidemiological figures, including those of the NIH, overwhelmingly suggest that the major variables that contribute to health status are not genetic but environmental (e.g., Edlin 1987; Sarkar 1998; Holtzman and Marteau 2000; Kaufman and Hall 2003; Kneese and Schulze 1977; U.S. NAS 1999). Even if a hereditable mutation seems to offer a statistically significant contribution to disease etiology—and evidence suggests that for the vast majority of illnesses the figure is on the very low end of a range between 1 and 20 percent (Collins, Guyer, and Chakravarti 1997)—attempting to address genetic causes makes less sense than pursuing studies and treatments directed toward mitigating behavioral and environmental causes of disease that offer substantial and proven benefits. Especially in the case of complex behavioral and health patterns such as depression, high blood pressure, diabetes, and asthma—all justifications for SNP research—data suggest that racial differences among these are best explained by institutional racism—the primary sources of which include large racial disparities in family wealth (e.g., Oliver and Shapiro 1995; Conley 1999), housing discrimination and segregation (e.g., Hunter 1995; LaVeist 1993; Massey and Denton 1993; Collins and Williams 1999), and stress from a range of subtle and blatant practices of prejudice (e.g., David and Collins 1997; Krieger 1990; Williams et al. 1997; Krieger and Sidney 1996).

It should be noted that ideas about the genetic basis for such diseases are almost impossible to disprove to a certain community of researchers who pursue their genetic hypotheses with apparently more fanaticism than reason. For instance, researchers have long puzzled over Black-White differences in hypertension that persist in the data even after regressions control for numerous variables. One popular hypothesis was that this was the result of genetic differences between Blacks and Whites. Once it was shown that contemporary Africans from West Africa—the origin of most Africans sold to plantations in the United States—have lower rates of hypertension than do contemporary African Americans and Whites, prominent population geneticists quickly regrouped. Acknowledging that there were no broad genetic differences between Negroids and Caucasians in their mix of genes that would predispose to hypertension, some hypothesized that contemporary African Americans underwent a process of natural selection rendering them genetically different from contemporary western Africans (Wilson and Grim 1991). Their hypothesis was that those

Africans who survived the arduous journey across the ocean passed down a gene for water retention and that it is this water-retention gene that is responsible for hypertension in U.S. Blacks being higher than that of U.S. Whites and Blacks in western Africa (Murray 1991; Curtin 1992). The conjecture tells us much about the allure of genes for explaining race differences and nothing about Black-White differences in hypertension (Cooper 1997; Cooper and Rotimi 1994; Krieger and Sidney 1996). Various studies that have controlled between races for environment or measured within-group changes following migration have demonstrated the irrelevance of these genetic-level etiologies.[23]

Prejudices about the genetics of race also continue to surpass sound judgment when it comes to protocols for collecting the data on diversity, another reason the NIH needs to step in and offer more guidance. Conventional subject consent procedures are insufficient: "Currently, it is standard practice to name ethnically, geographically, and linguistically identifiable populations in public databases and scientific publications. That practice, however, may entail collective risks that are shared by all member[s] of those populations, not just those who chose to participate in research studies" (Foster, Bernstein, and Carter 1998: 696; and see Knoppers, Hirtle, and Lormeau 1996). The practice of attempting to include representatives of potentially affected constituencies in the decision-making process (Greely 1998) is no prophylactic against the harms to which these group representatives may consent, as such leaders are institutionally predisposed to consolidating the existence of that group in ways that parallel the ambitions of population geneticists. On top of that, what counts as an ethnic group and its leader? Should the Israeli parliament vote before further genetic studies of Jews proceed?

Race itself is a code, one that presently instructs people to group with those whom they are thought to resemble by birth and to separate from those who are different. The form of our political institutions and the form of racial groups residing therein currently reflect governmental rules about birth and identity, not individual preferences. Whereas membership in a

23. One study compared measures of blood pressure and heart rate for West Point cadets who had been enrolled for at least one year and hence largely shared the same environment. Although their parents showed differences in blood pressure across race groups, the researchers reported, "Analysis of variance failed to reveal significant differences in any of these blood pressure regulatory mechanisms between any of the groups" (Horodyski et al. 1995). A study of Ethiopian immigrants to Israel compared 483 recent immigrants with a control group of Ethiopians who had settled in Israel two to three years earlier: "The Systolic and diastolic BP were considerably lower in recent immigrants of both sexes than among counterparts residing in Israel for two to three years" (Rosenthal et al. 1990). For an excellent critique of the slavery hypertension hypothesis, see Kaufman and Hall 2003.

social group is a matter of taste and disposition, a genetic group is regarded as impermeable, a natural difference that society respects and others will not abrogate, especially if membership in the group is hereditary and genetically stigmatized.

Heuristic Remedies: Establishing the Parameters of Research Interpretation

Public health policy in the area of racial heuristics seems caught between the proverbial rock and a hard place. On the one hand, racial denominators cause harms, but on the other hand, studying these harms seems to require the reiteration of race. One article carefully considering racialized sequence diversity research argues "against using race as a biological category in health research" but then states that "studies of the health effects of racism *per se* may be one arena where using traditional political categories of race is justified" (Lee, Mountain, and Koenig 2001: 40). This raises the question of how to distinguish these, that is, how to operationalize racialization as a category without reiterating genetic notions of race. Reflecting on the conundrum, these authors (ibid.: 63) quote Emerson: "A foolish consistency is the hobgoblin of little minds," but this seems only to beg the question.

Rather than calling on poor Emerson, it seems worthwhile to make explicit the bases of the intuition distinguishing racialization from race as a biological category. The problem is that race is not just a biological category. Colds, broken legs, and bad eyesight are also biological categories. One crucial difference between race and these other biological categories is that the latter impute biological difference to hereditary differences. Scholars worried about racialization are attempting to curtail research that harmfully and incorrectly represents groups as hereditary, but they do not want to prevent studying inequality resulting from racism. Studying race without connoting heredity seems to be a problem because race by definition seems heritable. The best evidence to settle any confusion about someone's race is not dress, speech, or even appearance, but the race of one's ancestors. Other factors of socioeconomic status, such as income or residency, do not share this characteristic and hence do not raise the same problems for these health researchers. That is, if I doubt that you really earn $1,000,000 annually, telling me that your parents are rich does not settle the case, even though statistically the wealth of one's family may be the best predictor of one's own wealth, but you can indisputably prove your race by documenting the race of your parents.

The task for health policy makers is to articulate a heuristic practice allowing for the disaggregation of race from heredity. Although at first this may seem a silly nominalism, if accomplished in the media of health research, it may dramatically change public intuitions about this classification. Earlier epochs witnessed equally stark movements from seemingly social to hereditary and back to social phenomenologies of legal status for serfs, slaves, and even the poor. With a bit of judgment and clear thinking, today's government guidelines for the use of race may be even more efficacious, especially for so-called ascriptive characteristics.

It is commonly thought that an ascriptive identity is one into which one is born, but the word has its root in the Latin *ascribere*, meaning "what is written."[24] The concept initially referred to the attributes taken from lists for the Domesday Book of eleventh- and twelfth-century England, when census takers sought to classify the occupations, incomes, and locations of residents throughout the realm recently conquered by Norman invaders. Over time, these categories became absorbed into the family names of the residents; for instance, millers, smiths, or people from particular parishes were assigned these or took them as family names. That one's father was a miller did not demand one to become one as well, but that did determine one was a Miller and hence revealed something about one's ancestry. Of course today, few associate such a hereditary detail of the Miller name with anything interesting about one's family occupation (though this does mark one as phenomenologically English) (Stevens 1999).

During this same period, feudal relations also depended on heredity: one was born a lord or a serf and that fact rendered these groups likewise infused with ancestral associations similar though not identical with our own conventions of ethnicity. Serfs were themselves soldiers in losing armies or descendants of such soldiers (Reynolds 1984). Eventually, just as the political ascriptions worked their way into hereditary ones, the hereditary ones became regarded as conventional. By the time of the English Civil War in the 1640s, the Bible was frequently used to rail against denominations and prerogatives of birth. God's children, not the Stuarts, had inherited the earth and all men were claimed to have the right to political participation on that basis (Locke 1960: First Treatise).

In light of the historicity and plasticity of forms of being such as lord, slave, White, Black—they may move between being experienced as contingent to inherited and then to contingent—and in light of the heightened

24. Much of the discussion in this section is based on findings from an earlier work (Stevens 1999, esp. chap. 5).

equality and freedom occurring when people are raised to believe they are endowed equal and free by birth, it makes sense to attempt such a transition from heredity to social beliefs about racial designations.

Specific Recommendations and Precedent

1. The Department of Health and Human Services should issue a regulation prohibiting its staff or grantees, including those receiving NIH funding, from publishing in any form—including internal documents and citations to other studies—claims about genetics associated with variables of race, ethnicity, nationality, or any other category of population that is observed or imagined as heritable unless statistically significant disparities between groups exist and description of these will yield clear benefits for public health, as deemed by a standing committee to which these claims must be submitted and authorized prior to their circulation in any form beyond the committee.
2. The NIH should issue a clarification of the current congressional requirement that "women and members of minorities and their subpopulations are included in all human subject research federally funded medical research," which has been interpreted to refer strictly to ethnic and racial groups (59 *Federal Register* 11,146 [9 March 1994]). The new regulation should specify that federally funded medical research study many populations, including those that vary by childhood residence, current residence, occupation, diet, exercise, age, wealth, income, and regularity of medical care.

The rules advocated above could be enforced by an NIH committee similar in purpose to the NIH Recombinant DNA (rDNA) Advisory Committee, but with more enforcement capabilities. Scientists using NIH funds for rDNA research must submit their proposals to the Advisory Committee, which then ascertains whether the experiments warrant public review. If the committee deems it necessary, for reasons of safety or ethical concerns, the scientists must make their plans available and receive public comment. Though the recommendations resulting from this review are not enforceable, the review procedure is: "Evidence of noncompliance may result in suspension or termination of NIH financial support and other sanctions applicable to the project researchers and their institutions" (Baram 2001). The model proposed for reviewing genetic etiologies associated with group differences would require the standing committee to

evaluate the public comments and, with these in mind, to determine whether the research can be published.

Adherence to the first recommendation would sharply curtail research references to race and ethnicity, with relatively little impact on genetic medical research agendas. Most of the studies funded by the NIH seem not to be centrally concerned with these differences but mention them in passing, seemingly as a matter of habit. Once pressed to supply more precise data and arguments on their relevance to public health, authors of these articles will likely be dissuaded from pursuing approval for these claims. For instance, if the authors of the *Journal of the American Medical Association* article on pharmocogenics (Phillips et al. 2001) had to prove their claims about genetically based racial differences in ADRs they would have to do more than cite the popular press and an offhand interview comment. Either they would need to conduct the research necessary to back up this observation or they would not bring up the topic. Though geneticists researching in this area may cringe at what appears to be a restraint on their freedom of speech and study, the intellectual basis for this ban is unassailable. There is no empirical evidence that populations taxonomized by descent yield more knowledge than those analyzed along other axes, while there is overwhelming evidence that nongenetic taxonomies offer more predictive value and robust information. Of course scientists can point to hundreds of articles studying genetics and ethnic associations with statistically significant differences, but frequently subsequent retesting shows these to be spurious, possibly a result of data mining. To ensure against this form of misdirection, scientists should disclose to the committee all of the suspected allele sites they investigated for correlations and adjust their standard error accordingly. Ideally, scientists should compare the racial and ethnic group genetic differences with those of groups not thought to be hereditary. If, using the same method they use for studying group differences, they find similar rates of statistically significant correlations for polymorphisms between arbitrarily selected groups—for instance populations divided by the last digit of their phone numbers—they should reconsider stating any conclusions about the role of heritable genes.

The second recommendation—expanding the number of variables studied—serves two purposes. First, it challenges the intuition that hereditary identities confer the most important differences among us. Studying race, ethnicity, and sex in the context of these other variables demonstrates these other contributions and may inspire viewing race, ethnicity, and even sex as also social. Such contextualization does not itself rule out

interpreting race and ethnic variables as diachronic or heritable, but at least it allows the consideration of inequalities associated with these attributes and invites their consideration as tied to the cross-sectional advantages and disadvantages of privilege and discrimination, respectively, and not to a group's inherited abilities and constraints.[25] One hesitation in requiring these additional variables stems from statistical concerns that lower *N*s will wash out results, as it will be very difficult to assemble a data set with sufficient numbers in the various boxes. There may not even be a New Hampshire counterpart to the Asian stockbroker who grew up in the rural Midwest near a power plant and lives now in New York City, for example. However, since we live in a world of these and many other variables, weak results more honestly reflect the uncertainty inherent in such studies. Rather than require skepticism on the part of the public, scientists should make explicit the uncertainty of their results.

The salutary effect of the NIH not funding publication of hereditary population characteristics is not that studies oversampling the genomes of White men are fair or that the findings lend themselves to accurate inferences about disease and risk for everyone else. Rather, because of the overwhelming similarities in the causes and treatments of the diseases the NIH is prioritizing—hypertension, diabetes, and asthma—the false universalization of heritable traits poses fewer health risks than a false particularization of such traits. Any misrepresentations at the margins—unavoidable for any study that goes beyond an individual genome—still means research avoiding hereditary population taxonomies will be more accurate and beneficial than the epistemic and medical consequences attendant obsessive reconstitution of hereditary groups.

Denying geneticists the ability to study heritable traits by large populations still allows researchers to compare family trees, and privately funded studies can pursue genetic racial and other population taxonomies. While the information presented above on breast cancer research suggests that for reasons of efficacy federal money might be better spent elsewhere, pursuit of autosomal genes for diseases can still use linkage studies of families, avoiding confusion about these as hereditary racial populations by refusing to cluster or name them as such.[26]

As racial differences are not just called socially constructed but analyzed as politically constructed, it is to be expected that they will recede

25. The same holds for sex difference, but to explain that is beyond the scope of this article.

26. The definition of a population is prone to the same infelicities as those of a species or a race (Hey 2001: 156–157).

as prominent distinctions in the public imagination. Just as serfs—also treated as a hereditary group—vanished as such with the elimination of the feudal legal structure, it is possible that abandoning the interpellation of race as biological by the governmental scientific community may also result in vanquishing the biological connotations of this group, so that being Black would be regarded as no more genetic than being a Manhattanite. In the fourteenth century, to think that a serf was a purely political convention and a woman might be a venture capitalist would be absurd. Developments in political economy change profoundly not just what we do but who we are. Albeit many times these changes are unforeseen, it is much better, especially for a democracy, if these changes are directed self-consciously toward the elimination of arbitrary inequalities and forms of alienation.

Since the government is funding this research, it is the prerogative of the government to decide on its priorities. Just as creationist researchers, using methods and premises the NIH rejects, do not receive funding, the NIH is free to exercise its judgment as to what it considers useful expenditures. One potential legal objection to this rule would be that it restricts free speech. However, the rule does not censor scientists, but denies them funding for particular types of studies, unless they go through a review. They are free to conduct these studies with private money and to publish them, albeit with the knowledge that scientists receiving NIH funding cannot cite them. One anticipates such a rule would take away any incentives for shoddy, inflammatory work, since presumably scientists would want their insights used by others and will spend time doing research where that is possible.

Related precedents suggest that while such a rule may anger a certain constituency, the rule is constitutionally sound. Analogous regulations tying funding to speech restrictions in the area of medicine as well as the arts have been held constitutional. In 1991, the U.S. Supreme Court upheld a federal regulation under Title X prohibiting family planning clinics receiving federal funds from providing any information about abortion or abortion referrals.[27] Nurses and doctors who asserted a First Amendment right to alert patients to medical treatments were told that the government had no obligation to pay for their exercise of this right. Relatedly, in 1998, the U.S. Supreme Court upheld, eight to one, Congress's requirement that the National Endowment for the Arts consider "general standards of decency and respect for the diverse beliefs and values of the American

27. *Rust v. Sullivan/State of New York v. Sullivan*, 500 U.S. 173 (1991).

public" when awarding grants, though artists protested this violated their First Amendment rights.[28] A rule prohibiting reference to variations associated with hereditary populations in federally funded research is no more an assault on free speech than is the NIH presumption against funding publications on whether signs of the zodiac correlate with health outcomes.

In fact, the pressing problem the human species poses to geneticists bent on discovering taxonomic rules of race among us is our own ability to rapidly change our so-called genes, based on changes in laws regulating kinship and citizenship and, by extension, ethnicity and race (Stevens 1999). For instance, the U.S. government has decided on the criteria determining membership in various sovereign Native American tribes, for which the evidence is largely government records and the practices of the individual, not physical appearance and certainly not DNA. Likewise at the level of family membership, legal authorities have asserted the state's right to determine paternity and even maternity so that the juridical family, the one recognized by law as "natural," may well be at odds with the genetic one.[29] Hence the ultimate determinants of the family and its respective intergenerational groups are not laws of nature, but laws of political society. These laws have the power to shape the very essence of who we are, requiring therefore the government-sponsored research community to be sensitive to how it may be inventing what it portends to discover.

References

Achen, C., and W. Phillips Shively. 1995. *Cross-Level Inferences.* Chicago: University of Chicago Press.

Altman, D. 2001. What's in a Name? Today, Not Much. *New York Times*, 23 August, A18.

Appiah, A. 1993. *In My Father's House: Africa in the Philosophy of Culture.* Oxford: Oxford University Press.

Associated Press. 1999. Assailing News Media, Judge Closes Trial Record. *New York Times*, 16 August, B6.

28. *National Endowment for the Arts v. Finley*, 524 U.S. 569 (1998).

29. For an extensive discussion of the role of the state in determining membership in political societies, nations, ethnic groups, races, and families see Stevens 1999: chap. 6 and forthcoming.

Austin, J. L. 1962. *How To Do Things with Words*. Oxford: Clarendon.

Bailey, L. R., N. Roodi, C. Verrier, C. Yee, W. Dupont, and F. Parl. 1998. Breast Cancer and CYPIa1, GSTM1, and GSTT1 Polymorphisms: Evidence of a Lack of Association in Caucasians and African Americans. *Cancer Research* 58:65–70.

Baram, M. 2001. Making Clinical Trials Safer for Human Subjects. *American Journal of Law and Medicine* 27:253–282. Available through the *AJLM* Web site at aslme.org/pub_ajlm.

Basile, V. S., V. Özdemir, M. Masellis, M. L. Walker, H. Y. Meltzer, J. A. Liebman, S. G. Potkin, G. Alva, W. Kalow, F. M. Macciardi, and J. C. Kennedy. 2000. A Functional Polymorphism of the Cytochrome P450 1A2 (*CYP1A2*) Gene: Association with Tardive Dyskinesia in Schizophrenia. *Molecular Psychiatry* 5:410–417.

Bates, R. 1998. *Analytic Narratives*. Princeton, NJ: Princeton University Press.

Borger, Julian. 2000. Researchers Suspected of Hiding Deaths in Gene Tests. *Guardian Unlimited*, 1 February. Available online at www.guardian.co.uk/genes/article/0,2763,191898,00.html.

Bullard, R. 1983. Solid Waste Sites and the Black Houston Community. *Sociological Inquiry* 53:273–288.

Cann, R. L., M. Stoneking, and A. C. Wilson. 1987. Mitochondrial DNA and Human Evolution. *Nature* 325:31–36.

Caruso-Nicoletti, M., M. Mancuso, G. Spadero, P. Samperi, C. Consalvo, and G. Schiliro. 1992. Growth and Development in White Patients with Sickle Cell Diseases. *American Journal of Pediatric Hematology/Oncology* 14(4):285–288.

Claus, E., N. Risch, and W. D. Thompson. 1991. Genetic Analysis of Breast Cancer in the Cancer and Steroid Hormone Study. *American Journal of Human Genetics* 48:232–242.

Colditz, G. A., et al. 1993. Family History, Age, and Risk of Breast Cancer: Prospective Data from the Nurses' Health Study. *Journal of the American Medical Association* 270:805–812.

Collins, C., and D. R. Williams. 1999. Segregation and Mortality: The Deadly Effects of Racism? *Sociological Forum* 14:493–521.

Collins, F., L. Brooks, and A. Chakravarti. 1998. A DNA Polymorphism Discovery Resource for Research on Human Genetic Variation. *Genome Research* 8:1229.

Collins, F., M. Guyer, and A. Chakravarti. 1997. Variations on a Theme: Cataloguing Human DNA Variation. *Science* 278:1580.

Collins, F., A. Patrinos, E. Jordon, A. Chakravarti, R. Gesteland, and L. Walters. 1998. New Goals for the Human Genome Project: 1998–2003. *Science* 282:682–689.

Conley, D. 1999. *Being Black, Living in the Red*. Berkeley: University of California Press.

Cooper, R. 1997. Hypertension in the African Diaspora: Genes and the Environment. In *Plain Talk about the Human Genome Project*, ed. E. Smith and W. Sapp. Tuskegee, AL: Tuskegee University Press.

Cooper, R., and C. Rotimi. 1994. Hypertension in Populations of Western African Origin: Is There a Genetic Predisposition? *Journal of Hypertension* 12:215–227.

Cowan, R. S. 1992. Genetic Technology and Reproductive Choice: An Ethics for

Autonomy. In *The Code of Codes: Scientific and Social Issues in the Human Genome Project*, ed. D. Kevles and L. Hood. Cambridge: Harvard University Press.

Curtin, P. D. 1992. The Slavery Hypothesis for Hypertension among African Americans: The Historical Evidence. *American Journal of Public Health* 82:1681–1686.

Darwin, C. 1964. *On the Origin of Species*. Cambridge: Harvard University Press.

David, R., and J. Collins Jr. 1997. Differing Birth Weights among Infants of U.S.-born Blacks, African-born Blacks and U.S.-born Whites. *New England Journal of Medicine* 337:1209–1214.

Drosnin, M. 1997. *The Bible Code*. New York: Simon and Schuster.

Durocher, F., D. Shattuck-Eidens, M. McClure, F. Labrie, M. Skolnick, D. Goldgar, and J. Simard. 1996. Comparison of BRCA1 Polymorphisms, Rare Sequence Variants and/or Missense Mutations in Unaffected and Breast/Ovarian Cancer Populations. *Human Molecular Genetics* 5:835–842.

Duster, T. 1990. *Backdoor to Eugenics*. New York: Routledge.

Easton, D. F. 2002. Personal communication (e-mail). 20 February.

Easton, D. F., D. T. Bishop, D. Ford, and G. P. Crockford. 1993. Genetic Linkage Analysis in Familial Breast and Ovarian Cancer: Results from 214 Families. *American Journal of Human Genetics* 52:678–701.

Edlin, G. 1987. Inappropriate Use of Genetic Terminology in Medical Research: A Public Health Issue. *Perspectives in Biology and Medicine* 31:47–56.

Egan, K. M., P. Newcomb, M. Longnecker, A. Trentham-Dietz, J. Baron, D. Trichopoulos, M. Stampfer, and W. Willet. 1996. Jewish Religion and Risk of Breast Cancer. *Lancet* 347:1645–1646.

Feuer, E. J., L. Wun, C. Boring, W. D. Flanders, M. Timmel, and T. Tong. 1993. The Lifetime Risk of Developing Breast Cancer. *Journal of the National Cancer Institute* 85:892–897.

Feuerstein, A. 2002. ImClone Bringing down the Biotech Neighborhood. Available online at www.thestreet.com/tech/adamfeuerstein/10007200.html.

Fodor, F., A. Weston, I. Bleiweiss, L. McCurdy, M. Walsh, P. Tartler, S. Brower, and C. Eng. 1998. Frequency and Carrier Risk Associated with Common BRCA1 and BRCA2 Mutations in Ashkenazi Jewish Breast Cancer Patients. *American Journal of Human Genetics* 63:45–51.

Ford, D., D. Easton, D. Bishop, S. Narod, and D. Goldgar. 1994. Risks of Cancer in BRCA-1 Mutation Carriers. *Lancet* 343:692–695.

Ford, D., D. F. Easton, and J. Peto. 1995. Estimates of the Gene Frequency of BRCA1 and Its Contribution to Breast and Ovarian Cancer Incidence. *American Journal of Human Genetics* 57:1457–1462.

Ford, D., D. Easton, M. Stratton, S. Narod, D. Goldgar, P. Devilee, D. T. Bishop, B. Weber, G. Lenoir, J. Chang-Claude, H. Sobol, M. D. Tearing, and J. Struewing. 1998. Genetic Heterogeneity and Penetrance Analysis of the BRCA1 and BRCA2 Genes in Breast Cancer Families. *American Journal of Human Genetics* 62:676–678.

Foster, M., D. Bernstein, and T. Carter. 1998. A Model Agreement for Genetic Research in Socially Identifiable Populations. *American Journal of Human Genetics* 63:696–702.

Freeman, H. 2000. The Meaning of Race in Science—Considerations for Cancer Research: Concerns of Special Populations in the National Cancer Program. *Cancer* 82:219–225.

Greely, H. 1992. Health Insurance, Employment Discrimination, and the Genetics Revolution. In *The Code of Codes: Scientific and Social Issues in the Human Genome Project*, ed. D. Kevles and L. Hood. Cambridge: Harvard University Press.

———. 1998. Legal, Ethical, and Social Issues in Human Genome Research. *Annual Reviews in Anthropology* 27:473-502.

Hartge, P., J. Struewing, S. Wacholder, L. Brody, and M. Tucker. 1999. The Prevalence of BRCA1 and BRCA2 Mutations among Ashkenazi Jews. *American Journal of Human Genetics* 64:963–970.

Healy, B. 1997. BRCA Genes—Bookmaking, Fortune-telling, and Medical Care. Editorial. *New England Journal of Medicine* 336:1448–1449.

Hey, J. 2001. *Genes, Categories, and Species*. New York: Oxford University Press.

Holtzman, N., and T. Marteau. 2000. Will Genetics Revolutionize Medicine? *New England Journal of Medicine* 343(2):141–144.

Hopper, J., and M. Jenkins. 1999. Modelling the Probability that Ashkenazi Jewish Women Carry a Founder Mutation in BRCA1 or BRCA2. Comment. *American Journal of Human Genetics* 65:1771–1776.

Horodyski, M. B., R. E. DeMeersman, P. M. Wanderburg, and D. Gallagher. 1995. With Environmental Control, the Effects of Race and Sex on Blood Pressure Regulatory Mechanisms Appear Diminished. *Journal of Human Hypertension* 9(2):107–111.

Hoskins, K. F., J. E. Stopfer, K. A. Calzone, S. D. Merajver, T. R. Rebbeck, J. E. Garber, and B. Weber. 1995. Assessment and Counseling for Women with a History Of Breast Cancer: A Guide for Clinicians. *Journal of the American Medical Association* 273:573–585.

Hunter, T. 1995. Fair Housing Testing—Uncovering Discriminatory Practices. *Creighton Law Review* 28:1127–1142.

Jackson, D. 1960. A Critique of the Literature on the Genetics of Schizophrenia. In *The Etiology of Schizophrenia*, ed. D. Jackson. New York: Basic.

Jackson, F. 1997. Assessing the Human Genome Project: An African American and Bioanthropological Critique. In *Plain Talk about the Human Genome Project*, ed. E. Smith and W. Sapp. Tuskegee, AL: Tuskegee University Press.

Joseph, J. 2001. Don Jackson's "A Critique of the Literature on the Genetics of Schizophrenia—A Reappraisal after 40 Years." *Genetic, Social and General Psychology Monographs* 127:27–57.

———. 2002. Twin Studies in Psychiatry and Psychology: Science or Pseudoscience? *Psychiatric Quarterly* 73:71–82.

Juengst, E. 1998. Identity and Human Diversity: Keeping Biology Straight from Culture. *American Journal of Human Genetics* 63:673–677.

Kapitany, T., K. Meszaros, E. Lenzinger, S. D. Schindler, C. Barnas, K. Fuchs, W. Sieghart, H. N. Aschauer, and S. Kasper. 1998. Genetic Polymorphisms for Drug Metabolism (CYPD6) and Tardive Dyskinesia in Schizophrenia. *Schizophrenia Research* 32:101–106.

Kato, C., et al. 2002. Molecular Genetic Studies of Schizophrenia: Challenges and Insights. Review Article. *Neuroscience Research* 43:295–304.

Kaufman, J., and S. Hall. 2003. The Slavery Hypertension Hypothesis: Dissemination and Appeal of a Modern Race Theory. *Epidemiology and Society* 14:111–118.

Keller, E. F. 1995. *Refiguring Life: Metaphors of Twentieth-Century Biology*. New York: Columbia University Press.

Khoury, M. J., and R. Thornburg. 2001. Will Genetics Revolutionize Medicine? 2 January. Available online at geneletter.com/01–02–01/features/medicine.html.

Khoury, M. J., and Q. Yang. 1998. The Future of Genetic Studies of Complex Human Diseases: An Epidemiologic Perspective. *Epidemiology* 9:350–354. Available online at www.cdc.gov/genetics/info/reports/research/future2.htm.

King, G., R. Keohane, and S. Verba. 1994. *Designing Social Inquiry: Scientific Inference in Qualitative Research*. Princeton, NJ: Princeton University Press.

Kneese, A., and W. Schulze. 1977. Environment, Health, and Economics—The Case of Cancer. *American Economic Review* 67:326–332.

Knoppers, B. M., M. Hirtle, and S. Lormeau. 1996. Ethical Issues in International Collaborative Research on the Human Genome: HGP and the HGDP. *Genomics* 34:272–282.

Krieger, N. 1990. Racial and Gender Discrimination: Risk Factors for High Blood Pressure? *Social Science Medicine* 30:1273–1281.

Krieger, N., and S. Sidney. 1996. Racial Discrimination and Blood Pressure: The CARDIA Study of Young Black and White Adults. *American Journal of Public Health* 86:1370–1378.

Lander, E. 1992. DNA Fingerprinting: Science, Law, and the Ultimate Identifier. In *The Code of Codes: Scientific and Social Issues in the Human Genome Project*, ed. D. Kevles and L. Hood. Cambridge: Harvard University Press.

LaVeist, T. 1993. Segregation, Poverty and Empowerment: Health Consequences for African Americans. *Milbank Quarterly* 71:41–64.

Lee, S. S-J., J. Mountain, and B. A. Koenig. 2001. The Meanings of Race in the New Genomics: Implications for Health Disparities Research. *Yale Journal of Health Policy, Law, and Ethics* 1:33–75.

Locke, J. 1960 [1689]. *Two Treatises of Government*. Cambridge: Cambridge University Press.

Luz, C. 1999. Socioeconomic Factors and Asthma Hospitalization Rates in New York City. *Journal of Asthma* 36:343–350.

Madsen, D. 1985. A Biochemical Property Relating to Power Seeking in Humans. *American Political Science Review* 79:448–457.

———. 1986. Power Seekers Are Different: Further Biochemical Evidence (research note). *American Political Science Review* 80:261–270.

Malone, K., J. Daling, J. Thompson, C. O'Brien, L. Francisco, and E. Ostrander. 1998. BRCA1 Mutations and Breast Cancer in the General Population: Analyses in Women before Age 35 Years and in Women before Age 45 Years with First-Degree Family History. *Journal of the American Medical Association* 279:922–929.

Mao, X. 1998. Chinese Ethicists' Views of Ethical Issues in Genetic Testing and

Screening: Evidence of Eugenics in China. *American Journal of Human Genetics* 63:688–695.

Marshall, E. 1997. Playing "Chicken" over Gene Markers. *Science* 278:2096.

———. 1998. DNA Studies Challenge the Meaning of Race. *Science* 282:654.

———. 1999. A High Stakes Gamble on Genome Sequencing. *Science* 284:1906.

Massey, D. S., and N. A. Denton. 1993. *American Apartheid: Segregation and the Making of the Underclass.* Cambridge: Harvard University Press.

Mayr, E. 1942. *Systematics and the Origin of Species.* New York: Columbia University Press.

McCreddie, M. R. E., et al. 1998. Breast Cancer in Australian Women under the Age of 40. *Cancer Cause Control* 9:189–198.

Micklos, D., and E. Carlson. 2000. Engineering American Society: The Lesson of Eugenics. *Nature Reviews* 1:153–158.

Molotsky, I. 1999. New Dawn for Flag That Was Still There. *New York Times*, 16 May.

Moshlehi, R., W. Chu, B. Karlan, D. Fishman, H. Risch, A. Fields, D. Smotkin, Y. Ben-David, J. Rosenblatt, D. Russo, P. Schwartz, N. Tung, E. Warner, B. Rosen, J. Friedman, J. Brunet, and S. Narod. 2000. BRCA1 and BRCA2 Mutation Analysis of 208 Ashkenazi Jewish Women with Ovarian Cancer. *American Journal of Human Genetics* 66:1259–1272.

Murray, R. F. Jr. 1991. Skin Color and Hypertension: Genetics or Environment? *Journal of the American Medical Association* 265:639–640.

Murray, T. 1997. Genetic Discrimination in Health Insurance and Why It Is Wrong. In *Plain Talk about the Human Genome Project*, ed. E. Smith and W. Sapp. Tuskegee, AL: Tuskegee University Press.

Nathanson, C. 1999. Social Movements as Catalysts for Policy Change. *Journal of Health, Policy and Law* 24:421–488.

Newman, B. 2002. Personal communication (e-mail), 21 January.

Newman, B., M. Austin, M. Lee, and M. King. 1988. Inheritance of Human Breast Cancer: Evidence for Autosomal Dominant Transmissions in High-Risk Families. *Proceedings of the National Academy of Sciences* 85:3044–3048.

Newman, B., H. Mu, L. Butler, R. Milikan, P. Moorman, and M. King. 1998. Frequency of Breast Cancer Attributable to BRCA1 in a Population-Based Series of American Women. *Journal of the American Medical Association* 279:915.

Noah, B. 1998. Racial Disparities in the Delivery of Health Care. *San Diego Law Review* 35:135–177.

Noronha, P. A. 1979. Sickle Cell Anemia in Two White American Children: Essential Laboratory Criteria for Diagnosis. *Pediatrics* 63:242–246.

Oddoux, C., J. P. Struewing, C. M. Clayton, S. Neuhausen, L. C. Brody, M. Kaback, B. Haas, L. Norton, P. Borgen, S. Jhanwar, D. Goldgar, H. Ostrer, and K. Offit. 1996. The Carrier Frequency of the BRCA2 6174delT Mutation among Ashkenazi Jewish Individuals Is Approximately 1%. *Nature Genetics* 14:188–190.

Oliver, M., and T. Shapiro. 1995. *Black Wealth/White Wealth: A New Perspective on Racial Inequality.* New York: Routledge.

Pennisi, E. 1997. NRC OKs Long-Delayed Survey of Human Genome Diversity. *Science* 278:568.

Peto, J., N. Collins, S. Barfoot, S. Seal, W. Warren, N. Rahman, D. F. Easton, C. Evans, J. Deacon, and M. R. Stratton. 1999. Prevalence of BRCA1 and BRCA2 Gene Mutations in Patients with Early-onset Breast Cancer. *Journal of the National Cancer Institute* 91:943–949.

Phillips, K. A., D. L. Veenstra, E. Oren, J. K. Lee, and W. Sadee. 2001. Potential Role of Pharmacogenomics in Reducing Adverse Drug Reactions (review article). *Journal of the American Medical Association* 286:2270–2279.

Reynolds, S. 1984. *Kingdoms and Communities in Western Europe: 900–1300*. Oxford: Clarendon.

Risch, N., E. Burchard, E. Ziv, and H. Tang. 2002. Categorization of Humans in Biomedical Research: Genes, Race and Disease." *Genome Biology* 3(7):2007.1–2007.12.

Roche, P., L. Glantz, and G. Annas. 1997. The Genetic Privacy Act: A Proposal for National Legislation. In *Plain Talk about the Human Genome Project*, ed. E. Smith and W. Sapp. Tuskegee, AL: Tuskegee University Press.

Rosenthal, T., E. Grossman, A. Knecht, and U. Goldbourt. 1990. Levels and Correlates of Blood Pressure in Recent and Earlier Ethiopian Immigrants to Israel. *Journal of Human Hypertension* 4:425–430.

Sadee, W. 1999. Pharmacogenomics (interview by Clare Thompson). *British Journal of Medicine* 319:1–4.

Sarkar, S. 1998. *Genetics and Reductionism*. Cambridge: Cambridge University Press.

Slattery, M. L., and R. Kerber. 1993. A Comprehensive Evaluation of Family History and Breast Cancer Risk: The Utah Population Database. *Journal of the American Medical Association* 270:1563–1568.

Smith, E., and W. Sapp, eds. 1997. *Plain Talk about the Human Genome Project*. Tuskegee, AL: Tuskegee University Press.

Stevens, J. 1999. *Reproducing the State*. Princeton, NJ: Princeton University Press.

———. 2002. Symbolic Matter: DNA and Other Linguistic Stuff. *Social Text* 20:106–140.

———. Forthcoming. Methods of Adoption. In *The View from Home: Philosophical and Feminist Issues in Adoption*, ed. S. Haslanger and C. Witt.

Stoneking, M. 1999. Comments at Human Evolution Meeting, Cold Spring Harbor Laboratory, Cold Spring, NY, 21–25 April.

Strachan, T., and A. P. Read. 1999. Genetic Mapping of Mendelian Characteristics. In *Human Molecular Genetics*, ed. T. Strachan and A. P. Read. Vol. 2. Oxford: BIOS Scientific.

Struewing, J., D. Abeliovich, T. Peretz, N. Avishai, M. M. Kaback, F. S. Collins, and L. C. Brody. 1995. The Carrier Frequency of the BRCA1 185delAG Mutation Is Approximately 1 Percent in Ashkenazi Jewish Individuals. *Nature Genetics* 11:198–200.

Struewing, J., P. Hartge, S. Wacholder, S. M. Baker, M. Berlin, M. McAdams, and M. M. Timmerman. 1997. The Risk of Cancer Associated with Specific Mutations of BRCA1 and BRCA2 among Ashkenazi Jews. *New England Journal of Medicine* 336:1401–1408.

Thomas, C., A. Ehrhardt, and M. Kay. 2003. Problems and Progress with the Use of Viral Vectors for Gene Therapy. *Nature Review Genetics* 415:346-58.

University of Pittsburgh Medical Center. 1999. University of Pittsburgh Medical Center Performs First *in Vivo* Gene Therapy for Hemophilia A. News release available online at www.upmc.edu/NewsBureau/science/hemophilia.htm.

U.S. Census Bureau. 1999. Revisions to the Standards for the Classification of Federal Data on Race and Ethnicity. 1 April. Available online through the Census Bureau Web site at www.census.gov/population/www/socdemo/race/Ombdir15.html.

———. 2000. "SIPPS Data Source Description" accompanying Table POP5.B: Percentage of Children under Age 18 Living in Various Family Arrangements. Available online at www.childstats.gov/ac2000/poptxt.asp; www.childstats.gov/ac2000/surveys.asp#sipp; and www.childstats.gov/ac2000/poptxt.asp.

U.S. Centers for Disease Control (CDC). 1997. *National Health Interview Survey*. Washington, DC: U.S. Government Printing Office.

U.S. Department of Energy (DOE). 1998. Human Genome News, January. Published online at www.ornl.gov/TechResources/Human_Genome/publicat/hgn/v9n1/20ednote.html.

———. 2000. Long-term Stewardship Study. Available online at www.em.doe.gov/ftplink/lts/ltsdraft.pdf.

U.S. Food and Drug Administration (FDA). 2001. FDA Approves Gleevec for Leukemia Treatment. FDA news release available online at www.fda.gov/bbs/topics/NEWS/2001/NEW00759.html.

U.S. National Academy of Sciences (NAS). 1999. Toward Environmental Justice: Research, Education, and Health Policy Needs. Available through the National Academies Press Web site at www.nap.edu/openbook/0309064074/html/13.html.

———. 2000. Clearing the Air: Asthma and Indoor Air Exposures. Available through the National Academies Press Web site at www.nap.edu/openbook/0309064961/html/19.html.

U.S. National Cancer Institute (NCI). 2000. Questions and Answers for Estimating Cancer Risk in Ashkenazi Jews: Cancer Facts. CancerNet Fact Sheet. Available online at cancernet.nci.nih.gov.

U.S. National Heart, Lung, and Blood Institute (NHLBI). 1997. Asthma Genes Linked to Regions Unique to Different Racial and Ethnic Groups, NHLBI Study Shows. NIH press release available online at www.nih.gov/news/pr/mar97.

U.S. National Human Genomics Research Institute (NHGRI). 1996. Prostate Cancer Gene Location Found on Chromosome 1. Available online at www.nhgri.nih.gov/DIR/LCG/PROSTATE/pros_media_rel.html.

———. 1999. Studies of the Ethical, Legal, and Social Implications of Research into Human Genetic Variation. 29 April. Available online at www.nhgri.nih.gov/Grant_info/Funding/RFA-HG-99-002.html.

U.S. National Institute for Allergies and Infectious Diseases (NIAID). 2000. International Team Accelerates Investigation of Immune-Related Genes. NIAID press release available (as of 16 May 2003) online at www.niaid.nih.gov/newsroom/releases/ihwg.htm.

U.S. National Institute of Arthritis and Muskuloskeletal and Skin Disease (NIAMS). 1998. An NIH-Funded Native American Study Finds Gene Site Associated with

Scleroderma. NIH press release available online at www.niams.nih.gov/ne/press/1998/10.29.

U.S. National Institutes of Health. 1997a. NIH Leads International Group That Identifies Gene for Familial Mediterranean Fever: Mutations Date Back to Biblical Times. Available online at www.nih.gov/news/pr/aug97/niams-21.htm.

———. 1997b. Researchers Locate Lupus Gene on Chromosome 1. Available online at www.nih.gov/news/pr/feb97/niams-19.htm.

U.S. National Research Council (NRC) Committee on Human Genome Diversity. 1997. *Evaluating Human Genetic Diversity*. Washington, DC: National Academy Press.

Wade, N. 2000. Whose DNA Is It? In a Way, Nobody's. *New York Times*, 27 June, F2.

———. 2002. Scientist Reveals Secret of Genome: It's His. *New York Times*, 27 April, A1.

Watson, J. D. 1987. *Molecular Biology of the Gene*. 4th ed. 2 vols. Menlo Park, CA: Benjamin/Cummings.

Whittemore, A., G. Gong, and J. Itnyre. 1996. Prevalence and Contributions of BRCA1 Mutations in Breast Cancer and Ovarian Cancer: Results from Three U.S. Population-Based Case-Control Studies of Ovarian Cancer. *American Journal of Human Genetics* 60:496–504.

Williams, D. R., Y. Yu, J. S. Jackson, and N. B. Anderson, 1997. Racial Differences in Physical and Mental Health. *Journal of Health Psychology* 2:335–351.

Wilson, J., M. Weale, A. Smith, F. Gratix, B. Fletcher, M. G. Thomas, N. Bradman, and D. B. Goldstein. 2001. Population Genetic Structure of Variable Drug Response. *Nature Genetics* 29:265–269.

Wilson, T. W., and C. E. Grim. 1991. Biohistory of Slavery and Blood Pressure Differences in Blacks Today: A Hypothesis. *Hypertension* 17(supp. 1):122–128.

Wittgenstein, L. 1968. *Philosophical Investigations*. 3d ed. New York: Macmillan.

Xu, X., and U. Arnason. 1996. The Mitochondrial DNA Molecule of Sumatran and a Molecular Proposal for Two (Bornean and Sumatran) Species of Orangutan. *Journal of Molecular Evolution* 43:431–437.

Zilinskas, R. 1997. Global Perspectives on the Human Genome Project. In *Plain Talk about the Human Genome Project*, ed. E. Smith and W. Sapp. Tuskegee, AL: Tuskegee University Press.