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Dealing with the Realities of Race and Ethnicity: A Bioethics-Centered Argument in Favor of Race-Based Genetics Research

Michael J. Malinowski
Louisiana State University Law Center, michael.malinowski@law.lsu.edu

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[*] Ernest R. and Iris M. Eldred Professor of Law, Paul M. Herbert Law Center, Louisiana State University. JD Yale Law School; BA, *summa cum laude*, Tufts University. This article was selected by international, interdisciplinary peer review for presentation at "One Origin, One Race, One Earth: Genetics, Human Rights and the Next Phase of Human Evolution," which was hosted by the University of Calgary on November 15-17, 2007. My sincere appreciation to event co-chairs Brian Seaman and Rose Geransar, and to all whose interactions greatly enriched this manuscript. The article also has benefited from participation in several additional events and presentations, most notably those given at a meeting hosted by Academia Sinica to launch the Taiwan Biobank, held in Taipei, Taiwan, August 2007, and the 21st Century Trust forum on genomics held at the Wellcome Trust's Sanger Institute, Cambridge, England, in August 2006. The present version will be discussed at "Ancestry in Health and Medicine Workshop: Expanding the Debate," a roundtable event to be held in Toronto April 8-9, 2008. My appreciation to the organizers of and participants in these events, and to colleagues Carl Coleman, Donna Gitter, Jonathan Kahn, and David Winickoff, who shared their expertise in the field and, as always, were generous with their time. Their contributions enriched this effort immensely. I also would like to thank Jim Figura and Damon Bowe for their excellent research assistance and thoughtful editorial input.

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Oct. 14, 2007

[Dr. James Watson, co-discoverer of the structure of DNA,] says that he is "inherently gloomy about the prospect of Africa" because "all our social policies are based on the fact that their intelligence is the same as ours—whereas all the testing says not really', and I know that this "hot potato" is going to be difficult to address. His hope is that everyone is equal, but he counters that "people who have to deal with black employees find this not true". He says that you should not discriminate on the basis of colour, because "there are many people of colour who are very talented, but don't promote them when they haven't succeeded at the lower level". He writes that "there is no firm reason to anticipate that the intellectual capacities of peoples geographically separated in their evolution should prove to have evolved identically. Our wanting to reserve equal powers of reason as some universal heritage of humanity will not be enough to make it so".[1]

Oct. 18, 2007

The Federation of American Scientists (FAS) is outraged by the noxious comments of Dr. James Watson that appeared in the Sunday [*London*] *Times* Magazine on October 14th. At a time when the scientific community is feeling threatened by political forces seeking to undermine its credibility it is tragic that one of the icons of modern science has cast such dishonor on the profession.

[1] Charlotte Hunt-Grubbe, *The elementary DNA of Dr. Watson,* THE SUN. TIMES, Oct. 14, 2007, at __.

The scientific enterprise is based on the promotion and proof of new ideas through evidence, however controversial, but Dr. Watson chose to use his unique stature to promote personal prejudices that are racist, vicious and unsupported by science.

While we honor the extraordinary contributions that Dr. Watson has made to science in the past, his comments show that he has lost his way. He has failed us in the worst possible way. It is a sad and revolting way to end a remarkable career.[2]

Oct. 18, 2007

Earlier this evening, the Cold Spring Harbor Laboratory Board of Trustees Decided to Suspend the Administrative Responsibilities of Chancellor James D. Watson, Ph.D., pending further deliberation by the Board.

This action follows the Board's public statement yesterday disagreeing with the comments attributed to Dr. Watson in the October 14, 2007 edition of *The Sunday Times* U.K.[3]

I. Introduction

[2] *The Federation of American Scientists Condemns the Comments of Dr. James Watson that Appeared in the Sunday Times Magazine on Oct. 14th*, *available at* http://fas.org/main/content.jsp?formAction=297&contentId=572.

[3] *Statement by Cold Spring Harbor Board of Trustees and President Bruce Stillman, Ph.D. Regarding Dr. Watson's Comments in The Sunday Times October 14, 2007*, *available at* http://www.cshl.edu/public/releases/07_statement2.html

"Race" and "ethnicity" compel reaction.[4] These concepts are social constructs,[5] and many commentators—drawing from a portfolio of disciplines that includes the natural sciences, the social sciences, medicine, and law—argue that the human population groupings they form

[4] The research, writing, and completion of this article coincides with a raw national debate over race, brought to a simmer and then beyond by a series of controversies. Race and gender charged the Democratic primary race between candidates Sen. Clinton and Sen. Obama. *See* Adam Nagourney, *Democrats Vote Reveals Deep Split Obama and Clinton Supporters Differ in Age, Race, and Gender,* INT'L HERALD TRIB., Feb. 8. 2008, at 5. During spring 2007, radio personality Don Imus was fired for racial and sexist remarks about the Rutgers University women's basketball team. *See* Dahleen Glanton, *Civil Rights Group Has Eye on Prize of Peace: Nation*, CHICAGO TRIBUNE, Aug. 3, 2007 (page nos. not available), 2007 WLNR 14904150. Soon after, charges from an alleged rape brought by an African American woman against Caucasian members of the Duke University male lacrosse team were dropped and the prosecutor himself faced charges. *See* Glanton, *Civil Rights Group*, *supra*; David Zucchino, *The Nation: Ex-Duke Players Get New Apology*, LA TIMES, July 27, 2007, at 13. Then, On September 20, the nation's attention was drawn to the small town of Jena, Louisiana, self-proclaimed to be "a nice place to call home," as more than 20,000 participated in a march led by the Reverand Jesse Jasckson and Al Sharpton. *See Black Leadership in America: Race, Justice and Jena*, ECONOMIST, Sept. 2007, at 71, 2007 WLNR 18968014 (no author identified). According to a report in the *Economist*,

> At a high school assembly on August 30th [2006], a black student asked if he could sit under a shady tree on campus where the white students usually hung out. The deputy principal said of course he could sit wherever he wanted. The next day, two nooses dangled from the tree. They were quickly removed, and the principal recommended that the three white students who hung them be expelled. But the school board let them off with a suspension, arguing that the incident was just a childish prank. . . . . On December 4th a black student named Mychal Bell jumped a white classmate from behind and knocked him out. Then he and six others kicked him as he lay on the ground. He was released in time to go out that evening, but retired home early complaining of pain. Five of the attackers were charged with attempted second-degree murder. That caused an outcry, so the charges were reduced to second-degree battery, which still carries heavy penalties. Mr. Bell was tried as an adult, though he was only 16 at the time of the attack. The prosecutor says this was because he had been arrested four times before for violent offences. He was convicted by an all-white jury. (Several blacks were summoned for jury duty, but non showed up.) . . . . But a higher court threw out his conviction and ordered that he be tried as a juvenile.

Id. (page numbers unavailable). Even before the House Judiciary Committee could hold a hearing on the "Jena Six" controversy (which took place on October 17, 2007), media reported on September 30 that a maintenance man found a noose hanging in the Hempstead, Long Island police department. *See* Joe Gould & Carrie Melago, *Noose Found Hanging in L.I. Police Station*, N.Y. DAILY NEWS, Sept 30, 2007, at 10; Dana Millbank, *Justice Denied, Sharpton Delayed*, WASH. POST, Oct. 17, 2007 (page numbers unavailable), 2007 WLNR 20337642. On October 13, a noose also was found hanging on the door of Professor Madonna Constantine, a black professor of psychology at Columbia University, and other "noose incidents" started arising across the nation. *See* Lester Holt, *Profile: In Depth; Nooses, an Old Symbol of Hate, Making Comeback*, NBC NEWS: NIGHTLY NEWS, Oct. 13, 2007 (page numbers unavailable). These incidents were two of more than forty (40) noose hanging incidents across the country during fall 2007. *See* Mark Potok, Luke Visconti, Barbara Frankel, & Nigel Holmes, *The Geography of Hate,* N.Y.TIMES, Nov. 25, 2007, at P11.

[5] *See* Pilar N. Ossorio, *About Face: Forensic Genetic Testing for Race and Visible Traits*, 34 J.L. MED. & ETHICS 277, 278-279 (2006); Statement of the American Sociological Association, The Importance of Collecting Data and Doing Social Scientific Research on Race, American Sociological Association, *available at* <http:// www.asanet.org/governance/racestmt.html> (last visited Feb. 15, 2007); A. Smedley & B. D. Smedley, *Race as Biology is Fiction, Racism as a Social Problem is Real,* 60 AMERICAN PSYCHOLOGIST 16-25 (2005). *See also infra* notes 13-19 and accompanying text.

are inconsistent with the scientific reality of human genetics.[6] The fundamental argument is that genetics groups us differently, often dramatically so, and it is scientifically and socially misguided and contrary to ample U.S. law and policy, perhaps even illegal, to approach contemporary population genetics with methodologies that embrace these constructs.[7] While the debate over race-based research has been of mixed opinion in the natural science and medical disciplines,[8] there is a discernable majority opinion among law academics that most race-based research is wrong on multiple levels.[9]

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[6] *See infra* notes 63-98 and accompanying text.

[7] *See generally id.*

[8] Contrary science positions on race-based research were juxtaposed in the November 2004 issue of *Nature Genetics*. *See* M. Bamshad, et al., *Deconstructing the Relationship Between Genetics and Race*, 5 NATURE GEN. 598-609 (2004); Francis Collins, *What We Do and Don't Know About 'Race,' 'Ethnicity,' Genetics and Health at the Dawn of the Genome Era,* 36 NATURE GEN. SUPP. S13-S15 (2004); E. J. Parra, R. A. Kittles, M. D. Shriver, *Implications of Correlation Between Skin Color and Genetic Ancestry for Biomedical Research,* 36 NAT. GENET. SUPP. S54-S60 (2004); J. L. Mountain, N. Risch, *Assessing Genetic Contributions to Phenotypic Differences Among `Racial' and `Ethnic' Groups*, 36 NAT GENET SUPP. S48-S53 (2004). *See also*, P. Sankar, Mildred K. Cho, C. M. Condit, et al., *Genetic Research and Health Disparities*. 291 JAMA 2985-9 (2004); K. R. Merikangas, N. Risch, *Genomic Priorities and Public Health*, 302 SCIENCE 599-601 (2003); E. G. Burchard, et al., *The Importance of Race and Ethnic Background in Biomedical Research and Clinical Practice*, 348 N. ENG. J. MED. 1170-71 (2003): R. S. Cooper, et al., *Race and Genomics*, 348 N. ENG. J.MED. 1166-67 (2003); N. A. Rosenberg, J. K. Pritchard, J. L. Weber, et al., *Genetic Structure of Human Populations*, 298 SCIENCE 2381-5 (2002); N. Risch, et al., *Categorization of Humans in Biomedical Research: Genes, Race and Disease*, 3 GENOME BIOLOGY 1-12 (2002): R. S. Schwartz, *Racial Profiling in Medical Research*, 344 N. ENG. J. MED. 1392-93 (2001); A. J. J. Wood, *Racial Differences in the Response to Drugs--Pointers to Genetic Differences,* 344 N. ENG. J.MED. 1393-96 (2001). The debate has intensified. *See, e.g.,* Bibbins-Domingo, K., & Fernandez, A*BiDil for Heart Failure in Black Patients: Implications of the U.S. Food and Drug Administration Approval*, 146 ANN INTERN MED 52-56 (2007); Guthery, S. L., Salisbury, B. A., Pungliya, M. S., Stephens, J. C., & Bamshad, M, The Structure of Common Genetic Variation in United States Populations, 81 AM J HUM GENET 1221-1231 (2007); Hafler, D. A., Compston, A., Sawcer, S., Lander, E. S., Daly, M. J., De Jager, P. L., et al., *Risk Alleles for Multiple Sclerosis Identified by a Genomewide Study*, 357 N ENGL J MED. 851-862 (2007); Wu, Y.-R., Chen, C.-M., Chao, C.-Y., Ro, L.-S., Lyu, R.-K., Chang, K.-H., et al., *A Nonsynonymous SNP in Human Cytosolic Sialidase in a Small Asian Population Results in Reduced Enzyme Activity: Potential Link With Severe Adverse Reactions to Oseltamivir*, 17 CELL RESEARCH 357–362 (2007); Neil Risch, *Dissecting Racial and Ethnic Differences*, 354 NEW ENG. J. MED. 408 (2006); M. Sinha, E. K. Larkin, R. C. Elston, S. Redline, *Self-Reported Race and Genetic Admixture*, 354 N ENGL J MED 421-2 (2006); Daar, A. S., & Singer, P. A, *Pharmacogenetics and Geographical Ancestry: Implications for Drug Development and Global Health*, 6 NAT REV GENET. 241-246 (2005); H. Tang, T. Quertermous, B. Rodriguez, et al., *Genetic Structure, Self-Identified Raceethnicity, and Confounding in Case-Control Association Studies*, 76 AM J HUM GEN. 268-75 (2005); A. E. Shields, M. Fortun, E. M. Hammonds, et al., *The Use of Race Variables in Genetic Studies of Complex Traits and the Goal of Reducing Health Disparities: a Transdisciplinary Perspective*, 60 AM PSYCHOLOGY 77-103 (2005). Opponents argue that race lacks any reliable biological basis and, for genetics research to contribute meaningfully to science and medicine, links between genes and disease should be made directly—for example, through single nucleotide polymorphisms ("SNPs") and other specific genetic characteristics associated with diseases and

This article proposes that responsible race-based genetics biomedical research—basic, clinical and epidemiological—is possible, and even desirable. A primary premise for the argument is that the concepts of race and ethnicity, like genetic science,[10] are neither innately good nor bad. Contrary to the dominant path followed by law academics,[11] which is to approach race-based research from anti-discrimination jurisprudence, this article approaches race-based

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responses to medications. *See generally* M. Bamshad, *Deconstructing*, *supra,* at 509. *See also infra* note 46 and accompanying text (SNPs addressed). Proponents argue that race does have a genetic basis—that, at the very least, it influences lifestyle choices resulting in shared environmental exposures, and DNA links people to geographic continents-regions that correspond with their self-identified racial classifications. *See id.* at 939-40. *See, e.g., Race, Ethnicity, and Genetics Working Group, The Use of Racial, Ethnic, and Ancestral Categories in Human Genetics Research*, 77 AM. J. HUM. GEN. 519-32 (2005); K Olden, SL White, *Health-Related Disparities: Influence of Environmental Factors*, 89 MED. CLIN. NORTH AM. 721-38 (2005); E. Gonzalez Burchard, L. N. Borrell, S. Choudhry, et al., *Latino Populations: a Unique Opportunity for the Study of Race, Genetics, and Social Environment in Epidemiological Research*, 95 AM J PUBLIC HEALTH 2161-8 (2005). *See also* C. W. MILLS, THE RACIAL CONTRACt (Ithaca, NY: Cornell University Press, 1997); P. KITCHER, IN MENDEL'S MIRROR: PHILOSOPHICAL REFLECTIONS ON BIOLOGY 239-45 (2003).

[9] *See, e.g.,* Jonathan Kahn, *Race-Ing Patents/Patenting Race: An Emerging Political Geography of Political Geography in Biotechnology*, 92 IOWA L. REV. 353 (2007); Erik Lillquist Charles A. Sullivan, *Legal Regulations of the Use of Race in Medical Research*, 34 J. L. MED. ETHICS 535-547 (2006); Dorothy Roberts, *Legal Constraints on the Use of Race and Ethnicity in Biomedical Research*, 34 J. L. MED & ETHICS 526-534 (2006); Sharona Hoffman, "*Racially-Tailored" Medicine Unraveled*, 55 Am. U. L. Rev. 395-456 (2005); Erik Lillquist & Charles A. Sullivan, *The Law and Genetics of Racial Profiling in Medicine*, 39 Harv. Civ. Rts-Civ. Lib. L. Rev. 442 391-483 (2004); Jonathan Kahn, *How a Drug Becomes 'Ethnic': Law, Commerce, and the Production of Racial Categories in Medicine*, 4 YALE J. HEALTH POL. L. & ETHICS 1-46 (2004). *See also infra* notes ___ and accompanying text. It is important to note that the law literature includes contributions to the race-based genetics debate from authors whose primary disciplines are in medicine and natural science, and they tend to be more receptive to, and even supportive of, this research. *See, e.g.,* Jay N. Cohn, *The Use of Race and Ethnicity in Medicine: Lessons From the African-American Heart Failure Trial*, 34 J.L. MED. & ETHICS 552 (2006); Raj Bhopal, *Race and Ethnicity: Responsible Use from Epidemiological and Public Health Perspectives*, 34 J. L. MED. & ETHICS 500 (2006), *citing* Raj Bhopal, *Is Research Into Ethnicity and Health Racist, Unsound, or Important Science?*, 314 BRIT. MED. J. 1751-56 (1997), *and* R. Bhopal, *Ethnicity as a Variable in Epidemiological Research*, 309 BRIT. MED. J. 327-28 (1994). *See also* Margaret A. Winker, *Race and Ethnicity in Medical Research: Requirements Meet Reality*, 34 J.L. MED. & ETHICS 520 (2006); Morris W. Foster, *Analyzing the Use of Race and Ethnicity in Biomedical Research from Local Community Perspective*, 34 J.L. MED. & ETHICS 508 (2006); Michael D. Ruel, Commentary, *Using Race in Clinical Research to Develop Tailored Medications*, 27 J. LEGAL MED. 225 (2006).

[10] Over the years, many have observed that the impact of genetic technology depends on how it is used. For example, in the context of one of the two most fundamental healthcare essentials, food (the other being water), genetic technology can be "democratically managed to the benefit of the most needy or skewed to the advantage of specific groups that hold the vital political, economical and technological power." Illenia M. Demenina, Note and Comment, *Genetically Modified Foods in the International Arena: Trade labeling Controversy and the Importance of Informed Consumer Choice*, 2 B.Y.U. Int'l. & Mngt. Rev. 311 (2006), *citing* Sara J. MacLaughlin, *Food for the Twenty-First Century: An Analysis of Regulations for Genetically Engineered Food in the United States, Canada, and the European Union*, 14 IND. INT'L & COMP. L. REV. 375, 405 (2003).

[11] *See, e.g.,* Lillquist & Sullivan, *Use of Race, supra* note 9; Hoffman, *Unraveled*, *supra* note 9.

research with the goal of promoting thoughtful bioethics compliance and with the legal mindset of inclusion analogous to the goals of affirmative action. This position is supported with arguments based in research pragmatism, genetic science, and applied bioethics—namely regulations to protect human subjects[12] and the fundamental principals documented in the Declaration of Helsinki[13] and the Belmont Report.[14]

The article begins with a discussion of the natural science context forming the background of the debate. Part II presents an overview of contemporary genetics research and medicine with a focus on the increased appreciation of the subtleties and pervasiveness of environmental influences on human genetics, and the heightened importance of population genetics following completion of the map of the human genome.[15] Part III summarizes the ongoing debate in the sciences, medicine, and law over race-based genetics research. Part IV

[12] In the United States, human subjects in research are protected through the Common Rule, 45 C.F.R. § 46 (2005), and separate Food and Drug Administration regulations, 21 C.F.R. § 50.20 (2005). *See also* Bonnie M. Lee, U.S. Food and Drug Administration, *Comparison of FDA and HHS Human Subject Protection Regulations*, 2000, *available at* http://www.fda.gov/oc/gcp/comparison.html (last visited July 27, 2007).

[13] World Medical Association, Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects (1964). The Declaration has been amended several times since 1964, including in 2002 and 2004. For more information, visit the internet site of the World Medical Association, *available at* http://www.wma.net/e/ (last visited Aug.2, 2007).

[14] The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research, at http://ohsr.od.nih.gov/mpa/belmont.php3 (last visited Aug. 4, 2007).

[15] The actual human genome map is available through the Encyclopedia of DNA Elements ("ENCODE") Project, a public research consortium launched by the National Human Genome Research Institute ("NHGRI"), information about which is *available at* http://www.genome.gov/10005107 (last visited July 28, 2007), and related sites, including UCSC Genome Bioinformatics, *available at* http://genome.ucsc.edu/ (last visited Aug. 2, 2007). Visit NHGRI, *ENCODE Overview*, *available at* http://www.genome.gov/10005107 (last visited May 4, 2007). Professor Bartha Knoppers addresses the importance of population genetics as a means to make medical sense out of the map of the human genome in *Biobanking: International Norms*, 33 J. L. MED. & ETHICS 7, 7-12 (2005); Bartha Maria Knoppers, *Overview of Law and Policy Challenges*, 66 LA. L. REV. 21, 21-31 (2005). For general discussion of genetic science and medicine in the aftermath of HGP, *see generally* JAMES D. WATSON, DNA: THE SECRET OF LIFE (Alfred A. Knopf ed., 2003); THE GENOMIC REVOLUTION: UNVEILING THE UNITY OF LIFE (Michael Yudell & Robert DeSalle eds., 2002) (concluding, "The knowledge gained [from HGP] could cure cancer, prevent heart disease, and feed millions. At the same time, its improper use can discriminate, stigmatize, and cheapen life through frivolous enhancement technologies."); Allen Guttmacher & Francis Collins, *Welcome to the Genomic Era,* 349 NEW ENG. J. MED. 996-98 (2004), *available at* www.nejm.org (last visited Aug. 3, 2007); *Climbing the Helical Staircase: A Survey of Biotechnology*, THE ECONOMIST, Mar. 29, 2003, at 1-24.

presents a hypothetical case study illustrating the scientific complications and potential group and social benefits of population genetics. This case study was selected to the side of the issue of the race controversy intentionally with three primary objectives: to focus on population genetics in the context of ongoing biomedical science and explain science fundamentals; to emphasize that groups organized by genetic disease, often seen as a preferable alternative, may in fact be no more homogenous than groups organized by race and ethnicity, even less so, while still serving as a valuable research resource; and to demonstrate that responsible biobanking may be beneficial on multiple levels regardless of the group collection criteria. The case study illustrates the pervasive disconnect between phenotype (physical characteristics) and genetics even in a group defined by a somewhat rare genetic disease; the bioethics benefits and pragmatism of working with *any* population on its own social and cultural terms; the potential control exercised by and benefits to the group under study; and the potential scientific and medical returns, which tend to transcend a group under study given the youth and genetics sameness of the human species. The overarching message is that responsible biobanking within any population enables research to move forward and may contribute tremendously to human health in sometimes very unpredictable ways.

The focus of Part V shifts back to race and ethnicity and proposes that recognition of and responsiveness to social constructs of race and ethnicity promotes the fundamental principles of contemporary bioethics. This argument rests heavily on the observations that, first, race and ethnicity are as real socially as genetics is scientifically. Second, these concepts, albeit social and cultural constructs,[16] have influenced, and in future generations will continue to influence,

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[16] *See supra* note 1 and accompanying text.

how people perceive themselves, whom they marry, their lifestyles, and how others perceive and interact with them—in other words, myriad environmental and genetic influences.[17]

The article concludes that, while the dangers of exploitation and discrimination must be underscored,[18] the concepts of race and ethnicity should be fully recognized and responded to in a receptive manner by the scientific communities. In fact, the article proposes that applied bioethics and scientific pragmatism favor recognizing race and ethnicity[19] as a *preferred* methodology for population genetics because this approach is most sensitive to self-identification by study subjects, communication with individual members of groups under study, realization of individual consent, recognition and assessment of group impact, and the development and realization of group consent in contemporary population genetics.[20] In addition, the article illustrates that "shoddy science" arguments against race-based genetics research are actually consistent with the goal of its advancement in a bioethics-sensitive manner, especially given the intensity of the surrounding debate and the critiquing environment that encompasses this research. As explained in the article, in the event the critics are correct, the

[17] "Beliefs about race, and behaviors that construct race, can be derived and analyzed using research methods from history, law, anthropology, sociology and psychology." Ossorio, *About Face*, supra note 2, at 278. *See generally* Race, Ethnicity, and Genetics Working Group, *The Use of Racial, Ethnic, and Ancestral Categories in Human Genetics Research*, 77 AM. J. HUMAN GENETICS 519-32 (2005); KITCHER, *supra* note 8. *See infra* notes 157-160 and accompanying text. Even Professors Lillquist and Sullivan, among the sharpest law academia critics of race-based research, have acknowledged that "it has been relatively safe, at least in the United States, to assume that race correlated with ancestry, although even in the United States the admixture of races is significant." Lillquist & Sullivan, *supra* note 9, at 544.

[18] Troy Duster, *Race and Reification in Science*, 307 SCI. 1050, 1050 (2005); Hoffman, *Unraveled*, *supra* note 6, at 420-27; Michael J. Malinowski, *Choosing the Genetic Makeup of Our Children: Our Eugenics Past—Present, and Future?*, 36 CONN. L. REV. 125, 172–97 (2003).

[19] It is important to note the distinctions and connections among race, ethnicity, and ancestry, which have been explained fully in both the science and law literature. *See, e.g.,* Race, Ethnicity, and Genetics Working Group, *The Use of Race, Ethnic, and Ancestral Categories in Human Genetics Research*, 77 AM. J. HUM. GEN. 519-32 (2005); Lillquist & Sullivan, *Use of Race*, *supra* note 6, at 536-537. *See generally* KITCHER, *supra* note 8.

[20] *See generally* Henry Greely, *Population Participation and Other Factors that Impact the Compilation and the Utility of Resulting Databases*, 66 LA L. REV. 79 (2005). *See also* Bartha Maria Knoppers, *Biobanking: International Norms*, 33 J. L. MED. & ETHICS 7, 10 (2005). *See infra* notes 177-198 and accompanying text.

advancement of race-based genetics will further establish the genetic fallacy of these groupings, create an opportunity for groups organized by race and ethnicity to participate in the genomics revolution on favorable terms as determined by them, and may result in genetic medicine applications that benefit the groups understudy directly and that transcend these groups and benefit the entire human species. This research also would advance fields of science such as epigenetics: the study of *heritable* changes in gene function that occur *without a change in DNA*, which some are referring to as the "other human genome."[21] Epigenetics is grounded in appreciation for the extent to which environment and lifestyle choices impact gene expression, for example, the environmental influences that often cause identical twins to become very different people as they progress through life.[22]

II. Measuring the Genetic Reality of Race, Then and Now

The present natural science debate over race-based genetics research is the progeny of another started nearly half a century ago[23]—one deeply influenced by the experience of grossly commingling life science in genetics and social science in eugenics at the turn of the Twentieth Century through the era of Nazi Medicine,[24] all in addition to the U.S. legacy of discrimination based upon race and ethnicity.[25] A particular field of science has driven each era in the debate,

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[21] *See generally* DAVID C. ALLIS, THOMAS JENUWEIN, & DANNY REINBERG, EPIGENETICS (2007); Adrian Bird, *Perceptions of Epigenetics*, NATURE, May 24, 2007, vol. 447, no. 7143 (May 24, 2007); JAMES A. GOODRICH, BINDING AND KINETICS FOR MOLECULAR BIOLOGISTS (2007); ERIC H. DAVISON, THE REGULATORY GENOME: GENE REGULATORY NETWORKS IN DEVELOPMENT AND EVOLUTION (2006); *Epigenetics*, SCIENCE, Aug. 10, 2001 (Spec. Iss.); *visit* Epigenetics, http://www.pbs.org/wgbh/nova/sciencenow/3411/02.html.

[22] *See generally supra* note 21.

[23] *See generally infra* Part II.A.

[24] Malinowski, *Choosing, supra* note 18, at nn. 25-67 and accompanying text.

[25] *See generally*, Ian F. Haney Lopez, *"A Nation of Minorities": Race, Ethnicity, and Reactionary Colorblindness*, 59 STAN. L. REV. 985 (2007); Daniel J. Sharfstein, *Crossing the Color Line: Racial Migration and the One-Drop*

which has been cumulative and has grown more complicated over time. The intensity and richness of the present debate, including the genetic science community's response to Dr. Watson's recent comments,[26] is the greatest assurance that race-based research and its outcomes will be scrutinized thoroughly—both scientifically and ethically.

A. Genetic Anthropology and Evolutionary Biology

The original post-World War II discourse over race-based genetics inspired several fields, including genetic anthropology[27] and molecular evolution,[28] which emerged in the 1960s and grew significantly throughout the 1970s.[29] By the 1980s, the debate had been largely quieted by an impressive body of scholarship that established persuasively that race is a social construct, not a genetic reality. Much of this scholarship is attributable to: Luca Cavalli-Sforza from Stanford University, widely recognized as the father of genetic anthropology;[30] Marcus Feldman, a Stanford colleague and collaborator of Professor Cavalli-Sforza, whose work centered on the

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Rule, 1600-1860, 91 MINN. L. REV. 592 (2007); KENNETH B. CLARK, DARK GHETTO: DILEMMAS OF SOCIAL POWER (1965).

[26] *See supra* notes 1-3 and accompanying text.

[27] *See infra* note 20.

[28] *See infra* note 22.

[29] This debate was a response to the jolt in understanding of human genetics following the discovery of the double helix structure of DNA by Dr. James Watson and Francis Crick in 1953. *See generally* JAMES WATSON, THE DOUBLE HELIX (1968).

[30] Professor Cavalli-Sforza's vast body of related scholarship before, during, and subsequent to the 1980s includes LUCA L. CAVALLI-SFORZA & W. BODMER, THE GENETICS OF HUMAN POPULATIONS (1999); LUCA L. CAVALLI-SFORZA, P. MENOZZI, AND A. PIAZZA, THE HISTORY AND GEOGRAPHY OF HUMAN GENES (1994); Luca L Cavalli-Sforza, *The Human Genome Diversity Project: Past, Present and Future*, 4 NAT REV GENET 333-40 (2005); Luca L. Cavalli-Sforza, *Studying Diversity*, 6 EMBO REP 713 (2005); Luca L. Cavalli-Sforza, *Man and the Diversity of His Genome. An Extraordinary Phase in the History of Population Genetics*, 46 PATHOL BIOL (PARIS) 98-102 (1998); Luca L. Cavalli-Sforza, *The DNA Revolution in Population Genetics*, 16 TRENDS GENET 60-5 (1998); Luca L. Cavalli-Sforza, P. Menozzi, A. Piazza, *Demic Expansions and Human Evolution*, 259 SCIENCE 639-46 (1993).

genetic evolution of complex systems;[31] and zoologist Richard Lewontin from Harvard University, who established the mathematical basis of population genetics and is often credited with founding the field of molecular evolution.[32] These scientists demonstrated that there was greater genetic variation within the racial groups they studied than between them, meaning that grouping based upon genetic commonality crossed the racial lines they tested. As stated by Professor Lewontin, "For the vast majority of human genetic variations, classical racial categories as defined by a combination of geography, skin color, nose and hair shape, and an occasional blood type or selected microsatellites make no useful prediction of genetic differences."[33] Consequently, during the last quarter of the last century, the natural science community, including the genetics community, largely abandoned race and ethnicity as biological categories.

B. The Social Scientists

Then, during the 1990s, the social science community reinvigorated the debate. The late Richard Herrnstein and Charles Murray published *The Bell Curve*, in which they attempted to measure the role intelligence plays in shaping social and economic differences between ethnic groups in America.[34] They claimed that intelligence is genetically inheritable in a predictable

[31] *See, e.g.,* LUCA L. CAVALLI-SFORZA & MARCUS W. FELDMAN, CULTURAL TRANSMISSION AND EVOLUTION (1981); Luca L. Cavalli-Sforza & Marcus W. Feldman, *The Application of Molecular Genetic Approaches to the Study of Human Evolution*, 33 NAT GENET (SUPP.) 266-75 (2003).

[32] *See* RICHARD C. LEWONTIN, THE TRIPLE HELIX: GENE, ORGANISM, AND ENVIRONMENT (2000); RICHARD C LEWONTIN, BIOLOGY AS IDEOLOGY: THE DOCTRINE OF DNA (1993). For a recent statement about race and genetics by Professor Lewontin, see Richard Lewontin, *Confusions About Human Races*, Apr. 20, 2005, *posted on* Is Race Real?, A Web Forum Organized by the Social Science Research Council, *available at* http://raceandgenomics.ssrc.org/Lewontin/ (last visited June 6, 2007).

[33] *Confusions*, *supra* note 32.

[34] *See generally* RICHARD HERNSTEIN & CHARLES MURRAY, THE BELL CURVE (1994).

manner, which they attempted to substantiate with research that relied on IQ scores.[35] Hernstein and Murray concluded that African Americans are less intelligent than Whites based upon a fifteen to sixteen point differential on IQ tests:

> Despite the forbidding air that envelops the topic, ethnic differences in cognitive ability are neither surprising nor in doubt. Large human populations differ in many ways, both cultural and biological. It is not surprising that they might differ at least slightly in their cognitive characteristics. That they do is confirmed by the data on ethnic differences in cognitive ability from around the world … The difference in test scores between African-Americans and European-Americans as measured in dozens of reputable studies has converged on approximately a one standard deviation difference for several decades. Translated into centiles, this means that the average white person tests higher than about 84 percent of the population of blacks and that the average black person tests higher than about 16 percent of the population of whites.[36]

Critics questioned the objectivity of IQ tests and attributed economic disparities to less quantifiable data, such as social circumstances.[37]

A year later, Michael Levin published *Why Race Matters: Race Differences and What They Mean*, in which he too claimed that African-Americans are less intelligent than whites,[38]

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[35] *See generally id.*

[36] *Id*. at 269.

[37] *See, e.g.,* CLAUDE S. FISCHER ET AL., INEQUALITY BY DESIGN: CRACKING THE BELL CURVE MYTH (1996); THE BELL CURVE WARS: RACE, INTELLIGENCE, AND THE FUTURE OF America (Steven Fraser ed., 1995).

[38] *See generally* MICHAEL LEVIN, WHY RACE MATTERS: RACE DIFFERENCES AND WHAT THEY MEAN (1997). In Levin's own words,

> [I]t always is assumed that Blacks are on average as intelligent as whites and as capable of passing any fair test in proportionate numbers. But there is now quite solid evidence that this assumption is not correct; the average black is significantly less intelligent than the average white. Therefore, the only adjustments in educational measures that will allow blacks their due number of successes amount to making course-work and tests easier and easier, and this is what has been going on for over thirty years. Conversely, if standards are going to be raised, cultural literacy reasserted and college education given its old depth and focus, the American policy will have to reconcile itself to an embarrassing failure rate for blacks. It has been amply confirmed over the last several decades that, on average, blacks are significantly less intelligent than whites. The black mean IQ is slightly more than one standard deviation below the white mean. In more familiar terms, that amounts to a difference of more than 15 points of IQ as measured by such standard tests as the Wechsler Adult Intelligence Scale.

Id. at __.

and then went much further. He concluded that African Americans are more aggressive, assertive, impulsive, and suffer from "an absence of conscience."[39] As with the work of Hernstein and Murray, Levin's work was heavily criticized and entirely dismissed by many.[40]

C. The Surge in Population Genetics

The turn of the Millennium has brought a surge in race-based genetics research[41] and genotype-phenotype connections associated with race.[42] Additionally, considerable ancestry-based research, though distinguishable,[43] raises implications that are spilling into the race-genetics controversy.[44] The increase in race-based genetics research is attributable to completion

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[39] *Id*. at 213, 322.

[40] *See generally* JOSEPH L. GRAVES, JR., THE EMPEROR'S NEW CLOTHES: BIOLOGICAL THEORIES OF RACE AT THE MILLENNIUM (2001). According to Professor Graves, both The Bell Curve and Why Race Matters were funded in part by the Pioneer Fund, "The purpose of [which] was to demonstrate the genetic inferiority of blacks." *Id.* at 154.

[41] *See* Neil Risch, *Dissecting Racial and Ethnic Differences*, 354 NEW ENG. J. MED. 408 (2006). *See generally supra* note 5. "There is a growing movement in medical genetics research and practice to develop, implement, and promote a model of race-based medicine." C. Condit & B. Bates, *How Lay People Respond to Messages About Genetics, Health, and Race*, 68 CLINICAL GENETICS 97 (2005).

[42] *See, e.g.,* C. A. Haiman, D. O. Stram, L. R. Wilkens, et al., *Ethnic and Racial Differences in the Smoking-Related Risk of Lung Cancer*, 354 N ENGL J. MED 333-42 (2006) ; X. Zhu, A. Luke, R. S. Cooper, et al., *Admixture Mapping for Hypertension Loci With Genome-Scan Markers*, 37 NATURE GENETICS 177-81 (2005); Richard S. Cooper, et al., *An International Comparative Study of Blood Pressure in Populations of European vs. African Descent*, 3 BMC MED. 2 (2005); M. Nakajima, T. Yokoi, *Interindividual Variability in Nicotine Metabolism: C-oxidation and Glucuronidation*, 20 DRUG METAB PHARMACOKINET 227-35 (2005); G. E. Swan, N. L. Benowitz, C. N. Lessov, P. Jacob III, R. F. Tyndale, K. Wilhelmsen, *Nicotine Metabolism: the Impact of CYP2A6 on Estimates of Additive Genetic Influence*, 15 PHARMACOGENET GENOMICS 115-25 (2005); N. Kaniwa, K. Kurose, H. Jinno, et al., *Racial Variability in Haplotype Frequencies of UGT1A1 and Glucuronidation Activity of a Novel Single Nucleotide Polymorphism 686C> T (P229L) Found in an African-American,* 33 DRUG METAB DISPOS 458-65 (2005); F. Innocenti, S. D. Undevia, L. Iyer, et al., *Genetic Variants in the UDP-Glucuronosyltransferase 1A1 Gene Predict the Risk of Severe Neutropenia of Irinotecan*, 22 J CLIN ONCOL 1382-8 (2004); N. L. Benowitz, E. J. Perez-Stable, B. Herrera, P. Jacob III, *Slower Metabolism and Reduced Intake of Nicotine from Cigarette Smoking in Chinese-Americans*, 94 J NATL CANCER INST 108-15 (2002); Neal L. Benowitz et al, *Ethnic Differences in N-Glucuronidation of Nicotine and Cotinine*, 291 J. PHARMACOLOGY & EXPERIMENTAL THERAPEUTICS 1196 (1999); Daniel L. Dries et al., *Racial Differences in the Outcome of Left Ventricular Dysfunction*, 340 NEW ENG. J. MED. 609, 616 (1999); Michael J. Klag, et al, *The Association of Skin Color With Blood Pressure in U.S. Blacks With Low Socioeconomic Status*, 265 J. AM. MED. ASS'N 599 (1991). For an insightful discussion of the clinical utility of race and ethnicity in medicine, *see generally* Cohn, *supra* note 9.

[43] For an excellent explanation of this distinction, see Ossorio, *About Face*, *supra* note 2, at 279-284.

[44] *See* Lillquist & Sullivan, *Regulation*, *supra* note 65, at 545-546. Note that NIH's National Human Genome Research Institute ("NHGRI") has distinguished ancestry from race and ethnicity in its International HapMap

of the map of the human genome in 2001,[45] the bioinformatics capabilities that enabled that accomplishment and which continue to expand by multiples, [46] and the broader understanding about human genetics that has followed. [47] Completion of the map of the human genome was both a remarkable accomplishment and humbling. As former President Bill Clinton observed at the time of its announcement:

> We are here to celebrate the completion of the first survey of the entire human genome. Without a doubt, this is the most important, most wondrous map ever produced by humankind.
>
> More than 1,000 researchers across six nations have revealed nearly all 3 billion letters of our miraculous genetic code. I congratulate all of you on this stunning and humbling achievement.
>
> Today's announcement represents more than just an epic-making triumph of science and reason. After all, when Galileo discovered he could use the tools of mathematics and mechanics to understand the motion of celestial bodies, he felt, in the words of one eminent researcher, "that he had learned the language in which God created the universe."

Project ("HMP"). *See* The International Haplotype Mapping Project, *available at* http://www.hapmap.org/ (last visited July 12, 2007). Nevertheless, HMP has raised many social, ethical and legal concerns about population genetics research that can be associated with race and ethnicity. *See generally* Ellen Wright Clayton, *Implications for Existing Law/Regulations*, 66 LA. L. REV. (Special Issue) 125, 129 (2005); Pilar N. Ossorio, *Race, Genetic Variation and the Haplotype Mapping Project*, 66 LA. L. REV. (Special Issue) 131 (2005).

[45] *See generally* 291 SCIENCE 1145 (Feb. 16, 2001) (issue entitled "The Human Genome"); 409 NATURE 745 (Feb. 15, 2001) (issue dedicated to the release of a draft map of the human genome). Timely information about the genomics revolution may be obtained from the National Human Genome Research Institute (NHGRI), *available at* http://www.nhgri.nih.gov (last visited May 24, 2007).

[46] *See generally* ESSENTIALS OF GENOMICS AND BIOINFORMATICS (C.W. Sensen ed., 2005); Robert Wells, *Intellectual Property/Ownership Interests,* 66 LA L. REV. 69, 70 (2006). As explained previously,

> Even before completion of the map of the human genome, the biomedical research community began employing bioinformatics to undertake a challenge dimensions greater than the basic genome mapping: translating this rambling string of letters that constitute the genome map into medical meaning. Consider that even just single-letter changes may cause variance in responsiveness to pharmaceuticals and susceptibility to diseases. The science community has been identifying these genetic idiosyncracies that appear in the human population with statistically significant regularity, known as SNPs, and compiling massive databases.

Michael J. Malinowski, *Technology Transfer in Biobanking: Credits, Debits, and Population Health Futures,* 33 L. MED & ETHICS 54, 56 (2005).

[47] *See generally* PAUL MARTIN & MICHAEL MORRISON; REALIZING THE POTENTIAL OF GENOMIC MEDICINE (2006). Most notably, we came to understand that all human diversity is attributable to just 25,000 or less active genes. *See* J. Michael McGinnis, *Population Health and the Influence of Medical and Scientific Advances*, 66 LA. L. REV. 9, 10 (2005).

> Today, we are learning the language in which God created life.
>
> Genome science will have a real impact on all our lives—and even more, on the lives of our children. It will revolutionize the diagnosis, prevention and treatment of most, if not all, human diseases.[48]

The map introduced perspective. Rather than the 100,000 or so genes expected by most at the outset of HGP, a mere 25,000 or fewer genes are responsible for all human diversity.[49] "Yet, one need only ride the New York City subway a few stops or people watch in Times Square to witness just how diverse we are, especially for such a young species. So, how do we resolve our genetic sameness with tangible human diversity?"[50] Genes multitask exponentially more than anticipated. Two unrelated human beings are separated by an estimated 3,000,000 distinct DNA variants.[51] With the map of the human genome in hand, those engaged in biopharmaceutical R&D and genetic medicine stepped into a universe of added complexity. Perspective has shifted: The scientific communities now have a significantly heightened appreciation for the dynamism of genetics, the intricacies of genetic expression, and the significance of interactions between genetics and environmental influences.[52] This shift is reflected in the emergence of epigenetics, which centers on environmental influences on, *not changes to,* DNA that become *heritable* changes in gene function.[53]

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[48] Visit http://www.genome.gov/10001356 (last visited May 16, 2007).

[49] McGinnis, *Influence*, *supra* note 38, at 10.

[50] Malinowski, *Futures*, *supra* note 46, at 56. Henry T. Greely, Daniel P. Riordan, Nanibaa' A. Garrison, Joanna L. *Mountain, Family Ties*; *The Use of DNA Offender Databases to Catch Offenders'* Kin, 34 J.L. MED. & Ethics 248, 249 (2006).

[51] *See* SNP Consortium Ltd., Single Nucleotide Polymorphisms for Biomedical Research, *available at* http://snp.cshl.org (last visited May 12, 2007). *See also* L. Brooks and M. Guyer, *National Human Genome Research Institute (HGRI), Resource for Studying Human Genetic Variation* (March 1998), *available at* www.georgetown.edu/research/nrcbl/nbac/transcripts/mar98/hbmr_spkrs.htm (last visited Feb. 18, 2005).

[52] *Cf.* Richard S. Cooper & Bruce M. Psaty, *Genomics and Medicine: Distraction, Incremental Progress, or the Dawn of a New Age?,* 138 ANNALS INTERNAL MED. 576 (2003).

[53] *See supra notes* 21-22 and accompanying text.

As overwhelming as this shift in scale is, bioinformatics,[54] the same technology that enabled completion of the map of the human genome is enabling scientists to make medical sense of it. Rather than working only at the gene or even protein level, scientists are reaching down further to study variations in single nucleotide bases and their impact on phenotype (physical characteristics), which are known as single nucleotide polymorphisms ("SNPs").[55] Single letter variants can be subtle—for example, a trigger that causes a gene to not make a needed protein that, through an intricate pathway of interactions, results in nonresponsiveness or over-responsiveness to a particular pharmaceutical. They also can be extreme, such as the deviation of one nucleotide that triggers Tay Sachs and takes a child's life.[56] Approximately two million of these subtle genetic variations with medical meaning have been identified—most a byproduct of the ongoing expenditure of tens of billions of dollars annually on biopharmaceutical research and development ("R&D").[57] Clusters of these variations inherited together are referred to as haplotypes.[58]

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[54] Bioinformatics is the combination of biology and information technology. *See generally*, ESSENTIALS, *supra* note 46; Wells, *Ownership, supra* note 46.

[55] SNPs are individual sites of genomic variation that occur with a frequency of at least 1% in the human population. *See The International SNP Map Working Group, A Map of Human Genome Sequence Variation Containing 1.42 million Single Nucleotide Polymorphisms*, 409 NATURE 928-933 (2001). For information about SNPs, visit the site of The SNP Consortium Ltd., *supra* note 44. *See generally* Helen Berman & Rochelle Dreyfuss, *Reflections on the Science and Law of Structural Biology, Genomics, and Drug Development*, 53 UCLA L. REV. 871, 882-883 (2006).

[56] Tay-Sachs is caused by a recessive genetic allele, a genetic variation on chromosome 15. For information, visit the Mayo Clinic internet site at http://www.mayoclinic.org/tay-sachs-disease/genetesting.html. More information is available via the National Tay-Sachs and Allied Disease Association, *available at* http://www.ntsad.org (last visited May 16, 2007).

[57] Some of these commercial entities have joined a collaboration, The SNPs Consortium Ltd., supra note 44, to put SNPs into the public domain. This effort is complemented by another consortium, the Wellcome Trust, which has a focus on structural genomics. *See* Wellcome Trust, Structural Genomics Consortium, http://www.wellcome.ac.uk/doc_WTD003502.html (last visited Oct. 31, 2005). For information about biopharmaceutical investment in drug research and development, visit the sites of the U.S. pharmaceutical trade organization, Pharmaceutical Researchers and Manufacturers of American, www.phrma.org, and the U.S. biotechnology trade organization, the Biotechnology Industry Organization, www.bio.org (last visited June 4, 2007).

[58] *See generally* International HapMap Project, What is the HapMap?, http://www.hapmap.org/whatishapmap.html.en (last visited Jan. 22, 2007).

Today's quest to find medical meaning in the genome has raised insatiable demand for human biological samples and accompanying medical information.[59] Appreciation for the scope of the universe of human genetic subtleties made discernable by the map of the human genome has expanded the scale of much genetics research from the study of families and disease groups to the study of entire populations.[60]

III. The Ongoing Debate Over Race-Based Research

Though the genetics science community and its research is at the center of the ongoing debate over race-based research, the social science and law communities also are actively engaged—making the present debate full-bodied, interdisciplinary, sophisticated and challenging.[61] As Professor Wolf has observed, "A number of conflicting proposals have been offered, some to discipline and improve the use of racial and ethnic categories, and some to eliminate such categories. This is a debate affecting researchers, funders, journal editors, research participants, and the broader community."[62]

A. Opponents

Those in the scientific and medical communities opposed to research based on race and ethnicity emphasize that these groupings are inconsistent with the scientific reality of human

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[59] *See* Paula W. Yoon, *Risk Prediction for Common Diseases*, 66 LA L. REV. 33, 40 (2005).

[60] *See generally Symposium: Regulation of Biobanks,* 33 J. L. MED. & ETHICS 1-188 (Mark Rothstein & Bartha Knoppers eds., 2005); Populations and Genetics: Legal and Socio-Ethical Perspectives (Ed. Bartha Maria Knoppers, 2003); Lorraine Sheremeta & Bartha Maria Knoppers, *Beyond the Rhetoric: Population Genetics and Benefit-Sharing,* 11 HEALTH L.J. 89, 90 (2003) (listing privacy as one of many concerns raised in present DNA testing).

[61] Professor Troy Duster, a sociologist, is an active participant. *See infra* note 58-59. Among law academics, Professors Sharona Hoffman, Eric Lillquist, Charles Sullivan, and Jonathan Kahn entered the debate early and have been fully engaged, and Professor Susan Wolf hosted a major symposium in the fall of 2006 which generated an issue of the Journal of Law, Medicine and Ethics dedicated to the topic. *See supra* note 9.

[62] Wolf, *Debating Use, supra* note 51, at 483.

genetics.[63] They draw from the ample body of literature by Professors Cavalli-Sforza, Lewontin and their contemporaries, and also reference recent findings which bolster the argument that race and ethnicity are more social constructs than genetic realities.[64] Opponents assert that a preferred methodology for population genetics is research centered on diseases or at least specific and more reliable genetic particulars.[65] They argue this approach will help avoid wasting resources, forcing outcomes, and chancing the affirmation of racial and ethnic groupings and social stereotypes. According to bioethicist and Ph.D. scientist Mildred Cho, the race and ethnicity categories are unworkable: "Because social perceptions of the meaning of race and ethnicity are extremely fluid, basing research findings on these categories or applying scientific findings based on perceived race or ethnicity is fraught with problems. Thus, attempts to "`better define [the racial and ethnic] structure [of drug response]' will be futile."[66]

Sociologist Troy Duster and many other opponents raise concerns about biologic determinism, meaning that genetic protocols crafted around race and ethnicity will become self-fulfilling prophecies. They emphasize the genetic commonality in any group due to the youth of

[63] *See, e.g.*, M. V. Osier, A.J. Pakstis, H. Soodyall, D. Comas, D. Goldman, K. Odunsi, F. Okonofua, J. Parnas, L. Schulz, J. Bertranpetit, B. Bonne-Tamir, R.-B. Lu, J.R. Kidd, and K.K. Kidd, *A global Perspective on Genetic Variation at the ADH Genes Reveals Unusual Patterns of Linkage Disequilibrium and Diversity*, 71 AM. J. HUM. GEN. 84, 84-99 (2002); N.A. Rosenberg, J.K. Pritchard, J.L. Weber, H.M. Cann, K.K. Kidd, L.A. Zhivotovsky, & M.W. Feldman, *Genetic Structure of Human Populations*, 298 SCIENCE 2381-2385 (2002). J.R. Kidd, A.J. Pakstis, H. Zhao, R.-B. Lu, F.E. Okonofua, A. Odunsi, E. Grigorenko, B. Bonne-Tamir, J. Friedlaender, L.O. Schulz, J. Parnas, & K.K. Kidd, *Haplotypes qnd Linkage Disequilibrium at the Phenylalanine Hydroxylase Locus (PAH) in a Global Representation of Populations,* 66 AM. J. HUM. GEN. 1882-1899 (2000).

[64] *See generally* Ossorio, *About Face*, *supra* note 2; Ossorio, *Genetic Variation*, *supra* note 37.

[65] *See generally* Ossorio, *About Face, supra* note 2; Gegg Bloche, *Market Incentives and Regulatory Constraints: Racial and Ethnic Categories in Pharmaceutical Research*, 34 J. L., Med. & Ethics 555-558 (2006); Raj Bhopal & L. Donaldson, *White, European, Western, Caucasian, or What?: Inappropriate Labeling in Research on Race, Ethnicity, and Health,* 88 AM. J. OF PUB. H. 88, 1303-07 (1998); Foster, *Analyzing Race*, *supra* note 6; Margaret A. Winker, *Race and Ethnicity in Medical Research: Requirements Meet Reality*, 34 J. L. MED. & ETHICS 520 (2006).

[66] Mildred K. Cho, *Racial and Ethnic Categories in Biomedical Research: There is No Baby in the Bathwater*, 34 J.L. MED. & ETHICS 497, 499 (2006), *quoting* Cohn, *supra* note 9.

the human species and its overwhelming genetic sameness.[67] Professor Duster also addresses the broader social implications of underscoring lines traditionally drawn around groups based upon race and ethnicity through genetics research protocols that suggest their validity. He warns that singling out these groups further affirms prejudices and increases their vulnerability to discrimination, exploitation, and health inequality.[68] According to Professor Duster, [69] the scientific community has shifted from "genetic sameness" as the mantra for mapping the human genome to a mantra of "genetic differentiation" through ongoing efforts to make medical sense out of the genome map, including population genetics,[70] pharmacogenomics,[71] and identification of SNPs.[72]

A number of law academics have entered the debate and have argued against the perpetuation of race in the biomedical context with cautions about the weighty social and legal implications involved.[73] In fact, there is a discernible majority opinion among law academics

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[67] *See generally* Troy Duster, *Lessons from History: Why Race and Ethnicity Have Played a Major Role in Biomedical Research,* 34 J.L. MED. & ETHICS 487 (2006); Prof. Troy Duster, Dinner Presentation, "The Globalization of Pharmaceutical Development: Race, Markets and Ethics" (Mar. 16, 2006, Santa Clara College of Law) (addressing the "shift from genetic sameness to individuality" pre- and post-HGP); Troy Duster, *Race and Reification in Science*, 307 SCI. 1050, 1050 (2005); Risch, *Dissecting, supra* note 8.

[68] Duster, *Dinner Presentation*, *supra* note 67. *See generally* Duster, *Reification*, *supra* note 67; Duster, *Lessons*, *supra* note 67. Sociologist Rose Brewer recently raised many similar concerns. *See generally* Rose M. Brewer, *Thinking Critically About Race and Genetics*, 34 J.L. MED. & ETHICS 513 (2006).

[69] Duster, *Dinner Presentation*, *supra* note 67.

[70] *See supra* notes 12, 32-50 and accompanying text.

[71] Complementary fields are pharmacogenomics, which is research centered on the expression of alleles shared by groups, and pharmacogenetics, the tailoring of health care and biopharmaceuticals to individual genetic profiles. *See generally* Michael J. Malinowski, *Law, Policy, and Market Implications of Genetic Profiling in Drug Development*, 2 H. J. OF HEALTH LAW & POL'Y 31-63, 31-43 (2003); L. Noah*, The Coming Pharmacogneomics Revolution: Tailoring Drugs to Fit Patients' Genetic Profiles,* 43 JURIMETRICS 1, 4-11 (2002).

[72] *See supra* notes 45-48 and accompanying text.

[73] *See supra* note 9 and accompanying text.

that race-based genomics research is undesirable on multiple levels and perhaps even illegal.[74] The literature includes articles by Professors Erik Lillquist and Charles Sullivan,[75] Professor Sharona Hoffman,[76] Professor Jonathon Kahn,[77] and a University of Minnesota symposium chaired by Professor Wolf which includes an article by Professor Dorothy Roberts.[78]

Proposals have been made to distinguish basic, clinical, epidemiological, and other forms of research, and to introduce legal restraints on the use of race and ethnicity in a manner tailored to each research specialty.[79] The general consensus among law opponents is that use of race and ethnicity in biomedical research always warrants caution and legal restraints, but there is a continuum: use of race in clinical research is least acceptable; use in epidemiological research, such as research on the correlation between race and health disparities, is most acceptable; and other types of research place between the two.[80] Also, the general consensus is that the use of race in research and medicine runs contrary to U.S. law and policy that broadly proscribes it. Professors Lillquist and Sullivan conclude that the use of race in research and medicine should be severely circumscribed, if not prohibited almost entirely.[81] Their proposed standard for using

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[74] *See id.*

[75] *See generally* Lillquist & Sullivan, *Regulations, supra* note 9. *See also* Lillquist & Sullivan, *Racial Profiling, supra* note 9, at 442.

[76] *See* Hoffman, *Unraveled*, *supra* note 9, at 395-456.

[77] *See generally* Kahn, *Racing Patent, supra* note 9; Kahn, *Racial Categories*, *supra* note 9, at 25.

[78] *See generally* Symposium, *The Responsible Use of Racial and Ethnic Categories in Biomedical Research: Where Do We Go From Here?,* 34 J.L. MED. & ETHICS 483 (fall 2006) (published outcomes of live symposium at Univ. of Minnesota); Roberts, *Legal Constraints, supra* note 6. Many of the contributors to this symposium were trained in disciplines outside of law and approached the topic accordingly. *See generally id.* For citations to the other symposium pieces, *see supra* note 0.

[79] *See* Lillquist & Sullivan, *Regulation, supra* note 9, at 543-547.

[80] *Id.* at 546.

[81] *See generally* Lillquist & Sullivan, *Racial Profiling, supra* note 9.

race in medical treatment is extremely restrictive. They would require a scientific basis to establish not simply that use of race is helpful in diagnosis and treatment, but that it is the best known method at the time.[82] Professor Hoffman declares that "'race-based' medicine is an inappropriate and perilous approach"[83] and proposes regulatory reforms to heavily restrain, if not entirely eliminate, both race-based research and medicine.[84] She proposes "attributes-based" identification as a race-neutral alternative.[85]

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[82] *Id*. at 442.

[83] Hoffman, *Unraveled, supra* note 9, at 397.

[84] *See generally id.*

[85] As Professor Hoffman explained,

> [T]o the extent that a group-oriented approach is pursued, it should be attribute-based rather than `race-based,' and scientists should invest considerable effort in accurately identifying the attribute or attributes at issue. . . . The variables that might be relevant for a particular procedure or therapy could include socioeconomic status, diet, exercise, stress level, exposure to environmental toxins, cultural and religious barriers to treatment compliance, specific genetic alterations that influence disease course or disease vulnerability, and other factors.

Id. at 398.

NIH is considering adoption of Professor Hoffman's attributes-based identification, at least according to a NIH representative during the question and answer session following Professor Hoffman's presentation at the 30th Annual Health Law Teacher's Conference in June 2006. Session on Race-Based Research, 30th Annual Health Law Teachers Conference, University of Maryland School of Law, June 1-3, 2006 (sponsored by the American Society of Law, Medicine, and Ethics; materials on file with author, including list of attendees). NIH regulations expressly require inclusion of minority groups in clinical research. NIH Policy on Reporting Race and Ethnicity Data: Subjects in Clinical Research, August 8, 2001, *available at* <http:// grants1.nih.gov/grants/guide/notice-files/NOT-OD-01-053.html (last visited June 12, 2006); U.S. Department of Health and Human Services, "Policy Statement on Inclusion of Race and Ethnicity in HHS Data Collection Activities" (1997), *available at* http://aspe.os.dhhs.gov/datacncl/racerpt/appendg.htm (last visited June 28, 2006). Under these rules, applicants for grant funding must measure and report the race and ethnic composition of their intended study population and provide a rationale for subject selection, in part to ensure inclusion of non-White populations traditionally understudied. National Institutes of Health, "Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research," last modified Oct. 11, 2001, *available at* http:// grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm (last visited Mar. 10, 2007).

Adoption of the attributes-based approach would introduce administrative and compliance complexity and inconsistency in federal policy, as recognized by the Office of Management and Budget ("OMB"), which has refused to stray from race and ethnicity classifications for these very reasons. Under OMB Directive 15, race and ethnic classifications are used for administrative practicality, as when conducting the national census. Statistical Directive No. 15: Race and Ethnic Standards for Federal Agencies and Administrative Reporting, 43 Fed. Reg. 19,269-70 (May 4, 1978) [hereinafter Statistical Directive 15]. The classifications also are used by government entities in a range of programs that require consideration of race with the objective of bringing about inclusion where there has been a legacy of the opposite, including in biomedical research. *See, e.g.,* CDC, "Racial and Ethnic Approaches to Community Health: Goals for 2010," *available at* http://www.cdc.gov/reach2010/goals.htm (last visited July 12, 2007). In other words, race and ethnicity are recognized to include and counter a legacy of exclusion and discrimination. Even Professor Dorothy Roberts who opposes the use of race and ethnicity in

Collectively, law academics generally approach race-based research from U.S. jurisprudence and public policy against discrimination and associated social and ethical concerns.[86] Their analysis of potential legal constraints on race-centered research begins with restrictions on intentional disparate treatment based on race by government entities under the Equal Protection Clause of the Fourteenth Amendment and the Due Process Clause of the Fifth Amendment.[87] They emphasize that government use of racial classifications triggers strict scrutiny, but recognize that government actions, including programs thoughtfully crafted to promote affirmative action, survive such scrutiny where there is a compelling government interest and the use of race is narrowly tailored to promote that interest.[88] They generally concede that, under established jurisprudence, government sponsorship of responsible race-based genetics research is likely to survive such challenges, though the present Court recently

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biomedical research supports their use to study and eliminate disparities in access to health care and medical treatment. *See* Roberts, *Legal Constraints*, *supra* note 9, at 532-533.

[86] *See, e.g. ,* Hoffman, *Unraveled*, *supra* note 9; Lillquist & Sullivan, *Regulation*, *supra* note 9.

[87] *See generally Grutter v. Bollinger*, 539 U.S. 306 (2003) (holding that the Univ. of Mich. Law School has a compelling interest in attaining a diverse student body and that its affirmative action admissions program was narrowly tailored to serve that compelling interest). Presently there is some uncertainty regarding permissible government action in the context of race integration, for the Supreme Court revisited the 1954 *Brown v. Board* decision in cases heard December 2006, *Parents Involved in Community Schools v. Seattle School District No. 1,* 551 U.S. __ , 127 S.Ct. 2738, 75 USLW 4577, 220 Ed. Law Rep. 84 (NO. 05-908, 05-915) (2007), and *Meredith v. Jefferson County Board of Education*, 127 S.Ct. 575 (Mem), 166 L.Ed.2d 407, 75 USLW 3247 (NO. 05-915) (2007). *See* Adam Liptak, *Brown v. Board of Education, Second Round*, N.Y. TIMES, Dec. 10, 2006, at 3. The Court considered whether school systems in Seattle, Washington, and Louisville, Kentucky, could take account of the races of students to achieve racial balance even though some students might be denied access to schools of choice due to race balance considerations. *See id.* The Supreme Court concluded that "The school districts have not carried their heavy burden of showing that the interest they seek to achieve [, namely racial diversification,] justifies the extreme means they have chosen—discriminating among individual students based on race by relying upon racial classifications in making school assignments." *Seattle, supra*, at Slip. Op. para. 2, p. 2.

[88] *See Grutter,* 539 U.S. at 306.

questioned the Seattle and Kansas City school diversity policies and subjected them to further inquiry. [89]

Professors Hoffman, Lillquist, and Sullivan also look to statutory schemes that expand protection against racial discrimination—namely section 1981,[90] Title VI,[91] and Title II of the Civil Rights Act of 1964. [92] However, again, they concede the limited applicability of these provisions to race-based research. First, as they address, while section 1981 reaches beyond government actions to contracts between private individuals, its prohibition on discrimination in contracts is limited to intentional disparate treatment.[93] The reach of Title II is limited to discrimination or segregation in places of public accommodation, and courts have limited the reach of Title VII in the medical context.[94] Although Title VII prohibits race discrimination in federally funded programs,[95] courts have held that doctors receiving Medicare funding are not "programs" within the meaning of the statute.[96] The case holdings suggest that medical research also would be beyond the statute's reach. Moreover, although Title VII allows private causes of

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[89] *See Seattle School District No. 1*, 551 U.S. at __, and *supra* note 77. Professors Lillquist and Sullivan have recognized that "The legal constraints on the use of race in research are more limited than might be expected given the strong ethical consensus against harmful use of racial categories. The three major sources of federal regulation, the Equal Protection Clause and two federal statutory schemes, together leave large areas untouched." Lillquist & Sullivan, *Legal Regulation*, *supra* note 6, at 540. Presumably the Supreme Court's *Seattle* decision underscores this observation..

[90] 42 U.S.C. § 1981 (2000).

[91] 42 U.S.C. § 2000d (2000).

[92] 42 U.S.C. § 2000a (2000).

[93] *See* Sullivan & Lillquist, *Legal Regulation*, *supra* note 9, at 540.

[94] *See* Hoffman, *Unraveled*, *supra* note 9, at 429-430.

[95] Title VII has been interpreted to prohibit both disparate treatment and disparate impact discrimination. See Hoffman, *Unraveled*, *supra* note 6, at 441-442.

[96] *See, e.g., Vuciecevic v. MacNeal Mem'l Hosp*., 572 F. Supp. 1424, 1430 (N.D. Ill. 1983). *See generally* Lillquist & Sullivan, *Racial Profiling*, *supra* note 6, at 445. In 1966, the Health, Education and Welfare Department decided to exempt physician Medicare participants from Title VII compliance. *See id.*

action for intentional discrimination, only the federal government can challenge policies on the basis of disparate impact.[97] Professors Lillquist and Sullivan also acknowledge that government restraints on private undertakings are limited by commercial free speech.[98]

B. Proponents

Contemporary biomedical research encompasses numerous methodologies centered on the study of populations, with the size of study groups varying from local communities to cross sections of the global human population.[99] Those in the science and medical communities who support race-based research generally accept that grouping the human species on a universal level according to the greatest genetic common denominators would likely cut through our socially drawn race and ethnicity lines.[100] The research of Professors Cavalli-Svorza, Lewontin, and their contemporaries is impressive and persuasive.[101] However, proponents of race-based genetics research also are receptive to the notion that clusters of genetic commonalities, acquired through ancestry or shared environmental exposures (defined to fully encompass social influences), may be more prevalent in racial and ethnic groups than in the general population.[102] In other words, they work with the premise that (a) comprehensive human species challenges to the genetic reality of race and (b) the utility of race and ethnicity in population genetics are not

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[97] Lillquist & Sullivan, *Racial Profiling, supra* note 9, at 447-448; Hoffman, *Unraveled, supra* note 9, at 441-442.

[98] *See* Lillquist & Sullivan, *Racial Profiling, supra* note 9, at 448-450. *See generally Wash. Legal Found. v. Henney,* 202 F.3d 331 (D.C. Cir. 2000) (declaring the marketing of pharmaceutical products commercial free speech and limiting restrictions).

[99] Foster, *Analyzing Race*, *supra* note 9, at 508.

[100] The research and scholarship of Professors Cavalli-Sforza, Feldman, and Lewontin remain persuasive on this point. *See supra* notes 30-33 and accompanying text.

[101] *See id.*

[102] *See generally* Cohn, *Lessons, supra* note 9; Bhopal, *Responsible Use, supra* note 9; Risch, *Dissecting, supra* note 8.

necessarily mutually exclusive. Rather, they perceive them as distinguished by scope and complementary—along the lines of the use of micro- and macroeconomics by economists.[103] Supporters assert that, at least in some instances, research centered on racial and ethnic groupings has the potential to be a population extension of classic family pedigree studies in which research is conducted on a scale necessary to address the genetic intricacies we more fully discern and appreciate post completion of the human genome map. [104] A crisp illustration is an ongoing multiple sclerosis (MS) study carried out by the University of California at San Francisco and Harvard University under the International Multiple Sclerosis Genetic Consortium to identify genetic variants that account for the difference in the risk of developing MS between Africans and Europeans.[105] The scientists are scanning DNA from African American MS patients for regions that have an unusually high proportion of European or African ancestry.[106] Their hypothesis is that, as the occurrence of MS is much higher in people of European ancestry, African Americans with MS have inherited a higher than average proportion of European

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[103] The basic distinction is that microeconomics is about how markets operate while macroeconomics is about how economies function. *See generally* SILK ET AL., MAKING CAPITALISM WORK 175 (1996); DOUGLASS C. NORTH, ECONOMIC PERFORMANCE THROUGH TIME, PRIZE LECTURE IN ECONOMIC SCIENCE IN MEMORY OF ALFRED NOBEL (Dec. 9, 1993); PETER HOWITT, MACROECONOMICS: RELATIONS WITH MICROECONOMICS, IN 3 THE NEW PALGRAVE: A DICTIONARY OF ECONOMICS 273-75 (John Eatwell et al. eds., 1989) (outlining the disjunction between micro and macro economics).

[104] *Cf.* Bhopal, *Responsible Use*, *supra* note 9, at 500.

[105] Daar & Singer, *Geographical* Ancestry, *supra* note 8 (editorial surveys ongoing pharmacogenetics research projects and identifies the potential benefits of this research for developing economies).

[106] This project is using 'admixture mapping', a type of haplotype association mapping. *See* David Reich, Nick Patterson, et al., Letters, *A Whole-Genome Admixture Scan Finds a Candidate Locus for Multiple Sclerosis Susceptibility*, 37 NATURE 1113, 1113-1118 (Oct. 2005). For explanation and discussion of haplotype mapping, *see supra* note 58 and *infra* notes 110-118 and accompanying text.

chromosomal regions.[107] The first part of this study already has brought science closer to interesting candidate genes.[108]

Additional research results substantiate the scientific merit of this methodology: Race and ethnicity-based genetics research is bestowing medical benefits to groups under study. A notable example is identification of the genetic causes of adverse drug reactions ("ADRs") to some commonly prescribed medications disproportionately prevalent in patients of South Asian descent, not a common focus group in biopharmaceutical research and development. The use of oseltamivir, commonly known as Tamiflu and widely stockpiled for use in a possible avian influenza pandemic, has been associated with neuropsychiatric disorders and severe skin reactions primarily in patients of Japanese origin.[109] ADRs from Tamiflu eventually were linked to a genetic aberration present in a small percentage of persons with Japanese origin.[110]

Asian populations also have experienced a disproportionately high ADR incident rate—ten percent—with rosuvastatin (commonly named Crestor), a routinely prescribed statin inhibitor. The side-effects of muscular myopathy and rhabdomyolysis were observed during the Phase IV (post marketing) clinical testing period. The severity of these ADRs prompted a drug

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[107] Daar & Singer, *Pharmacogenetics*, *supra* note 8, at 242.

[108] *See generally* Reich, et al., *Whole-Genome Admixture*, *supra* note 106.

[109] *See generally* Li, et al, *Nonsynonymous SNP*, *supra* note 8.

[110] This allele (genetic variation) is a nonsynonymous SNP (single nucleotide polymorphism) near the region of DNA coding for the enzymatic active site of human cytosolic sialidase, a homologue of virus neuraminidase that is the target of oseltamivir. This SNP, not observed in persons of European and African American descent, occurs in 9.29 percent of Asian populations. ADRs to oseltamivir in Asian populations have been associated with the tendency of this SNP to reduce sialidase activity (Li et al., 2007). The governing theory is that its presence increases the unintended binding affinity of human sialidase to oseltamivir carboxylate, the active form of oseltamivir, thus reducing sialidase activity. In addition, this SNP itself results in an enzyme with an intrinsically lower sialidase activity. *Id.*

advisory memorandum from the FDA that specifically regulated the dosage of Crestor for persons of Asian descent.[111]

These and other ADRs in populations associated with racial classifications have inspired several countries with Asian populations, populations not traditionally a study focus for biopharmaceutical R&D based in the U.S. and Europe, to unite and form The Pacific Pan-Asian SNP Initiative ("Pan-Asian Initiative").[112] The Initiative, hosted by the Genome Institute of Singapore, has brought scientists together to research the breadth of genetic diversity and the extent of genetic similarity within Asian populations.[113] This information will form the basis for future studies in genomic medicine focused on Asian populations. Data from the Pan-Asian study will provide a platform for researchers in Asia to study why some populations seem predisposed to certain diseases, do not respond to certain drugs, or experience adverse drug reactions.[114] Participating countries with complementary population genetics programs of their own include Japan,[115] Taiwan,[116] and China.[117]

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[111] FDA Public Health Advisory on Crestor (rosuvastatin) (2005).

[112] *See generally* Daar & Singer, *supra* note 8.

[113] *See id.*

[114] *See id.*

[115] Japan begain the BioBank Japan Project in 2003 with the goal of collecting DNA, serum samples, and clinical information from 300,000 patients. Triendl, R. *Japan Launches Controversial Biobank Project*, 9 NAT MED. 982 (2003). Biobank Japan is focused on elucidation of ADRs associated with oncological chemotherapy. The overall goal of the BioBank Japan Project is to achieve personalized patient dosing capabilities to maximize positive responsiveness and avoid ADRs, *See generally* Y. Nakamura, *The BioBank Japan Project*, 5 CLIN. ADV'S IN HEMATOLOGY & ONCOLOGY 696-697 (2007).

[116] The Taiwan Biobank was inspired by identification of hereditary and external risk factors unique to the Taiwanese. *See generally* Wu, Y.-R., Chen, C.-M., Chao, C.-Y., Ro, L.-S., Lyu, R.-K., Chang, K.-H., et al., *Glucocerebrosidase Gene Mutation is a Risk Factor for Early Onset of Parkinson Disease Among Taiwanese*, 78 J. NEUROL NEUROSURG PSYCHIATRY 977-979 (2007). The purpose of Taiwan Biobank is to investigate the gene factors behind common chronic diseases in Taiwan, such as cancer, high blood pressure, and diabetes, and the interactions of genetic and external risk factors. *See id.* Early findings include identification of a mutation common in a subsection of the Taiwanese population that predisposes such patients to early onset of Parkinson's disease. *See id.*

These ADRs also have inspired the FDA to conduct pharmacogenomic studies that require evaluation of toxicity in separate race-based groups. A recent example is FDA approval of alosetron hydrochloride for irritable bowel syndrome—the drug Lotronex by GlaxoSmithKline.[118] After an initial approval through the FDA, the drug was voluntarily withdrawn by GlaxoSmithKline because of ADRs.[119] However, because of its efficacy, Lotronex was re-approved by the FDA in 2002 with market restrictions.[120] Currently, GlaxoSmithKline is studying the relationship between adverse events and genetic profiles as part of FDA-imposed post-marketing commitments.[121]

The FDA also has required race identification in clinical trial design. In 2003, the FDA demanded greater scrutiny of data from subpopulations and required incorporation of racial catagories specified by the Census Bureau to ensure consistent evaluation of drug safety profiles across racial groups. Then, in 2005, the FDA issued its first approval of a "race-specific"

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[117] China has several biobanking initiatives underway that position the nation for leadership in pharmacogenomic studies. *See generally*, Jiang, C., Thomas, G. N., Lam, T. H., Schooling, C. M., Zhang, W., Lao, X., et al., *Cohort Profile: The Guangzhou Biobank Cohort Study, a Guangzhou-Hong Kong-Birmingham collaboration*, 35 INT. J. EPIDEMIOL 844-852 (2006). The Guangzhou biobank (GBCS), for example, is a collaborative project between the UK and China and focuses on older people aged at least 50 years in a mega-city of approximately 10 million. See id. Of these, 6.4 million are permanent residents with locally registered households, and the remainder are mostly migrants from other parts of the country. *See id*. Guangzhou, the provincial capital of Guangdong province in southern China, is one of the most economically developed regions of China. *See id.* The overall study population design calls for 30,000 participants who are evaluated regularly by the bank. *See id.* The elderly population in Guanzhou is uniquely exposed to two unique macroenvironments. Prior to 1949, this was a rural region. *See id*. After formation of the People's Republic of China, the region was industrialized. See id. Thus, potential early genetic cues may differ substantially between the elderly population that developed through adolescence prior to the 1949 transition. *See id.*

[118] Webster, W., Martin, P., Lewis, G. & Smart, A., *Integrating Pharmacogenetics Into Society: In Search of a Model*, 5 NATURE REV. GENET. 663–669 (2004).

[119] *See id*

[120] *See id.*

[121] *See id.*

therapy— a fixed-dose combination of isosorbide dinitrate and hydralazine, now known as BiDil, NitroMed, for use in African Americans with heart failure. [122]

These events culminated in a 2005 FDA recommendation to pharmaceutical companies that they include racial and ethnic data in their safety assessment protocols. The FDA adopted the "Guidance for Industry: Collection of Race and Ethnicity Data in Clinical Trials," originally issued by the Office of Management and Budget (OMB).[123] This Guidance advises pharmaceutical companies how to incorporate race and ethnicity in a standardized fashion within existing protocols for pharmaceutical safety assessment of drugs.[124] Under OMB Directive 15, race and ethnic classifications are used for administrative practicality, based on the definitions provided in the United States Census (Statistical-Directive-15, 1978). [125] The classifications also are used by government entities in a range of programs that require consideration of race with the objective of achieving inclusion where there has been a legacy of the opposite, including in biomedical research.[126] Consequently, inclusion of race in pharmacogenomic safety assessment profiles for new drug applications is an increasingly accepted practice in the United States.

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[122] Bibbins-Domingo, K., & Fernandez, A., *BiDil for Heart Failure in Black Patients: Implications of the U.S. Food and Drug Administration Approval*, 146 *Ann Intern Med.* 52-56 2007. *See also infra* notes 144-150 and accompanying text. Originally, the FDA rejected the drug because its efficacy in treating heart failure could not be demonstrated statistically in a clinical trial in the general population Franciosa, J. A., *Fixed Combination Isosorbide Dinitrate-Hydralazine for Nitric-Oxide-Enhancing Therapy in Heart Failure*, 7 EXPERT OPIN PHARMACOTHERAPY 2521-2531 (2006). However, the results of a subsequent doubleblind, randomized clinical trial in 1,050 self-identified African-American patients who had experienced heart failure were impressive enough to compel the FDA's race-specific approval. *See id*.

[123] *Finding-Solutions-to-Health-Disparities: Racial and Ethnic Approaches to Community Health (REACH) in the U.S. (Oct. 11, 2007)*, *available at* http://www.cdc.gov/reach/reach_2010/index.htm.

[124] *Id*.

[125] *Id*.

[126] *Id*.

. Supporters emphasize the jolt in the scale of genetics research post completion of the map of the human genome in 2001 to a level of intricacy dimensions beyond the capabilities of genetic science in the years before.[127] Today, many scientists are working at the level of alterations in single nucleotides (just one adenine, cytosine, quinine, or thymine nucleotide base among an individual's three billion base pairs), and some even are identifying *hereditary* genetic differences through environmental exposures that occur *without changes in DNA*.[128]

These proponents point to the ample positive outcomes of race and ethnicity-based research, including findings from research in Amish[129] and Ashkenazi Jewish populations,[130] and the higher incidence of some diseases associated with specific racial and ethnic groups, such as Tay Sachs in Ashkenazi Jews[131] and cystic fibrosis in Caucasians with Northern European ancestry.[132] They assert that race and ethnicity should be accepted as a possible research variable especially in light of how environmental factors interact with and influence genetics, the influence of race and ethnicity on how we group ourselves socially, the impact of these

[127] *See supra* notes 55-58 and accompanying text.

[128] This field, epigenetics, is addressed *supra* notes 21, 22, 53, *infra* note 117, and in the accompanying text.

[129] *See, e.g.,* Robert Wells, *Intellectual Property Ownership Issues*, 66 LA. L. REV. 69, 74 (2005) (discussing collaboration between Affymetrix and Amish populations to identify the gene responsible for Swyer Syndrome and a gene responsible for a new form of sudden infant death syndrome).

[130] *See, e.g.,* S.V. Hodgson et al., *Risk Factors for Detecting Germline BRCA1 and BRCA2 Founder Mutations in Ashkenazi Jewish Women with Breast or Ovarian Cancer*, 36 J. MED. GENETICS 369 (1999).

[131] National Institute of Neurological Disorders and Stroke, *available at* http://www.ninds.nih.gov/disorders/taysachs/taysachs.htm (last visited June 4, 2007).

[132] National Heart Lung and Blood Institute, *available at* http://www.nhlbi.nih.gov/health/dci/Diseases/cf/cf_risk.html (last visited June 9, 2007).

groupings on environmental exposures, and the fact that race and ethnicity have influenced social groupings for centuries.[133] As explained by some researchers:

> For example, individuals living in sub-Saharan rural Africa have close to 100% of what are called African alleles, whereas African Americans living in the United States show about 26% Caucasian admixture 18. Some groups (for example, African-American, Caribbean and Panamanian populations) are likely to show a large degree of allelic diversity, whereas other groups (for example, sub-Saharan Africans, Inuits and Finns) are less genetically diverse. Old Amish individuals share more alleles than do individuals in other populations because they marry within their own community and as a result have a higher than-average incidence of inborn errors of metabolism 19, as do some Arab consanguineous communities. Because of founder effects and enforced segregation, Ashkenazi Jews also share a large number of alleles.[134]

Much more subtle, the field of epigenetics is demonstrating that environmental exposures and lifestyle choices—again, factors highly influenced by social, cultural and geographic groupings—impact gene expression in a heritable manner without changes in DNA.[135]

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Proponents also emphasize the potential good that could be done for the populations of developing countries, while also improving the safety and efficacy of biopharmaceuticals across subpopulations in developed ones, by recognizing the disparate impact pharmaceuticals have on subpopulations organized by race, ancestry, and ethnicity in advance of their market distribution.[136] They emphasize that, today, the measures for market access in the United States are crude—the standard is better than placebo, biopharmaceuticals are often put on the market with a showing of efficacy in only thirty-percent of the subjects, and usually only after being

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[133] *See generally Race, Ethnicity, and Genetics Working Group, The Use of Racial, Ethnic, and Ancestral Categories in Human Genetics Research*, 77 AM. J. HUM. GEN. 519-32 (2005); *See generally* Cohn, *Lessons*, *supra* note 9; Bhopal, *Responsible Use*, *supra* note 9; Burchard, *Importance of Race, supra* note 9.

[134] Daar & Singer, *Pharmacogenetics*, *supra* note 105, at 242.

[135] *See supra* notes 22 & 53 and accompanying text. [Damon, please research tangible successes in epigenetics research to date].

[136] *See, e.g., id.*

tested on the general populations of Europe and North America.[137] And, in fact, countries largely excluded from biopharmaceutical R&D are responding by establishing their own ancestry-based genotyping initiatives—countries including China, India, Indonesia, Japan Korea, Malaysia, Mexico, Nepal, the Philippines, Singapore, Taiwan, and Thailand[138]—and even transnational efforts, such as The Pan-Asian Initiative.[139]

C. The Debate Applied: HapMap and BiDil

One of the most controversial research undertakings in recent years is the International Haplotype Mapping Project ("HMP"),[140] a collaboration among scientists and funding agencies from Canada, China, Nigeria, the United Kingdom, and the United States.[141] The goal of HMP

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[137] *Id.* at 243. The *number of adverse events and performance disappointments with biopharmaceuticals in recent years speaks to this. See generally* Congressional Committee Report (Dec. 2007); Institutes of Medicine Report 2006; General Accountabililty Office Report (2006).

[138] Populations outside of North America and Europe are recognizing the problems of exclusion and potential benefits of inclusion in biopharmaceutical R&D, and they are undertaking initiatives, sometimes in collaboration:

> India and Thailand are both embarking on SNP-genotyping studies. Hosted by the Genome Institute of Singapore, an important regional initiative has recently brought scientists from China, India, Indonesia, Japan, Korea, Malaysia, Nepal, the Philippines, Singapore, Thailand and Taiwan to establish the Human Genome Organization (HUGO) Pacific Pan-Asian SNP Initiative, which is expected to begin in the middle of 2005. The goal of this initiative is to uncover the breadth of genetic diversity and the extent of genetic similarity within Asian populations. This information will form the basis for future studies in genomic medicine focused on Asian populations. Data from the Pan-Asian study will provide a platform for researchers in Asia to study why some populations seem predisposed to certain diseases, or do not respond to certain drugs. Cost reductions and new technologies are opening up the study to all researchers, including those with less well-developed research infrastructures. Asia is not alone in such initiatives. Mexico has a newly-created, well-funded federally mandated Institute of Genomic Medicine, headed by Gerardo Jimenez-Sanches. Genotyping the diverse Mexican populations is one of its top priorities.

Daar & Singer, *Pharmacogenetics*, *supra* note 105, at 242.

[139] *See supra* notes 112-117 and accompanying text.

[140] For more information, visit the official site of the International Haplotype Mapping Project, at http://www.hapmap.org/ (last visited June 2, 2007) and the National Human Genome Research Institute (NHGRI) HapMap Page, http://www.genome.gov/page.cfm?pageID=10001688 (last visited July 12, 2007). *See generally* Clayton, *Implications,* supra note 34; Ossorio, *Haplotype Mapping Project*, supra note 34.

[141] *Visit* Haplotype site, *supra* note 34; NHGRI HapMap Page, *supra* note 35. *See generally* Daar & Singer, *Pharmacogenetics*, *supra* note 105, at 242.

is to take the concept of familial-pedigree studies up to the population level—to compare genetic sequences to identify chromosomal regions where genetic variants are shared, and to identify clusters of variations that are inherited together.[142] Stage I of HMP, commenced in October 2002 and completed in fall 2006, consisted of analyzing DNA from populations with African, Asian, and European ancestry.[143] This chapter of HMP resulted in a haplotype map consisting of more than 1 million SNPs.[144] The Consortium's goal for Phase II, financed with $3.3 million in public-private support, is to create a map five-times denser.[145] Data is made available to the global science communities on an ongoing basis through free public databases.[146] HMP already has enabled considerable population-based genetics research through its contributions to cost-effectiveness.[147]

In addition to the science that HMP has generated, the project has made a tremendous bioethics contribution to the field of population genetics and genetics research in general. HMP has introduced a prototype ethics model for population genetics research with ancestry, race and

[142] Visit Haplotype site, *supra* note 34; NHGRI HapMap Page, *supra* note 35.

[143] Samples were collected from 270 people in these three groups: Africans (30 sets of familial samples from the Yoruba people of Ibadan, Nigeria); Japanese (45 unrelated individuals from the Tokyo area); Chinese (45 unrelated individuals from Beijing); and Europeans (30 trio samples from European-Mormon families in the U.S.). Visit *Haplotype Mapping*, *supra* note 52.

[144] NIH News Release, International HapMap Consortium Expands Mapping Effort (Feb. 7, 2005), *available at* http://www.genome.gov/13014173 (last visited May 27, 2007).

[145] *See id.* This support includes the Wellcome Trust, London, $624,000; Genome Canada/Genome Quebec, $260,000; Bristol-Myers Squibb Co., New York, $100,000; Pfizer Inc., New York, $100,000; Perlegen Sciences, at least $1.2 million (based on "in kind" services); and NHGRI, $1 million. *Id.*

[146] These databases include the HapMap Data Coordination Center, www.hapmap.org (last visited June 12, 2007), the NIH-funded National Center for Biotechnology Information's dbSNP, http://www.ncbi.nlm.nih.gov/projects/SNP (last visited June 6, 2007), and the JSNP Database in Japan, http://snp.ims.u-tokyo.ac.jp/ (last visited July 23, 2007).

[147] *See generally* Daar & Singer, *Pharmacogenetics*, *supra* note 105, at 243-244.

ethnicity implications.[148] The Ethics Committee for HMP, co-chaired by Professors Ellen Wright Clayton and Bartha Knoppers, has generated guidance and algorithms used in the project, which include obtaining group consent when practicable and appropriate.[149]

Another significant controversy in race-based genetics that has raised the volume of the debate was the Food and Drug Administration's approval of BiDil for treatment of heart failure specifically in African Americans ("blacks" is used on the label insert).[150] The decision, issued on June 23, 2005, was the first FDA approval of a pharmaceutical use limited to a specific racial or ethnic group.[151] The drug did not originate from a race-based population genetics methodology,[152] but it was approved based upon one—a study of 1,050 self-identified black patients with severe heart failure who had already been treated with the best available therapy.[153] According to the FDA, this study demonstrated that black patients on BiDil experienced a forty-

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[148] *See generally*, *Implications, supra* note 35. The HMP also has a staff committed to related ethical, legal, and social implications issues, which includes Vivian Ota Wang, Jean McEwen and Lisa Brooks. The staff may be contacted at:

National Human Genome Research Institute
National Institutes of Health
5635 Fishers Lane
Suite 4076, MSC 9305
Bethesda, MD 20892-9305
Phone: (301) 496-7531
Fax: (301) 480-2770

[149] *See generally* Clayton, *Implications, supra* note 35. *See supra* note 17.

[150] *See supra* note 112 and accompanying text. According to the BiDil package insert, "BiDil is indicated for the treatment of heart failure as an adjunct to standard therapy in self-identified black patients to improve survival, to prolong time to hospitalization for heart failure, and to improve patient-reported functional status." BiDil Package Insert at p. 9 (on file with author).

[151] *See* Kahn, *Racial Categories, supra* note 9, at 15-16; Hoffman, *Unraveled*, *supra* note 9, at 396; Rene Browser, *Race As A Proxy for Drug Response: The Dangers and Challenges of Ethnic Drugs*, 53 DEPAUL L. REV. 1111, 1112 (2004); Gregory M. Lamb, *A Place for Race in Medicine*?, THE CHRISTIAN SCI. MONITOR, Mar. 3, 2005, at 14.

[152] Two general population studies indicated no clinical benefit, but sponsors spotted a potential benefit in a subpopulation of subjects who self-identified as black. FDA News, *FDA Approves BiDil Heart Failure Drug For Black Patients* (June 23, 2005), *available at* http://www.fda.gov/bbs/topics/NEWS/2005/NEW01190.html (last visited July 12, 2007).

[153] *Id.*

three percent reduction in death, a thirty-nine percent decrease in hospitalization for heart failure compared to a placebo, and a decrease of heart failure symptoms.[154] Although the BiDil sponsor's methodology, data, and patent practice were challenged and criticized intensely in the law literature,[155] the FDA's decision stands and the underlying data has survived scientific and clinical scrutiny from the medical and science communities.[156]

Nevertheless, challenges from the law and social science communities linger. One concern is that, because members often identify with racial and ethnic groups strongly, they will demand drugs associated with their racial and ethnic group affiliations regardless of other good medicine considerations and options, and physicians will give into those demands.[157] Such a scenario could exacerbate standing differences in health care quality due to race-based medicine, as documented by the Agency for Health Care Research and Quality (AHCQ).[158] Another is that

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[154] *Id.*

[155] Professor Jonathan Kahn has challenged the integrity of re-analysis of the general population trial data and the sponsor's associated patent claim based upon the race-specific science findings, which extended patent protection of BiDil from 2007 to 2020 and made the large African-Americans trial and commercialization post-approval commercially viable. Kahn, *supra* note 9, at 15-16. *See also* Bhopal, *Responsible Use*, *supra* note 9. Professor Roberts has repeated Professor Kahn's concern and declared "race-based pharmaceuticals promise to be a lucrative field of invention." Roberts, *Legal Constraints, supra* note 9, at 528-529. However, it would not make economic sense for sponsors of pharmaceuticals to choose to limit their use to a particular race if they can demonstrate safety and efficacy in the general population. The scientific outcome of the African American clinical trial of Bidil supports the integrity of the underlying patent claim, and the patent system appears to have worked: a drug with clinical utility in African Americans which would not have been developed now is available to them and their doctors as a treatment option for a life-threatening condition. *See generally* Cohn, *Lessons*, *supra* note 9.

[156] *See generally* Cohn, *Lessons*, *supra* note 9; Bhopal, *Responsible Use*, *supra* note 9.

[157] Hoffman, *Unraveled, supra* note 9, at 419-426.

[158] *Id.* AHRQ has documented significant treatment disparities for major diagnostic related groups ("DRGs") where there was a baseline of coverage and access to care. In comparison with Caucasian patients in the same DRGs, doctors provided significantly fewer and less aggressive treatments for patients with ethnic and racial affiliations. *See* AHRQ, National Health Care Disparities Report 2006 (2006), *available at* http://www.ahrq.gov/qual/nhdr06/nhdr06.htm (last visited July 17, 2007). In fact, tremendous disparity in health care treatment for common and serious conditions has been documented in the U.S., causing some to suggest that, rather than an art or science, medicine in the U.S. is guesswork. John Carey, *Medical Guesswork: From Heart Surgery to Prostate Care, the Health Industry Knows Little About Which Common Treatments Really Work*, 3986

the biopharmaceutical sector will accomplish the same commercial responsiveness through aggressive marketing, thereby exploiting racial and ethnic groups and detracting from their health care.[159] Professors Lillquist and Sullivan suggest that the medical community will not move beyond race-specific data—meaning they will not engage in significant off-label use in patients with the disease but without the race affiliation—to the potential medical disadvantage of other populations.[160] Others worry about the success of BiDil encouraging more race-based research and exploitation of groups associated with the clinical study on African Americans.[161]

Dr. Jay Cohn, Director of the Rasmussen Center for Cardiovascular Disease Prevention at the University of Minnesota and a renowned clinical researcher, has responded to these challenges to BiDil with arguments based in science and a focus on good medicine.[162] Dr. Cohn was the lead investigator and inventor on a patent for BiDil (combining isosorbide dinitrate and

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BUS. WK. 72-84 (May 29, 2006). Presumably, over time, increased precision from genomics will spill into medicine and lessen these disparities.

[159] Question and answer session of *Race-Based Research Session*, Health Law Teachers Annual Meeting (June 2006) (attended by the author). It is important to note, however, that the sponsor of BiDil first attempted to establish the safety and efficacy of its drug in the general population, which proved unsuccessful. FDA approval for use in the general population accompanied with the release of data suggesting greater efficacy in African Americans would have proven a more profitable market strategy, but one not supported by the clinical data. *See supra* notes 111-112 and accompanying text. It is unlikely that biopharmaceutical companies will intentionally limit the scope of their market approvals, for they have been hesitant even to introduce pharmacogenomic data out of fear that the use of their products will be conditioned on genetic screening and the presence of particular genetic alleles. *See generally* Janet Woodcock, *FDA Policy on Pharmacogenomic Data in Drug Development*, 66 LA. L. REV. 91 (2005).

[160] *See also* Lillquist & Sullivan, *supra* note 9, at 542. However, the medical profession does engage in extensive off-label use, and the sponsors of pharmaceuticals limited to a specific racial group would have every economic incentive to undertake post-marketing clinical research to broaden their market access—i.e., find safety and efficacy in additional populations.

[161] Prof. Troy Duster, Dinner Presentation, "The Globalization of Pharmaceutical Development: Race, Markets and Ethics" (Mar. 16, 2006, Santa Clara College of Law) (addressing the "shift from genetic sameness to individuality" pre- and post-HGP); Troy Duster, *Lessons from History: Why Race and Ethnicity Have Played a Major Role in Biomedical Research,* 34 J.L. MED. & ETHICS 487 (2006); Troy Duster, *Race and Reification in Science*, 307 SCI. 1050, 1050 (2005).

[162] Cohn, *Lessons*, *supra* note 9, at 1.

hydralazine).[163] As stated by Dr. Cohn, from the perspective of a medical doctor and clinical investigator,

> The debate . . . should not be over the existence of population differences, but how to describe those differences with more precision. Those who argue against our current approach may wish that differences did not exist, but they do. They are identified by statistical differences among definable populations in prevalence and physiological mechanisms. These population differences cannot in the first instance be classified as genetic, geographic, or environmental. They are observed differences in populations identified by a variety of demographic criteria. Railing against what some claim are misguided efforts to use racial, ethnic, or geographic distinctions does not make the differences disappear. We should be working toward better approaches in dealing with the differences, not raising legal and moral arguments, as Professor Roberts has, claiming that any effort at distinction is wrong.[164]

IV. An Illustrative Case Study in Population Genetics

Responsible biobanking in any group introduces the potential to benefit the group under study regardless of how that group is organized. These benefits include opportunities to increase the level of communication between the group and the research community to raise sensitivity to the group's particular social and cultural norms, to participate at the forefront of genetics research, to control the terms of that participation, and to realize commercial benefits and scientific and medical returns. More generally, the endeavor advances bioethics through population genetics case study applications and, scientifically and medically, introduces the possibility of benefiting humankind well beyond the group under study due to the youth and genetic sameness of our species.

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[163] Wolf, *Debating Use, supra* note 52, 483.

[164] Cohn, *Lessons*, supra note 9, at 556. Professor Roberts proposes applying law to "discourage or prohibit the use of `race' as a genetic or biological category, but encourage or require the use of `race' as a sociopolitical category to understand and investigate ways to eliminate disparities in health status, access to health care, and medical treatment." Roberts, *Legal Constraints*, *supra* note 9, at 532-533.

To illustrate these points, the scientific complexities and unpredictability of population genetics, and the potential benefits of any serious, responsible population genetics undertaking, consider the incidents of dwarfism embodied by Matt Roloff, his wife Amy, and their son Zach. The Roloff case study places population genetics in a tangible context that utilizes a genetic disease-based organizing criteria much more acceptable to opponents of race and ethnicity based genetics research. The case study also is responsive to some of the fundamental challenges to race and ethnicity-based genetics research raised by these opponents. First, it demonstrates the extent to which groups organized by genetic disease may be no more homogenous than groups organized by race and ethnicity, and even less so. Second, this case study underscores that, regardless of the collection criteria, responsible biobanking may be advantageous on multiple levels, including group communication, empowerment, and benefits.

Matt, Amy, Zach are dwarfs who are featured in the television show "Little People, Big World" along with Zach's siblings—Jeremy, Molly, and Jacob—who do not have dwarfism.[165] To the casual observer, the Roloffs represent an extreme in genetic homogeneity given their biological ties to each other and the incidence of dwarfism in their immediate family. Many would be comfortable extending this perceived genetic grouping to encompass other people with

[165] For information about the show and the Roloff family, visit the Roloff Family internet site at http://www.mattroloff.com/ (last visited June 9, 2007). Slide Show, *Dwarfism*, http://www.mansfield.osu.edu/~jbradley/102Ppts/Dwarfism.ppt. (last visited Feb. 7, 2007). Information about DD is available at Little People of America Online, FQs, http://lpaonline.org/resources_faq.html (last visited May 28, 2007); Luise Bonafe & Andrea Superti-Furga, *Diastrophic Dysplasia*, (posted Nov. 15, 2004), *available at* Gene Review, http://www.genetests.org/query?dz=diastrophic-d (last visited May 24, 2007). *See also* PBS, *What is Dwarfism*, *available at http*://www.pbs.org/pov/pov2005/bigenough/special_dwarfism.html (last visited Apr. 16, 2007).. *See generally* PBS, "Big Enough", aired Aug. 8, 2006; *Clinical Implications of Basic Research: The Genetic Basis of Dwarfism*, NEW ENG. J. MED., vol. 332, no. 1, 58-59 (Jan. 5, 1995). Information about achondroplasia dwarfism is available at Clair A. Francomano, Achondroplasia, *available at* GeneReviews, http://www.geneclinics.org/profiles/achondroplasia/details.html (updated Jan. 9, 2006) (last visited Feb. 7, 2007); March of Dimes, *Quick Reference and Fact Sheets: Achondroplasia, available at* http://www.marchofdimes.com/professionals/681_1204.asp (last visited Feb. 7, 2007). The popularity of Little People, Big World has inspired "The Foos Family," the real TV profile of a family with dwarfism throughout. For information about the Foos, visit http://www.advancedmedical.tv/shows/mtf.htm#synapsis (last visited Apr. 14, 2007).

dwarfism given that it is commonly recognized as a genetic condition. However, there are more than two hundred forms of dwarfism, which appears throughout recorded history and affects both sexes and all races.[166] Matt has diastrophic dysplasia ("DD"), the third most prevalent type of dwarfism, which occurs once in every 110,000 births in the U.S.[167] Although DD arises in all races and sexes, there is a higher incidence rate in Finland.[168] Symptoms associated with DD include a cleft pallet, a "hitchhiker thumb" (a thumb permanently distended), club feet, and other orthopedic and joint problems that impact shoulders, elbows, hips and knees.[169] The gene for DD, SLC26A2, is on chromosome 5q32-q33.1 and it is recessive.[170] A parent may carry the gene but not have DD, and both parents must carry the gene—not necessarily have DD—to have a child with DD.[171] Typically, children with DD are born to two parents who each carry the DD gene but do not have DD.[172] Under these circumstances, there is a fifty percent chance that each child will be a carrier of DD but not have dwarfism, a twenty-five percent chance that the child

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[166] Official The Learning Channel (TLC) homepage for "Little People, Big World", *available at* http://tlc.discovery.com/fansites/lpbw/lpbw.html. (last visited Mar. 19, 2007).

[167] Little People of America Online, FQs, http://lpaonline.org/resources_faq.html (last visited June 2, 2007). Information about DD is available at Diastrophic Dysplasia, Genetics Home Reference, *at* http://ghr.nlm.nih.gov/condition=diastrophicdysplasia;jsessionid=A16D3AB4538E86E2F34B6065DCEDA343 (last visited Feb. 7, 2007); Greenberg Center for Skeletal Dysplasis, *available at* http://www.hopkinsmedicine.org/greenbergcenter/tutorial.htm (updated Sept. 12, 2002) (last visited Feb. 7, 2007). The most common form of dwarfism, achondroplasia, occurs in one per 26,000-40,000 births. *Id.* The entire world-wide dwarf population was estimated to be 6,250,000,000 in 2002. Dwarfism.Org, at http://www.dwarfism.org/ (last visited June 7, 2007).

[168] Greenberg Center for Skeletal Dysplasis, *available at* http://www.hopkinsmedicine.org/greenbergcenter/tutorial.htm. (updated Sept. 12, 2002) (last visited Feb. 7, 2007).

[169] *Id.*

[170] *See generally id.*

[171] http://www.pixelscapes.com/ddhelp/DD-booklet/ (last visited Apr. 14, 2007).

[172] *See generally* Bonafe & Andrea, *supra* note 124.

will have DD (have a pair of SLC26A2 genes, one from each parent), and a twenty-five percent chance that the child will be unaffected.[173]

Matt's wife Amy and son Zach have achondroplasia ("AP"), the most prevalent form of dwarfism, which occurs in one out of every 25,000 births and, like DD, affects both sexes and all races.[174] However, the gene for AP, FGFR3, is dominant, so it is symptomatic in everyone who carries FGFR3.[175] Eighty percent of AP children are born to parents of normal stature, meaning that AP usually is the result of a de novo gene variation.[176] When both parents have AP, each carries the FGFR3 gene and its non-AP counterpart, meaning that they have a fifty percent chance of having a child with AP (one FGFR3 gene paired with a non-AP counterpart), a twenty-five percent chance of having a child without AP (two non-AP genes), and a twenty-five percent chance of having a child with two FGFR3 genes.[177] This latter condition, known as homozygous AP or double homozygosity, usually is fatal.[178]

The Roloffs had no chance of having a child with DD because Amy is not a carrier of SLC26A2.[179] Matt does not have AP and does not carry FGFR3. Therefore, with each pregnancy, Amy and Matt had a fifty percent chance of parenting a child with AP, and all the Roloff children—including Jeremy, Molly, and Jacob who are of normal stature—are carriers of

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[173] *See generally id*.

[174] *See generally* A Francomano, *GeneReview*, *supra* note 124.

[175] *See id*

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[176] *See id.*

[177] *See id.*

[178] *See id.* There are exceptions, however, such as one of the children in the Foos family. *See supra* note 123.

[179] Roloff Family, Internet site, *supra* note 124.

DD.[180] Among Matt, Amy, and Zach, all are dwarfs according to phenotype and, therefore, they share many challenges posed by their environment on a daily basis—for example, extreme stress on their hips and knees due to the size of their heads and torsos in relation to their limbs. Their symptoms overlap significantly, though some are distinguishable—for example, the severity of Matt's joint and orthopedic problems associated with DD, which cause him to rely upon walkers and occasionally electronic ambulatory machinery for movement.[181] However, genetically, their DD and AP differences make them highly distinguishable. Combining these fundamental genotype and phenotype characteristics, there is a lot of genetic complication within the Roloff family: according to phenotype, three incidents of dwarfism among a family of six, with both overlapping and distinguishable symptoms; two forms of dwarfism with completely different genetic causes, one a dominant gene and the other a recessive gene, on different chromosomes; and four children who are carriers of DD, including three who are of normal stature.[182]

Although the societal perceptions used to group the Roloffs and people with dwarfism in general are at best an exaggeration of genetic reality, the Roloffs could advance the realization of bioethics principles in population genetics and make significant contributions to genetics research in and beyond dwarfism. Imagine that the Roloffs decide to use their celebrity to advance research on dwarfism by establishing littlepeopleBiobank ("lpBiobank"), a biobank of families in the U.S. with at least one occurrence of a child with dwarfism.[183] Little people with

[180] With each pair of genes, offspring get one version of the relevant gene from each biological parent. Matt only has DD genes to pass onto each child.

[181] TLC Homepage, *supra* note 124.

[182] *See supra* notes 125-131 and accompanying text.

[183] Biobanks are the collection and organization of biological samples, medical information, and sometimes environmental data for research use. For a comprehensive treatment of biobanking, see generally Symposium: Regulation of Biobanks, 33 J. L. Med. & Ethics 1-188 (Mark Rothstein & Bartha Knoppers eds., 2005). A number of governments have undertaking biobanking initiatives, including Estonia, Iceland, Japan, Singapore, Sweden, and

dwarfism in the United States are highly organized on the national, regional, and local levels through the not-for-profit organization Little People of American ("LPA"), and they share strong social group identification.[184] Throughout its half-century of existence, LPA has united the community through its many social activities, including conferences and other events, and by serving as an information resource.[185] LPA has earned the trust of its members, as evidenced through their active and ongoing participation.[186] The organization of the group and its governance structure suggests a means to work through bioethics issues such as individual consent, group impact, and group consent with sensitivity and insight.[187] LPA also could provide a means to identify acceptable conditions for research protocols and workable terms for technology transfer around the lpBiobank, such as the requisite quid pro quo for researcher access.[188] Presumably the scope of the lpBiobank, both in terms of samples and accompanying medical information, and the sophistication of its organization and ability to meet individual researcher needs would be somewhat proportional to the group's bargaining power with researchers and research institutions.[189]

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the United Kingdom Representatives from these biobanks were gathered in August 2007 for the Meeting to Launch the Taiwan Biobank, in which the author participated. Proceedings, Meeting to Launch the Taiwan Biobank, Academia Sinica, Taipei, Taiwan, Aug. 12-15, 2007.

[184] For more information, visit LPA Online at http://www.lpaonline.org/lpa_intro.html (last visited Feb. 9, 2007). LPA membership to which is offered to individuals 4' 10'' and shorter. *See id.*

[185] *See supra* note 143.

[186] LPA has over fifty local chapters which meet monthly and hosts a range of activities, including an annual week-long national conference that typically draws 1,000 or more attendees. Visit LPA Online at http://www.lpaonline.org/lpa_intro.html (last visited Feb. 9, 2007).

[187] *See generally* Henry Greely, *Population Participation and Other Factors that Impact the Compilation and the Utility of Resulting Databases*, 66 LA L. REV. 79 (2005). *See also* Bartha Maria Knoppers, *Biobanking: International Norms*, 33 J. L. MED. & ETHICS 7, 10 (2005).

[188] Malinowski, *Technology Transfer, supra* note 37, at 59.

[189] For an excellent case study in biobanking, see the discussion of Pseudoxanthoma Elasticum (PXE) in David E. Winickoff, *Governing Population Genomics: Law, Bioethics, and Biopolitics in Three Case Studies*, 43

If lpBiobank were formed, the basic phenotype characteristics associated with dwarfism would unite people who embody a range of distinct genes that cause their distinguishable version of the condition—meaning a phenotypically homogenous group, idiosyncratically so to the layperson, that actually embodies a lot of genetic diversity.[190] It is theoretically possible that there could be less overall genetic commonality among the lpBiobank members than among another group that, based on phenotype, appears more genetically diverse to society. For example, there may be more genetic commonality among the one hundred and seventy-five 1Ls at Yale Law School, a heavily screened group selected, among other things, to achieve diversity as defined by society (or at least law school administrators).[191] Greater genetic commonality might also be found between the subpopulation of the lpBiobank with DD and the Yale 1Ls, for SLC26A2 is but one of the 3,000,000 distinct DNA variants estimated to separate any two unrelated human beings.[192] Similarly, the females in lpBiobank may share more overall genetic commonality with the first year class at Wellesley College, an all-women school, than with their male lpBiobank co-members. Also, given the higher incidence of DD in Finland, the DD members of the group may share more overall genetic commonality with the population of one

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JURIMETRICS J. 187, 222-226 (2003). *See generally* Malinowski, *Technology Transfer, supra* note 37 (discussing PXE and other case studies). Another excellent case study of how groups may use biobanking to advance research they desire is that of The Pan Asian Initiative, which is addressed *infra* in notes 112-117, 213 and accompanying text.

[190] *See generally* LPA Online at http://www.lpaonline.org/lpa_intro.html (last visited Feb. 9, 2007); PBS, *What is Dwarfism*, *available at* http://www.pbs.org/pov/pov2005/bigenough/special_dwarfism.html (last visited Aug. 6, 2007).

[191] This conclusion is suggested by the body of work generated by Luca Cavalli-Sforza. *See supra* notes 22-23 and accompanying text.

[192] *See supra* note 42 and accompanying text.

or more of the small, scattered, isolated settlements in Northern and Eastern Finland than with their lpBiobank counterparts.[193]

Nevertheless, lpBiobank may prove a valuable resource to develop bioethics algorithms for researchers working on DD and AP and population genetics in general. Moreover, even if the lpBiobank membership were limited to people with DD and AP dwarfism, researchers working on other forms of dwarfism also may take interest because some of the more fundamental phenotype characteristics (shared cellular differentiation) of dwarfism transcend the groupings. Comparing and contrasting the expression of a particular phenotype characteristic among subpopulations in the lpBiobank could prove a means for identifying and understanding the intricate pathways of gene and cellular expression that connect the common phenotype characteristic to the highly distinguishable genetic triggers for dwarfism. In fact, because members of the human species are 99.9 percent the same genetically, the lpBiobank could prove useful for a wide array of genetics research not necessarily associated with dwarfism depending on how extensive the biobank is and the type and quantity of medical information available to researchers. It follows that research findings by those working within the lpBiobank may readily transcend the DD population—for example, fundamental understanding about genetic expression and cellular differentiation in the general human population. Moreover, in addition to any direct benefits to members of lpBiobank, the endeavor could contribute immensely to population genetics in general through development of thoughtful recruitment, consent algorithms, and technology transfer precedents. Working within a group defined by society that self-identifies would provide a means to insightful deliberation of group impact. LpBiobank also might

[193] Today, almost twenty percent of Finland's population lives in such settlements. *See* Andra Aldea-Partoren, Esko Lehto, & Jukka Oksa, *Access to Services in Rural Finland: Examples from Esko Lehto and Jukka Oksa* (Oct. 2004), *available at* http://cc.joensuu.fi/~alma/deserve/raportit/rep04-finland.doc (last visited June 18, 2007).

contribute to genetics research and society in general by inspiring similar biobank efforts among other groups, thereby creating resources needed to accelerate the process of making medical sense out of the human genome map.

V. A Proposal in Favor of Race-Based Genetics Research

The reckless words of Dr. Watson published by the *London Sunday Times* on October 14, 2007[194] speak to the dangers of using social science to make conclusions about human genetics that are not substantiated by existing genetic science.[195] This is a lesson learned over the last century at tremendous cost to human life, extraordinary human suffering, and incalculable lost research opportunities when Charles Davenport, a Cold Spring Harbor predecessor of Dr. Watson, established the Station for Experimental Evolution at Cold Spring Harbor and the Eugenics Record Office next door.[196] Dr. Davenport used Cold Spring Harbor and the Eugenics

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[194] *See supra* note 1 and accompanying text. According to the New York Times,

> In announcing his retirement, in an oddly oblique e-mailed dispatch, he expressed hope that the latest biological research, at Cold Spring Harbor and elsewhere, would lead to treatments for mental illness and cancer. Invoking his `Scots-Irish Appalachian heritage' and a faith in reason and social justice passed on by his parents, he sounded sad and confused, as though this time he had succeeded in dumbfounding even himself.

George Johnson, *Bright Scientists, Dim Notions*, NEW Y. TIMES, Oct. 28, 2007, at 5.

[195] Although this author's professional discipline is legal academia and he approaches this material from a base in the social sciences, holds deep respect for quality social science research, and appreciates that such research may help to frame meaningful natural science research protocols, he is adamantly opposed to overreaching from the social sciences to suggest natural science genetic truths. Last century's experience with eugenics makes this author extremely uncomfortable with some social science-based behavioral biology, which gained significant popularity in legal academia in conjunction with the advancement of natural genetics science through HGP. *See, e.g.*, Owen D. Jones & Timothy H. Goldsmith, *Behavioral Biology,* 105 COLUMBIA L. REV. 405 (2005). Related emerging fields that invite speculation about natural science genetics far removed from established genetics science research include "Law and Emotions" and some social science approaches to neurogenetics, a genetics science priority set by Dr. Watson for Cold Spring Harbor prior to his resignation. This is, in the spirit of *The Bell Curve* (see supra notes 38-41 and accompanying text), potentially reaching too far beyond established natural science, inviting the substitution of extensive speculation for established genetics science, and perhaps influencing law and policy based upon that speculation in areas fundamental to the human condition and society. *See* Grubbe, *Elementary DNA*, *supra* note 1. "Law and Emotions" is the subject matter of a major conference hosted jointly by Vanderbilt University and the School of Law (Boalt Hall), which will take place Feb. 8-9, 2007. For more information, visit Law and Emotions, at http://law.vanderbilt.edu/academics/scholarly-events/past-events/law-and-the-emotions/index.aspx (last visited Oct. 26, 2007).

[196] *See* Malinowski, *Choosing, supra* note 18, at notes 25-181 and accompanying text. The Station was seeded in 1904 by a $10 million grant from the Carnegie Institute of Washington, a grant that surpassed the total endowment

Record Office to collect shoddy data that substantiated centuries of social observation about the human condition, however tainted by prejudices.[197] His work gave credibility to a eugenics movement that started with a sputter of "fitter families contests" in America's heartland but then roared into an international movement that included involuntary sterilization legislation and forced sterilizations in the United States and beyond, provided some precedent for the murder of millions the Third Reich deemed "undesireables", and served as a pretext for the torture of tens of thousands, including many children, under the guise of medical research.[198]

The immediate outrage of today's genetics and broader natural science communities in response to Dr. Watson's comments and the global resonation of that protest attest to the extent to which the field of human genetics has evolved over the last century, even if some of Dr. Watson's thinking has not.[199] The lines between natural science in genetics and the social sciences must be respected. Crossing them is essential, but that must be done with thoughtfulness and professionalism—for example, the Ethical, Legal, and Social Implications Program counterpart to HGP.[200] Just as social science findings should not be substituted for established genetic science truths, the legitimacy of responsible genetic science research should not be undermined scientifically where the driving force is actually to preempt avoidable social harms. There simply is too much potential benefit to human health at stake to make the lines that

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for research in United States universities, while the Records Office was financed through generous support from Ms. Mary Harriman, a philanthropic socialite. *Id.* at notes 33-35.

[197] *Id.* at notes 37-38 and accompanying text.

[198] *Id.* at notes 68-101 and accompanying text.

[199] *See, e.g., supra* notes 2-3 and accompanying text.

[200] Dr. Watson himself and the other founders of the HGP recognized the necessity of accompanying genetics research with the social science disciplines to probe ethical, legal, and social implications of the underlying research the same, and ELSI has proven an essential counterpart. Today, there are ELSI counterparts to virtually all major genetics research undertakings, including HMP. For information about ELSI, visit the site of the Human Genome Research Institute at http://www.genome.gov/ (last visited Oct. 26, 2007).

faint and fluid. Identifiable and ominous potential social harms necessitate caution, but the answer is to move research forward thoughtfully and responsibly with the strong presence of responsive law and policy.

As articulated thoughtfully by Dr. Raj Bhopal,[201] "Race and ethnicity are closely related, contentious concepts that have been abused and misinterpreted through history, but have a vast potential for good, at least in the health sciences."[202] Similarly, as observed by Dr. Margaret Winker, Deputy Editor of the Journal of the American Medical Association, "Despite the many difficulties posed by categorizing race, in some instances it can be important to assess race and ethnicity."[203]

Race and ethnicity are as real socially and culturally as genetics is scientifically[204] and "[i]t is well known that disease does not affect the population equally[.]"[205] The reality of these constructs is made evident by the reactions they compel, their impact on human history, and their influences on culture, society, and how individuals perceive themselves and others.[206] Race and ethnicity influence where people live, how they live, what they consume, and whom they partner

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[201] Dr. Bhopal, M.D., M.P.H., FRICP (E), CBE, became Professor and Head of the Department of Epidemiology and Public Health at Newcastle University in 1991, Alexander Bruce and John Usher Professor of Public Health at the University of Edinburgh in 1999, and Head of the Division of Community Health Sciences 2000-03. He is Chairman of the Steering Committee of the National Resource Centre for Ethnic Minority Health, Scotland, and honorary consultant in public health to the Lothian Health Board.

[202] Bhopal, *Responsible Use*, *supra* note 9, at 500.

[203] Winker, *Race and Ethnicity in Medical Research: Requirements Meet Reality*, 34 J. L. MED. & ETHICS 520, 521 (2006).

[204] *See supra* note 14 and accompanying text. *See* Ossorio, *About Face, supra* note 2, at 278. *See generally* Working Group, *Use*, *supra* note 13.

[205] Neil Risch, *Dissecting Racial and Ethnic Differences*, 354 NEW ENG. J. MED. 408 (2006). *See also* notes 92-99 and accompanying text. *See generally* Cohn, *Lessons*, *supra* note 6; Bhopal, *Responsible Use*, *supra* note 6.

[206] *See id.*

and propagate with—often significantly.[207] Moreover, they have done so for many generations; historically, race and ethnicity have profoundly impacted what environmental exposures people have been subjected to, and their influence continues. "Put simply, place has a huge impact on health for a variety of reasons. Indeed, increasing globalization may weaken the cumulative effects that place has on health. Nonetheless, many people still reside and work in the same place for many years. This pattern is particularly pronounced in rural areas."[208] Moreover, the populations of developing economies more heavily influenced by ancestry, race, and ethnicity than the population in North American Europe have been largely excluded in biomedical R&D even when they are recipients of resulting biopharmaceuticals, and many of their most pressing health care needs continue to be unmet and relatively low priorities in ongoing biomedical R&D.[209]

Completion of the map of the human genome has raised appreciation for the extent to which, especially over time, shared environmental exposures can make a collective genetic difference—perhaps most notable through advancement in the field of epigenetics.[210] The map has illuminated a universe of intricacies, complexities, and subtleties in human genetics beyond the appreciation of most prior to its completion.[211] Consequently, the map has shifted perspective and increased comprehension of the influence of environment exposures in the study

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[207] This point has been persuasively articulated by Dr. Bhopal in the context of epidemiology and conceded by Professors Lillquist and Sullivan. *See generally* Bhopal, *Responsible Use*, *supra* note 6. *See* Sullivan & Lillquist, *Legal Regulation*, *supra* note 9, at 537-538.

[208] Foster, *Analyzing Race*, *supra* note 9, at 508.

[209] *See generally* Daar & Singer, *Pharmacogenetics*, *supra* note 105, at 242-246.

[210] *See supra* notes 21-22, 53, 117, 110 and accompanying text.

[211] *See supra* notes 38-40, 102-118 and accompanying text.

of gene expression, and it has inspired research within populations grouped over time by social and cultural notions of race and ethnicity.[212]

The approach is supported by significant past success engaging in genetics research within groups identified by the social constructs race, ethnicity, and religion, including the country members of The Pan Asian Initiative and their populations,[213] as well as populations of Ashkenazi Jews, Amish, and Mormons within the U.S.[214] There are ample examples of disease rate differences documented with sound epidemiological data that correlate with groupings based upon race and ethnicity.[215] The intricacies of human genetics have shifted much genomics research up to the population level on par with traditional epidemiological research.[216] Moreover, biotechnology has begun to introduce a generation of biopharmaceuticals developed around specific genetic alleles,[217] including precedent for developing and delivering medicines

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[212] The most notable example is HMP. *See supra* notes 100-106 and accompanying text.

[213] *See supra* note 112-117 and accompanying text.

[214] *See supra* notes 95-98, 102-118 and accompanying text.

[215] *See generally* Daar & Singer, *Pharmacogenetics*, *supra* note 105, at 242-246; Bhopal, *Responsible Use*, *supra* note 6; Working Group, *Use*, *supra* note 14. *See also infra* notes 95-98 and accompanying text.

[216] *See supra* notes 32-50 and accompanying text.

[217] *See generally* Kristin Cho, *Personalized Prescriptions, Legal Actions Will Help Determine the Success of Using Genetics to Improve Drug Treatments*, 92 ABA J. 42 (Sept. 2006). One of the most prominent examples is over expression of the Her2neu protein associated with an aggressive form of breast cancer, which inspired development of the drug Herceptin and an associated genetic test. *See generally* ROBERT BAZELL, HER-2: THE MAKING OF HERCEPTIN, A REVOLUTIONARY TREATMENT FOR BREAST CANCER (1998). A recent example is FDA's market approval of a genetic test that predicts the likelihood of breast cancer returning within 5-10 years after an initial cancer. FDA News, *FDA Clears Breast Cancer Specific Molecular Prognostic Test* (Feb. 6, 2007), *available at* http://www.fda.gov/bbs/topics/NEWS/2007/NEW01555.html (last visited May 12, 2007). This is the first test cleared by the FDA that profiles genetic activity. *Id*. Two additional recent examples include response differences to Warfin, a drug used to stop blood clots from forming and growing, associated with particular alleles and the same regarding mercaptopurine (6MP), a drug used in the treatment of acute lymphoblastic leukemia--a childhood leukemia. *See generally* Jeffrey L. Moe, *Commercialization Considerations for Individualized Diagnostic and Drug Therapies Resulting from Pharmacogenomics*, 66 LA. L. REV. 103 (2005). However, the biopharmaceutical sectors have demonstrated reluctance introducing pharmacogenomic data, and the medical profession has demonstrated some reluctance working predictive genetic testing into the delivery of care. *See generally id*; Woodcock, *Pharmacogenomic Data*, *supra* note 118. Physicians balked at a required 6MP test due to cost and confidence that they could identify slow metabolizers of the drug simply by monitoring blood levels. *See id.*

with attention to genetic differences that are associated with race.[218] Race-based research is generating results—increased understanding about diseases, such as MS,[219] and the means to make biopharmaceuticals help and avoid harm in groups organized by race and ethnicity.[220]

The law and social science opponents to race-based genetics research challenge the soundness of the underlying science.[221] They also draw heavily from the legacy of use of classification based upon race and ethnicity, both inside and outside of the biomedical context, to discriminate and exclude and, when combined with science, to exploit and affirm racist notions of inferiority.[222] Rounding up and focusing upon this legacy, a strong argument can be made that the social dangers of race-based genetics research are too great to justify, especially given alternative research methodologies—most notably, disease based and allele-specific population genetics.[223]

Incendiary debate and ongoing critiques, especially in an age of global communication and unprecedented transparency, police use of race-based genetics research and the integrity of associated research.[224] The professional consequences to Dr. Watson from his words attest to the same.[225] This check accompanies a trilogy of considerations that support responsible race and

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[218] See the discussion of BiDil, *supra* notes 109-123 and accompanying text.

[219] *See supra* notes 105-108.

[220] *See supra* notes 122, 153-156 (Bidil), 109-117 (Theraflu in Asian populations) and accompanying text.

[221] *See supra* notes 53-57 and accompanying text.

[222] *See supra* notes 57-58 and accompanying text. *See, e.g.*, Roberts, *Legal Constraints*, *supra* note 9.

[223] *Cf.* Lillquist & Sullivan, *Regulations, supra* note 9; Lillquist & Sullivan, *Racial Profiling, supra* note 9; Hoffman, *Unraveled*, *supra* note 9.

[224] *See supra* notes 8-9 and Part III.

[225] *See supra* notes 1-3 and accompanying text.

ethnicity-based genetics research, each of which is discussed below. First, strict adherence to thoughtful application of bioethics law and policy demands maximum communication with potential research subjects and full consideration of the impact of proposed research on study participants.[226] Recognition of race and ethnicity from the individual subject's perspective—sensitivity towards an individual's association with a particular race and the impact of race and ethnicity on one's self-identification—is fundamental to maximize communication and fully assess the impact upon potential subjects, both individually and collectively.[227] Second, directly recognizing, addressing, and understanding race and ethnicity is a means to confront and offset a legacy of discrimination through responsible inclusion in biomedical research, which is consistent with the pragmatic exercise of sample collection so necessary in an age of population genetics.[228] Third, advancement of responsible race and ethnicity-based genetics research is consistent with the science arguments of its opponents as well as its proponents.[229]

A. Bioethics

The National Institutes of Health (NIH), the Food and Drug Administration (FDA), and institutional review boards (IRBs) should scrutinize research protocol proposals for race-based

[226] *See infra* Part V.A.

[227] As recognized by the American Medical Association Council on Ethical and Judicial Affairs, "The patient's right of self-decision can be effectively exercised only if the patient possesses enough information to enable an intelligent choice." Statement of the American Medical Association Council on Ethical and Judicial Affairs (adopted by the House of Delegates, Mar. 1981), *available at* http:/www.ama.-assn.org/ceja (last visited July 12, 2007). *See generally* CARL. H. COLEMAN, JERRY A. MENIKOFF, ET AL., THE ETHICS AND REGULATION OF RESEARCH WITH HUMAN SUBJECTS (2005).

[228] *See infra* Part V.B.

[229] *See infra* Part V.C.

genetics research and oversee the research they enable to ensure compliance with regulations to protect human subjects.[230] Existing law requires nothing less.[231]

The regulations to protect human subjects favor race consciousness over race neutrality in fundamental ways. First, population genetics necessitates the collection of large numbers of samples with accompanying medical information.[232] The connection to medical information means that samples are identifiable, even if encrypted, which triggers the informed consent requirement.[233] Voluntary, informed consent is the touchstone tenet of applied bioethics, as recognized in the Nuremberg Code,[234] Declaration of Helsinki,[235] and Belmont Report,[236] and as codified in U.S. law under the Common Rule[237] and FDA regulations.[238]

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[230] The Common Rule requirements are triggered whenever research is federally funded, or conducted by an institution that receives federal funding and has filed an assurance that it will conduct all research in a manner that complies. *See generally* Common Rule, 45 C.F.R. § 46 (2005), and separate Food and Drug Administration regulations, 21 C.F.R. § 50.20 (2005). *See also* Bonnie M. Lee, U.S. Food and Drug Administration, *Comparison of FDA and HHS Human Subject Protection Regulations*, 2000, *available at* http:// www.fda.gov/oc/gcp/comparison.html (last visited June 7, 2007); Food and Drug Administration regulations, 21 C.F.R. § 50.20 (2005). *See also* Bonnie M. Lee, U.S. Food and Drug Administration, *Comparison of FDA and HHS Human Subject Protection Regulations*, 2000, *available at* http:// www.fda.gov/oc/gcp/comparison.html (last visited June 9, 2007); Coleman, *supra* note 173.

Field Code Changed

[231] *See id.* For guidance on application of human subjects protection regulations, see NIH, Research on Hman Subjects, *available at* http://www.cdp.ims.nci.nih.gov/brochure.html (last visited May 7, 2007). *See also* the Office for Human Subjects Research Protections, Human Subject Regulations Decision Charts, *available at* http://www.hhs.gov/ohrp/humansubjects/guidance/decisioncharts.htm (last visited May 7, 2007).

[232] Yoon, *Prediction, supra* note 48. *Cf generally* MARTIN & MORRISON, *supra* note 38.

[233] The requirements are triggered when samples are identifiable, even if encrypted, but IRBs may wave the requirement where subjects are exposed to minimum risk. *See* Decision Charts, *supra* note 177.

[234] The Nuremberg Code, in 2 Trials of the War Criminals Before the Nuremberg Military Tribunals Under Control Council Law No. 10, 181-82 (Government Printing Office, 1949), *available at* http:// www.hhs.gov/ohrp/references/nurcode.htm (last visited May 12, 2007).

[235] World Med. Ass'n, Declaration of Helsinki 1964), http:// www.wma.net/e/policy/pdf/17c.pdf (last visited May 12, 2007).

[236] Ethical Principles and Guidelines for the Protection of Human Subjects of Research, at http:// ohsr.od.nih.gov/mpa/belmont.php3 (Apr. 18, 1979) (last visited May 17, 2007).

[237] *See generally* 45 C.F.R. pt. 46 (2005).

[238] 21 C.F.R. §§ 50, 56 (2005).

The realization of informed consent presupposes meaningful communication—a meeting of the minds between study sponsors and subjects.[239] Recognition of race and ethnicity from the individual subject's perspective—sensitivity towards whether the individual self-identifies with a particular race or not—is fundamental to maximize communication and to fully assess the impact upon potential subjects, both individually and collectively. As explored through Critical Race Theory in the law literature for decades[240] and in the social sciences for much longer,[241] race and ethnicity often have a profound impact on how people self-identify, interpret information, and relate with others and society in general.[242] "Arguably, classifying people using large-scale categories such as `African-American' or `Native American' can be helpful in understanding community practices with respect to external sources of care, because such practices are based on conditions of discrimination and economic disparity that are more or less consistent throughout the United States."[243] An interesting recent phenomenon that underscores this point is the receptiveness of African Americans to genetic ancestry services, which has been explained as a desire to bridge the gap in recorded ancestry attributable to slavery.[244]

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[239] *See generally* 45 C.F.R. §46.116(a); TOM L. BEAUCHAMP & RUTH R. FADEN, INFORMED CONSENT: MEANING AND ELEMENTS, IN 3 ENCYCLOPEDIA OF BIOETHICS 1277, 1279 (3d ed. 2004).

[240] *See, e.g.,* Mari Matsuda, *Voices of America: Accent, Antidiscrimination Law, and a Jurisprudence for the Last Reconstruction*, 100 YALE L. J. 1329 (1991).

[241] Ossorrio, *About Face*, *supra* note 5, at 279.

[242] *See generally* Cheryl I Harris, *Whitewashing Race: Scapegoating Culture,* 94 CAL. L. REV. 907 (2006); Cheryl I. Harris, *Critical Race Studies: An Introduciton,* 49 UCLA L. REV. 1215 (2002).

[243] Foster, *Analyzing Race*, *supra* note 9, at 509-510.

[244] *See generally* John Simons, *Out of Africa,* 155 FORTUNE 37 (Feb. 19. 2007) ("African Ancestry's business has doubled in each of the past four years; all told, it has served 10,000 customers."). An estimated 460,000 people in the U.S. have taken genetic tests to determine ancestry even though they cost hundreds of dollars and individually provide incomplete pieces of information. *See* Ron Nixon, *DNA Tests, Find Branches But Few Roots*, N.Y. TIMES, Nov. 25, 2007, at 1, 7 (identifying companies engaged in genetic research to trace ancestry). "The demand has spawned an industry. Almost two dozen companies now offer such services, up from just two or three only six years ago. The field is so hot that private equity investors have moved in: Spectrum Equity Investors recently

In addition to individual consent, HMP and other population genetics efforts have raised recognition of the importance of group consent, and HMP has generated some algorithms for obtaining it.[245] Group consent is necessitated by the reality of group harm. In fact, the National Geographic Society's project to collect 100,000 indigenous DNA samples to trace migrations patterns of the human species, the Genographic Project, was suspended while an Institutional Review Board at the University of Pennsylvania worked on the informed consent process.[246] Directly addressing race and ethnicity in population genetics is a means to fully assess group impact, including group harm, and to develop this second dimension of consent. [247]

Bioethics also demands full deliberation of the racial and ethnic composition of study subjects. Specifically, the Common Rule and NIH regulations incorporate the fundamental ethics principles identified in the Belmont Report. [248] Justice, the second of the three principles,

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bought Ancestry.com, an online geneology site, for about $300 million shortly after the site added genetic testing as a service." *Id*. at 7. For one of the many companies offering these services, visit DNAPrint Genomics, Ancestry by DNA, *available at* http://www.ancestrybydna.com/ (last visited March 3, 2007). The impact of race and ethnicity on self and social identification is captured in *Motherland: A Genetic Journey*, a documentary by the British Broadcasting System, which follows three people who participated in a study allowing subjects with African features to use contemporary genetics to trace their ancestry. *See generally* BBC, *Motherland: A Genetic Journey* (Feb. 14, 2003). The impact of the results on these individuals' self-identification was profound and often unpredictable from the subjects' perspectives. *See id.*

[245] *See* Clayton, *Implications*, *supra* note 35. *See generally supra* note 17. The U.K. effort to build a biobank of biological, environmental, and medical data from 500,000 individuals qged 40-69 also has generated much ethics consideration and guidance. See generally UK Biobank Ethics and Governance Council, Annual Report 2004-2005 (2006).

[246] *See* Amy Harmon, *Question Stalls DNA Tracking: What's the Benefit for the Tribe?,* N.Y. TIMES, Dec. 10, 2006, at A1, A30. Visit the Genographic Project home page at https://www3.nationalgeographic.com/genographic/index.html (last visited Mar. 19, 2007). The project quickly generated group harm to the Havasupai tribe in the form of identity confusion, and virtually all tribes in North America recognized by the federal government have refused to participate. *See* Harmon, *supra* note 9, at A1, A30. The tribe's ancestors were linked to Asia, while tribe members have been raised to believe the Grand Canyon is the birthplace of humanity. *Id.*

[247] *See* Clayton, *Implications, supra* note 35. *See generally supra* note 17.

[248] *See supra* note 74 and accompanying text; The Belmont Report, Ethical Principles and Guidelines for the Protection of Human Subjects in Research (Apr. 18, 1979), *available at* NIH, Office of Human Subjects Research, http://ohsr.od.nih.gov/guidelines/belmont.html (last visited June 10, 2007).

demands recognition of race and ethnicity for research impact assessment and that such assessment be undertaken. As explained in the Report,

> [T]he selection of research subjects needs to be scrutinized in order to determine whether some classes (e.g., welfare patients, particular racial and ethnic minorities, or persons confined to institutions) are being systematically selected simply because of their easy availability, their compromised position, or their manipulability, rather than for reasons directly related to the problem being studied. Finally, whenever research supported by public funds leads to the development of therapeutic devices and procedures, justice demands both that these not provide advantages only to those who can afford them and that such research should not unduly involve persons from groups unlikely to be among the beneficiaries of subsequent applications of the research.[249]

In accordance with the justice principle, NIH rules require researchers to describe the composition of study populations and to provide a rationale for subject selection.[250] The realities of race and ethnicity are utilized to police against discrimination and exclusion, the very concerns fueling opposition to race-based genetics research.[251]

B. Research Pragmatism and a Means for Access

The social constructs of race and ethnicity, like genetic science, are neither intrinsically good nor bad. Their social impact depends upon how they are used. The ethical, legal, and social legacies of race and genetics are damning,[252] especially at their nexus, which mandates caution moving forward.[253] However, learning from the past and proceeding with caution must be distinguished from allowing the past to control the future, especially when the context is

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[249] Belmont, *supra* note 193, at Prin. III.

[250] *See supra* note 75 and accompanying text.

[251] *See id.* Even Professor Dorothy Roberts, who is strongly opposed to race-based biomedical research, is supportive of the use of race and ethnicity as sociopolitical classifications in order to counteract exclusion of these groups and health care disparities. Roberts, *Legal Constraints*, *supra* note 6, at 532-533. *See also supra* note 123.

[252] *See supra* note 15 and accompanying text.

[253] *See generally* Duster, *Lessons*, *supra* note 57; Hoffman, *Unraveled*, *supra* note 6; Roberts, *Legal Constraints*, *supra* note 6.

human health and there are opportunities to include where there has been exclusion, to lessen health care disparities, and to improve human health.[254]

Making medical sense out of the map of the human genome map necessitates accessing samples and medical information.[255] Race and ethnicity are strong influences on how populations are organized and self-identify,[256] especially in developing economies, [257] and utilization of such groupings could provide a means for the extensive sample collection necessary to advance the translation of the map into medical meaning.[258] Research pragmatism, the simple act of approaching and interacting with populations to collect needed samples and accompanying medical information on acceptable terms, favors recognizing and embracing race and ethnicity. Moreover, groups organized by race and ethnicity, such as country participants in The Pan Asian Initiative, have an unprecedented opportunity to leverage their organization to draw research to their priority areas, and do so on terms favorable to them.[259] Research contributions are being made, such as enablement of the MS study mentioned earlier[260] and race-based research to improve the efficacy and safety of biopharmaceuticals for the groups

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[254] Daar & Singer, *Pharmacogenetics*, *supra* note 105, at 242-246.

[255] *See supra* Part II.C. *Cf. generally* MARTIN & MORRISON, *supra* note 38.

[256] *See supra* notes 14, 157-160 and accompanying text.

[257] Daar & Singer, *Pharmacogenetics*, *supra* note 105, at 242-246.

[258] *See Yoon*, supra note 49, at 40. *See generally* Knoppers, *International Norms, supra* note 12.

[259] *See supra* note 147 (PXE case study).

[260] *See supra* notes 105-108 (MS study). Howard University's biobank is profiled in *Motherland, supra* note 189, when Howard's relatively sophisticated database is used to clarify some confusion for one of the subjects attempting to trace his genetic ancestry to Africa. Both the Howard University and PXE case studies are discussed in Winickoff, *supra* note 147, and Malinowski, *Technology Transfer*, *supra* note 36. At this time, the Howard biobank has been administratively shifted to its clinical center due in part to difficulties recruiting participants. Communication between Damon Bowe and Howard University Administrators, November 13, 2007. *See also* Kaiser, J., *GENETICS: U.S. Hospital Launches Large Biobank of Children's DNA*, 312 SCIENCE 1584a-1585 (2006).

involved.[261] "Racial and ethnic categories can be particularly important in securing resources to reduce structural barriers to prevention and care, especially where racial and ethnic categories are embedded in health care and research infrastructure and policy."[262] Globally, the need for change could not be greater: "Only 16 of the 1,393 new drugs that were marketed between 1975 and 1999 were registered for diseases that predominantly affect people in developing countries, and through of those were for tuberculosis, which is not restricted to developing countries."[263] Singling groups out on the basis of race and ethnicity to benefit their health is desirable, presumably a legitimate state interest, and not discrimination for the purposes of U.S. antidiscrimination jurisprudence.[264] It follows that, within the discipline of law, race and ethnicity in genetics research should be approached with the mindset of responsible bioethics and affirmative action/inclusion, not with a presumption of discrimination. We should think openly in terms of race and ethnicity to raise participation in the genomics revolution. Professor Hoffman's proposed attributes-based identification runs contrary to a function-based approach to affirmative action, which is premised upon recognizing race meaningfully in order to accomplish objectives such as inclusion and diversification.[265] "Prohibiting the use of racial identity labels

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[261] *See infra* notes 122, 153-156 (Bidil in African Americans); 109-117 (Theraflu in Asian populations).

[262] Foster, *Analyzing Race*, *supra* note 5, at 512.

[263] Daar & Singer, *Pharmacogenetics*, *supra* note 105, at 243.

[264] *See generally Grutter,* 539 U.S. at 306. *But see generally Seattle School District*, *supra* note 89, and accompanying text.

[265] *See* Hoffman*, Unraveled, supra* note 5. *See generally* Tseming Yang, *In Affirmative Action, the Census, and a Colorblind Society*, 11 MICH. J. RACE & L. 367, 402-415 (2006). In contrast, FDA policy demands recognition of U.S. Census classifications in order to promote inclusion where there has been exclusion. *See* Daar & Singer, *Pharmacogenetics*, *supra* note 105, at 242.

and ignoring prejudice and discrimination will not make them disappear. The very persistence of discrimination creates a need for a tool to monitor and redress its effects."[266]

C. The Underlying Science

Race-based research is producing results—results that include increased understanding of diseases such as MS and explanations for the prevalence of adverse events from common biopharmaceuticals in populations organized by race and ethnicity.[267] Nevertheless, ironically, advancement of responsible race and ethnicity-based genetics research also is consistent with the scientific arguments of its opponents, as illustrated by the lpBiobank case study.[268] To the extent opponents are proven correct, research outcomes and associated health care applications will transcend the racial and ethnic groups under study to benefit the entire human species. Advancement of the research will establish the extent to which race and ethnicity are genetic fictions. Groups organized by race and ethnicity will gain the opportunity to bargain for inclusion with both the science and medical communities, and the doctrine of group consent will be further developed.[269] To the extent the critics are incorrect, the groups under study will benefit disproportionately through scientific understanding and greater likelihood of medicinal applications tailored to their genetic idiosyncrasies.

The law, bioethics, and social science communities have raised concerns that the fluidity of race and ethnicity make them scientifically imprecise enough to necessitate regulating them

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[266] *Id.* at 416.

[267] *See supra* notes 105-108; 122, 153-156; 109-117 and accompanying text.

[268] *See generally supra* Part IV.

[269] For discussion of supportive case studies, including PXE, *see generally* Winickoff, *supra* note 148; Malinowski, *Technology Transfer*, *supra* note 37.

away from many biomedical research purposes.[270] These concerns embody several presumptions about the natural science communities. First, they presume that the natural science communities are incapable of accounting for the imprecision of what they recognize to be social constructs.[271] Second, they presume that the natural science and medical communities are not capable of policing the validity of scientific claims that arise from race and genetics-based research and engaging in meaningful, ongoing peer review. In fact, the natural science and medical communities utilize peer review extensively, in contrast with legal academia, which entrusts most journal publication selection and production to law students. Third, they presume that it is not possible to carry out race and ethnicity based research with responsible application of bioethics and sensitivity to group impact.

In fact, the immediate, definitive, and global response to Dr. Watson's comments about genetics and race[272] and the rigorous debate over this research within the natural science and medical communities suggest the contrary.[273] The broader debate within the global science, medical, bioethics, law, sociology, and other social science communities provides an even firmer check on the integrity of resulting claims and the threat of abuse of science for social injustice.[274] The role of law and policy in this debate should be to enforce regulations that protect human subjects to ensure race-based genetics research is carried out in a responsible manner, meaning with attention to consequences for individual subjects and the groups they represent.

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[270] *See, e.g.,* Cho, *Bathwater, supra* note 57.

[271] *See supra* notes 3, 19-25 and accompanying text.

[272] *See supra* notes 1-3 and accompanying text.

[273] *See generally supra* note 9.

[274] *See generally supra* notes 9-10

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VI. Conclusion

Race-based genetics research is advancing understanding about human disease and directly benefiting populations under study.[275] Entire nations are organizing themselves to reap these benefits, both individually and collectively.[276]

Law is largely a reflective endeavor; the precedent of the past is highly influential and often persuasive. However, mistakes of the past should not determine the present nor the future of genetic science and medicine, especially given the opportunities for inclusion and to improve human health associated with responsible genetics research.[277] Rather than allowing past mistakes in scientific research and medicine and a legacy of discrimination and exploitation based on race and ethnicity to shackle science, the law should be applied to ensure that research, including race, ethnicity, and ancestry-based population genetics, advances responsibly.

This article has analyzed the use of race and ethnicity in genetics research with sensitivity to past controversies and present inequities, but with an emphasis on applied bioethics, scientific pragmatism, and ongoing biopharmaceutical R&D. A major theme is that the lines between natural genetics science and the social sciences should not be made too faint and fluid. Doing so from the base of natural genetic science invites speculation about genetic truths and introduces susceptibility to prejudices. Doing so from the base of the social sciences invites overreaching far beyond the existing state of genetic science and the substitution of speculation for scientific reality in areas fundamental to human health and society.

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[275] *See, e.g., supra* notes 112-118, 105-108, 109-117, 122, 153-156.

[276] *See, e.g., supra* notes 112-117, 213 (Pan Asian Initiative).

[277] This opportunity is illustrated through the lpBiobank hypothetical case study presented in Part IV and several real world case studies addressed in Winickoff, *supra* note 147 and Malinowski, *Technology Transfer*, *supra* note 37.

The article's proposal promotes several important goals: heightened sensitivity towards people's self-identification, group identification, and group impact in the context of population genetics research on human subjects;[278] an increase in the rate of translation of the map of the human genome into medical meaning through more group participation in biomedical research;[279] an increase in participation in the genomics revolution by groups organized socially and culturally by race and ethnicity;[280] and a lessening of negative, documented disparities in the delivery of health care for these groups.[281]

Responsible race-based research is possible and desirable, and the law should be applied to accomplish nothing less. This position rests solidly on footings of applied bioethics,[282] research pragmatism, [283] and natural science.[284] Proposals to stretch U.S. antidiscrimination jurisprudence to regulate away the use of race and ethnicity in genetics research are misguided at best.

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[278] *See supra* Part V.A.

[279] *See supra* Part V.B.

[280] *See supra* Parts IV, V.B, and V.C.

[281] *See supra* Parts V.B and V.C.

[282] *See supra* Part V.A

[283] *See supra* Part V.B

[284] *See supra* Part V.C