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Race, Genetic Variation, and the Haplotype Mapping Project

Pilar N. Ossorio*

We have heard an overview of the Haplotype Mapping Project ("HapMap Project") and about the Project’s sampling strategy. During its first phase, the Project will collect and analyze samples from 270 people. 1 One group from whom samples will be collected is the Yoruba people living in Nigeria. The Yoruba are members of a tribal and language group. The Project will also collect samples from Han people in China. The Han are one of fifty-four ethnic groups recognized by the Chinese government. 2 Additional samples from Chinese immigrants in Denver, Colorado (U.S.), may also be included. Another set of samples will be collected from Japanese people who live in and around Tokyo. Researchers believe that individuals from many regions of Japan will be included in this sampling. Finally, researchers will study samples collected from Mormons who live in Utah (U.S.), and whose biological samples were already in a repository at the Centre d’Etude du Polymorphisme Humain (CEPH). 3

Organizers plan a second phase for the Project, during which they intend to sample several additional populations. These will likely include: a group from Kenya; another as yet undefined African group; Mexican-Americans in California; Asian-Indians in Texas (an immigrant community primarily from Gujarat, India); African-Americans in Oakland, California; Italians, probably in Italy; Finnish people, probably in Finland; and perhaps Moroccans.

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3. The Centre d'Etude du Polymorphisme Humain (CEPH) is a research laboratory created in 1984 by Professor Jean Dausset (Nobel Prize, medicine and physiology, 1980). This laboratory constructs maps of the human genome. The original idea of Professor Dausset was to provide the scientific community with resources for the human genome mapping. See Fondation Jean Dausset, More About the Fondation Jean Dausset - CEPH, http://www.cephb.fr/ceph_presentation.html.
Work with some of these groups, such as Mexican-Americans, is already underway.

From the description above it should be obvious that the HapMap sampling does not draw from commensurate types of groups. Among other things, the groups differ with respect to the likely degree of shared ancestry within each one. They differ in the extent to which members share a cultural affiliation or language. Han people, for instance, may speak any one of several languages, including Cantonese and Mandarin, languages which are linguistically farther apart than Spanish and Italian. The initial HapMap sampling was designed to study patterns of genetic variation among people from three well-separated points on what most scientists believe is a geographic gradient of human genetic variation around the world. Secondarily, the sampling was done by convenience—it reflects the availability of scientists who were eager to participate and technically capable of conducting HapMap research, the existence of governments or other parties willing to fund the research, and the prior existence of samples for which new consent could be obtained without undue burden on participants or researchers.

When introduced to the HapMap Project, many people hear Yoruba, Han, Japanese, and Utah Mormons and think Black, Asian, and White. They say, “You are sampling three races.” Some ask, “Where are the Native Americans?” In early discussions, project organizers and advisors suspected that we would have to contend with people’s inclinations to over-generalize, for instance, to view one sample of a single tribal group in Nigeria as representing an entire race of black people. Nevertheless, the degree to which the HapMap sampling strategy resonates with folk notions of race, and perhaps reinforces these notions or enhances their salience and significance, has surprised me. In a different world, the Project might have had the time and resources to begin with samples from groups that did not fit neatly into racial categories, such as people from Syria, Saudi Arabia, Sri Lanka, some group or groups from India, some group or groups from Indonesia or the Philippians, several groups of Africans, and groups of American Indians/Alaskan Natives.

An alternative sampling approach would, however, have opened up different fronts for criticism. Sampling from groups that do not fit neatly into racial categories could have left the Project open to the charge that researchers were spending large sums of money to create maps that might not be the most useful for the greatest numbers of people in the world. Furthermore,
sampling that included indigenous people, or people from smaller, less-industrialized countries, could have been viewed as a pernicious attempt to transfer biological resources from the have-less to the have-mores, an attempt by the wealthier nations and scientists to plunder from the less-wealthy.

Questions about sample descriptors are intimately tied to sample collection. In community engagements associated with the HapMap Project, investigators asked potential participants, "How would you like to be described? Are there racial or ethnic descriptors that researchers should use or avoid? What geographic descriptors would be best? What additional information should be included to describe you and the specimens derived from you?" Sample descriptors are both an ethical and technical scientific issue. Descriptors are pertinent to the meaning of any data generated—who do the samples represent, what type of representation does this sampling constitute, what generalizations and conclusions can legitimately be drawn from the data generated using these samples? The choice of descriptors may also influence people's tendency to view the sampled groups in racial terms.

So, sampling by race is not what most HapMap Project organizers thought they were doing, but that is how the Project is often perceived. Some pundits wonder whether the HapMap will find genetic categories that coincide with folk notions of race, whether the Project will reinforce some people's mistaken belief that there are separate, distinct, biological categories of humans. Will the Project alter or disrupt personal identities? Will it change prevailing, popular concepts of race? These questions can be situated within a decade-long debate that continues to rage in the biomedical sciences literature, about whether or how race should be used as a variable. Numerous articles in major journals attempt to elucidate the proper use of race in biomedical science and medicine, or attempt to clarify the meaning of data in which race was used as a variable.4 This scientific dispute is not primarily

about the quality or validity of the data; rather, it is about the interpretation and meaning of the data. What kinds of knowledge should or could existing data produce?

Unfortunately, the "race in science" question is often formulated as a "binary trap," an argument framed so that each disputant must take one of two mutually exclusive positions—that race is always an important and useful variable when collecting and analyzing data on humans, or that race is never a useful or appropriate variable. People line up behind one of these categorical positions and battle it out with opponents.

There are several important and unexamined assumptions behind the race-in-science debate. Perhaps the most important assumption is that the reality or existence of race can be adjudicated using genetic data—we will find "The Answer" to questions of whether human races exist by sampling more populations and looking at more loci. A second assumption is that, if we do not find an answer to the race question in genetic data, then we should not be using race as a demographic variable in biomedical research or health care. If race is not "genetically real" then it has no meaning and no place in research or medicine. I would like to challenge both of these assumptions.

Prior to discussing the assumptions, however, it is useful to ask what most people, including most scientists, mean when they use the term "race." Why would people think that we could find race in our genes or in collections of haplotypes? There is a large body of scholarship detailing people's different conceptions of race, and the ways in which race is deployed to achieve certain goals in

society. In the U.S., we all grow up with folk notions of race, according to which races are distinct categories of people. These racial categories are treated as fixed and stable, reflective of essential, intrinsic, pervasive properties of persons. Race-based divisions in society are believed to reflect natural divisions. When we perceive race, we are perceiving an asocial feature of reality. Although attempts to define race or delineate racial groups typically flounder on the shoals of over- or under-inclusivity, like pornography, most people "know it when they see it." Part of the reasoning behind the race-in-science debate is that if we view race as an asocial quality of the world, of our biological selves, then we should be able to measure, characterize, and delineate it by using the proper scientific tools for studying human biology, the tools of biomedical science.

Folk notions of race developed prior to modern molecular genetics. Nonetheless, molecular genetics is easily incorporated into these folk notions. If race is an intrinsic, immutable, pervasive, and natural property of persons, then what is more immutable, essential, and natural than his or her genome? What is more likely to be a root cause of these perceived biological differences than genes? The coalescing of beliefs about race with beliefs about the power of genetic explanations is probably one reason that issues of race are particularly prominent in debates about genetics research. Another reason, of course, is that the field of human genetics grew out of the pernicious field of eugenics.

Returning to the assumptions underlying the race-in-science controversy, I will argue that the existence or nature of human races is not something we can find or determine using genetic


tools. We have not found and will not find race in our genomes or as a genetic reality, particularly if what we mean by the commonly used phrase "genetic reality" is that races consist of distinct genetic categories of people. No clear or consistent pattern of genetic variation or set of alleles separates humans into four or five groups and only those groups; no major genetic discontinuities separate people into races.

What have scientists discovered so far about human genetic variation and racial groups? They have discovered that we are a very young species, far less genetically diverse than most other species that have been studied. For example, humans are approximately four times less genetically diverse than a single species of chimpanzee. Modern human beings probably arose in Africa, and a small subset of humans migrated out of Africa, in one or more waves, approximately thirty to fifty thousand years ago. Because we are a young species that expanded rapidly to populate the earth, we have not had time to develop much genetic heterogeneity. Nor has any human population experienced the requisite degree of reproductive isolation to separate into a genetically distinct sub-species.

Studies have not identified any "pure" races, and no genetic variants are found in all people of one race but no people of another. Approximately eighty-five percent of all human genetic variation is found within any human population or group—the vast majority of human genetic variation does not distinguish between groups, even when the groups being compared are composed by


Seven to fifteen percent of the human genetic markers vary between two groups from the same continent. Only four to five percent of genetic variation occurs primarily between groups from different continents. This between-continent variation represents a tiny fraction of our entire genomes (5% of 0.1%). Geneticists can use statistical models that analyze data from hundreds of genetic markers per person to cluster people according to degrees of relatedness or shared ancestry. Recently, it has become popular to cluster individuals according to their ancestors’ continents of origin. Many people think of contemporary racial groups as representing ancestral populations that resided for long periods on different continents, and one could view the ability to construct continental clusters as a finding of race in our genomes. However, different and equally valid statistical manipulations of the same data sets can produce clusters in which people from different continents are grouped together, or can separate people from one continent into different clusters. There is nothing intrinsically more important about statistically constructed genetic groupings that map onto continents. That tiny bit of the genome that varies between continents is not more important in understanding human health and illness, human evolution, or individual and collective identity, than that vastly greater portion of the genetic variation that occurs between two individuals within any group. Genetic differences between and among people do exist, but this variation does not sort the species discretely and unambiguously into a small number of biological categories consistent with folk notions of race. There are many different ways of finding genetic similarity and difference among individuals and groups.

The weight of existing evidence makes it extremely unlikely that additional findings will change our current understandings of human genetic variation and human races, no matter how many

12. Marks, supra note 9.
13. Id.
15. See, e.g., Rosenberg et al., supra note 11; Tang et al., supra note 14; David Serre & Svante Paabo, Evidence for Gradients of Human Genetic Diversity Within and Among Continents, Genome Research, Nov. 2004, at 1679.
more sequences or haplotyped genomes scientists generate. The genetic data, like anthropological data from an earlier era, do not support folk notions of races as discrete, fundamentally, and pervasively different, natural groups of humans. Does this mean that race is not real? No! Race is real even if it is not a genetic construct.\(^{16}\) Marriage, childhood, and public school are just a few of the institutions, relations, or status positions that are real but not genetically defined or genetically distinct entities. In considering the primary assumption of the race-in-science debate, we must consider the possibility that races exist and can be measured and evaluated with the tools of history, sociology, law, geography, and psychology, even if they cannot be delimited with the tools of genetics.

If folk notions of race are not supported by genetic research, then what is race? Contemporary race theorists are not unified in their views of the meaning and nature of race, but most would likely agree that race involves the mapping of meaning onto people’s physical and behavioral traits.\(^{17}\) Relevant physical traits include hair color and texture, eye shape and color, and of course, skin color. In addition, racial meanings are attributed to ancestry, language(s) spoken, accents, religion, nationality or national origin, and political philosophies. Race is social and relational, we create it through our interactions. Thus, it is fluid and contingent on historical and geographical circumstances. A person may be black in one census and white or “colored” in the next, may be white on her birth certificate and black on her death certificate, may be white in the Bahamas but black in the U.S.

Despite its fluid and contingent nature, race is one of the most pervasive and deeply entrenched social stratifying practices in U.S. society—as we create race, we create racial hierarchies and we

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16. Care should be taken, however, not to push this insight [that race is not a set of biological categories but a social construct] to its constructionist extreme and claim that race is merely a social contrivance and therefore not “real”... if things are defined as real, they are real in their consequences. The concepts of race and ethnicity are social realities because they are deeply rooted in the consciousness of individuals and groups, and because they are firmly fixed in our society’s institutional life.

America Becoming, supra note 5, at 3.

17. See, e.g., Omi & Winnant, supra note 5; Statement, supra note 5; Smedley, supra note 5; Lopez, The Social Construction, supra note 5; Ossorio & Duster, supra note 4.
instantiate these hierarchies in our institutions, our geography, and perhaps, our biology. Through our practices, including scientific and medical ones, we concretize and materialize racial ideologies. Some racially-stratified features of U.S. society that may influence health include: access to health care; access to health insurance; residential segregation and the quality of housing; employment opportunities; exposures to toxins; access to affordable, fresh, nutritious food; and access to safe spaces for physical exercise. Even if race is not genetic, many factors that correlate with race or that come into existence as a function of race, can have impacts on drug responses, on disease progression, and on immune system functioning.

The discussion above helps explain why I believe that there are legitimate reasons to use race as a variable in answering some research questions or in making some medical decisions. Race variables may generate data that point towards new medical interventions or cures, or towards better understandings of the causes of health problems. At times, race may be proxy for some cause that we cannot yet measure or have not figured out that we should measure. Race variables may also be useful in assessing the effects of racism and institutional inequalities in access to health care or other health-promoting goods in society. Finally, race variables may capture aspects of a person’s cumulative life experience, effects that are difficult or impossible to disaggregate into separate variables; the same could be true for gender and class variables. Viewed this way, race could be understood as a biological consequence, not a genetic cause. It is something that may be measurable now, and have health effects, but it is neither immutable nor essential. Race as a consequence or effect is not genetic destiny; rather, it is a contingent result of living in a racially stratified society.

Here, I want to emphasize that not all biological variation is caused by genetic variation. Too often, commentators discuss genetic variation and biological variation as though these are interchangeable concepts; they are not. If we compare two individuals or two groups of organisms, they might differ in a biological characteristic such as height or disease state even if they possess the same relevant alleles or genetic variants. Biological variation has many causes, including differing diets, differing

exposures to toxins, and different access to health care to name just a few. Genetics is only one of many determinants of biological variation. Difficult as it is to believe in this geneticized era, genes are probably the least important factor in creating the biological variation that we describe as racial health disparities.

Returning to the race-in-science controversy, I would argue that race may be a legitimate and useful variable in biomedical research, even if folk notions of race are incorrect. On the other hand, race will not always be the most useful or informative taxonomy for answering biomedical research questions or for guiding health care decisions. There may be better ways of allocating people into groups, of lumping or splitting them when we need to categorize to understand or intervene in a phenomenon. Race ought not be used as a proxy for other, measurable variables. Race ought not be used simply out of habit or convenience.

From its inception, the concept of race has involved social stratification and social hierarchies—some racial groups have always been viewed as more beautiful, more intelligent, more civilized, more law-abiding, or perfected than others. After reflecting on this legacy, some scholars object to any use of race in science because they believe it is terribly difficult, if not impossible, to disentangle racist beliefs from any use of racial categories. While the danger of inadvertently importing racist assumptions is real, I disagree with the proposition that it should entirely preclude the use of race in biomedical science. A better approach is to use race in a far more educated, reflective, and cautious manner. It would be difficult to make sense of, or even describe, this very racialized society without resorting to some concept of race.

Even when inter-racial comparisons are useful and legitimate, nobody should forget that such comparisons reflect statistical, mean differences between groups. They do not provide information about the outcome for any particular individual. Dr. Kidd emphasized this point during his presentation, but it cannot


be repeated often enough. For most research observations, the within-racial-group variation in treatment outcome (or other dependant variable) is greater than the between-group variation. Thus, even if the white-subject sample in a particular study responds less-well, on average, to drug X than does the Asian-subject sample, it is true that some white people will respond to drug X better than some Asian people.

Unfortunately, both medical experts and non-medical members of our society have a tendency to transform statistical claims into categorical ones. Reports of a mean difference between racial or ethnic groups in response to a drug become common knowledge, and soon “we all know that black people do not respond to drug X” or “Asians are particularly sensitive to drug Y.” Such common knowledge about racial, ethnic, or national groups is often wrong, or at least misleading, and should always be viewed with suspicion. Similarly, even when a particular gene variant or a particular haplotype is reported as being more common than average in people of one ethnic group, race, or nationality, this does not mean that all people of that group have the reported variant or haplotype.

Returning to a general discussion of the race-in-science controversy, we should not view the use of race as an all or nothing proposition. Rather than falling into the binary trap and then chewing off our own—or each other’s—legs to get out, we should take a case-by-case approach and ask what work a racial taxonomy is doing in any particular instance. Scientists and physicians should justify their use of racial taxonomies. Likewise, colleagues and critics should always examine the assumptions underlying particular uses of race in science. In cases such as the HapMap Project, scientists should take care not to generalize their conclusions inappropriately. Scientists and others associated with the Project should note the error of imagining that a few hundred people could ever represent the genetic diversity of the millions or hundreds of millions of people included in each of the four or five races.

One contributor to unreflective uses of race variables in biomedical research is the federal law and guidance that requires many federally-funded studies to be designed using the Office of Management and Budget’s (“OMB’s”) categories for race and
ethnicity.\textsuperscript{21} In some cases, the law requires researchers to search for and report inter-racial and inter-ethnic differences.\textsuperscript{22} We find racial differences because we construct our research to look for them, and in finding them we reinforce our beliefs that people of different racial groups are naturally and inevitably different from each other. We almost never design experiments that could elucidate the causes of these differences,\textsuperscript{23} perhaps because the causes are presumed to be genetic. The law and guidance documents mandating the search for racial and ethnic differences were undoubtedly well-motivated, but they may cause the scientific community to focus on race and racial differences to the exclusion of other factors that have greater power to explain health and medical outcomes.

The ethical questions raised by the use of race variables must be considered early and often in designing any biomedical research project. There are many concerns about justice that should receive heightened attention in the context of a large-scale government effort such as the HapMap Project. Dr. Clayton introduced some of these ethical concerns in her presentation. Ethical concerns may be dismissed with comments such as, “Oh, you are talking about potential harms, but they are distant and unlikely to eventuate,” or “The harm is speculative—it has never happened before.” Those statements are incorrect when applied to the use of racial categories in research and medicine. The U.S. has a reprehensible history of biomedical research on human participants in which people of color have been abused; these abuses were sometimes incorporated directly into the research design.\textsuperscript{24} The U.S. has a history of using racist science to justify discriminatory law and

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\item Cooper & Kaufman, \textit{supra} note 4.
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policies. This legacy should encourage particular vigilance by scientists and by those who regulate and oversee research.

Patricia King, a law professor at Georgetown and one of my heroes, has used the phrase "the dilemma of difference" in pointing out that we must negotiate a treacherous terrain when conducting science, or regulating it, with the intention of improving the lives of people of color. On the one hand, our biomedical research may need to take race and ethnicity into account if it aims to identify and diminish racial and ethnic health disparities. On the other hand, simply finding and studying differences can reinforce those norms and institutions that create health disparities in the first place. The study of racial differences must be undertaken with the utmost thought and care, or we chance reinforcing antiquated racist notions and, in the end, we may repeat history by building scientific support for discriminatory policies, we may exacerbate unjust inequalities.

Some people fear that the HapMap Project, and other studies of human genetic variation, will produce data that will be used to support unjust policies. The Project could have pernicious effects merely by studying genetic variation in human subject groups that evoke racial categories, regardless of the data generated. In my opinion, the chances of perpetuating racial injustice increase if biomedical researchers cannot communicate the complexities of human genetic variation, and if they lack sophisticated theories of race to guide them in project design and analysis. I am confident that, in the long run, the study of human genetic variation will reveal the rich tapestry of within-race variation—data that can undermine simple, geneticized folk notions of race. I am also confident that the many non-genetic sources of health and illness will someday receive a much larger share of scientific attention, a development that would decouple simple, genetic notions of race from views about health disparities and policies to improve health. I am less confident that we will avoid harm, or produce benefit, in the short run.
