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Concerns and priorities in genetic studies: Insights from recent African American biohistory

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Concerns and Priorities in Genetic Studies: Insights from Recent African American Biohistory

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I. INTRODUCTION AND CENTRAL CONCERNS

Advances in Deoxyribonucleic Acid (DNA) technology have made widespread genetic testing highly feasible and virtually inevitable. DNA sequencing of the human genome under the aegis of the Human Genome Project (HGP) is expected to be completed before 2000 C.E. This is largely the result of the application of automated DNA sequencing, improved sampling handling, advanced bioinformatics, and other technological innovations to the project. Additionally, an increased number of researchers are devoting their most productive career years to genomic research, further accelerating the rate of identification and description of important genomic sequences.

The HGP is the most important molecular taxonomic effort of this century.[1] By setting the taxonomic norm for *Homo sapiens,* the HGP establishes a baseline from which future comparisons such as the data from the Human Genome Diversity Project (HGDP) will be made. The HGP will provide the "structural periodic table" from which functional genomics will emerge.[2] Which alleles should contribute to this taxonomic norm? General guiding principles from population biology suggest several appropriate alternative sampling strategies: (1) identify sequences from the oldest (i.e., deepest) lineages of our species to obtain

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[1] A detailed critique of the taxonomic implications of the HGP was presented by the author at the Tuskegee University Conference on the Human Genome Project, Sept. 26-28, 1996, and at the 1997 Human Biology Association annual meeting in St. Louis, Missouri, Apr. 1-2, 1997.

[2] *See* Eric S. Lander, *The New Genomics: Global Views on Biology*, SCI., Oct. 1996, at 536. Functional genomics is seen as the sequel to structural genomics. While structural genomics provides information on disease gene sequence and expression, functional genomics represents a new paradigm to elucidate gene function and gene pathway. Frequently non-human systems (e.g., the fruit fly or the mouse) are used to discover the function and genetic pathway of human disease genes. Using non-human systems is generally more rapid and less costly than the more traditional biochemical approaches.

the most commonly shared variants among all of humanity;[3] (2) collect sequences from the most frequently encountered contemporary phenotype(s) to increase the likelihood that any derived sequences would at least be common among contemporary humans;[4] (3) sample proportionally from each geographical region of the human range based upon current population densities to ensure that the final genome is inclusive;[5] and (4) sample probabilistically on an international basis.[6] That none of these basic strategies are being employed in the selection of sequences for HGP analysis may severely limit the broad scientific and biomedical utility of this massive technological effort as well as weaken its taxonomic accuracy.[7]

The overwhelming majority of the genes being sequenced for the HGP come from an extremely limited number of North Atlantic European-American lineages. No serious attention has been paid to the issue of the representativeness of these lineages to the rest of humanity and their appropriateness for forming the taxonomic baseline for the human genome. Thus, upon completion of this "generic," "average," and "normal" genome (the stated goal of the project), the question will be then, as it is now, whose genome does it represent? How will this information benefit Americans of African descent and other citizens of color who have shared in the expense and sacrifice for this highly touted project? How will their inevitable variation from the molecular baseline generated by the HGP be addressed? How will molecular variants frequently observed in African Americans be categorized?

In some cases, these very variants may more closely represent original genes rather than their derivations; will "wild types" be confused with mutants? Will future taxonomic assessments based upon evolutionary peripheral lineages be skewed? These questions are more than simply academic. Aside from the recurrent socioeconomic issues of stigma and disenfranchisement associated with variation from the "norm," re-

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[3] This sampling strategy would mandate the selection of alleles from lineages in eastern and southern Africa where the oldest anatomical, molecular, and behavioral evidence for modern humans exists.

[4] This sampling strategy would encourage researchers to focus on the most commonly encountered contemporary human phenotype, ethnic Han Chinese females.

[5] Specifically, this sampling strategy is for proportional random sampling based upon current population distributions.

[6] Although randomized, this sampling strategy would have the potential to oversample sparsely populated areas of the human range and undersample more dense regions or more biodiverse groups.

[7] *See generally* Fatimah Jackson, *Bioanthropological and African American Concerns About the Human Genome Project*, *in* PROCEEDINGS OF THE TUSKEGEE UNIVERSITY CONFERENCE ON THE HUMAN GENOME 1996 (forthcoming 1997); Fatimah Jackson, *The Taxonomic Implications of the HGP*, 9 AM. J. HUM. BIOLOGY 130 (1997).

cent advances in the genetics of human disease have caused many researchers to modify our old working models of genetic diversity. In a recent summary of these advances,[8] Kenneth Weiss notes that new DNA sequence data have shown that most mutations are unique, rather than recurrent, that there are many (tens, even hundreds, not just two) alleles at a typical locus, and that variation in any geographic area is composed of clones of related alleles (therefore, cases of a given disease in a specific geographic area are usually genetically related; this same disease in another geographic area may involve a different set of genetically related alleles).[9] What will be the real potential for identifying the most relevant disease-related genes for use in evaluating disease causation across geographical groups? If identification is based on a taxonomically nonrepresentative set of alleles, will we have the most appropriate disease-gene sequences to facilitate the development of highly specific diagnostic and therapeutic products for the majority of humanity in the HGP?

Finally, when and if the systematic inclusion of African Americans and other groups into "biology's periodic table"[10]—the human genome—occurs, what will be the associated costs and the liabilities of being part of the data base? Will inclusion be coupled with improvements in the provision of health and education services to the African American community or will inclusion simply facilitate, at a molecular level, for example, the coercive and oppressive aspects of previous "bad science" on this group such as the forty-year use of uninformed and untreated African

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[8] *See* Kenneth M. Weiss, *Is There a Paradigm Shift in Genetics? Lessons from the Study of Human Diseases*, 5 MOLECULAR PHYLOGENETICS & EVOLUTION 259-65 (1996).

[9] For example, the specific alleles for cystic fibrosis that are common in Europeans are not necessarily the same alleles responsible for cystic fibrosis in non-European groups. Therefore, screening and gene therapy intervention strategies that are appropriate for one geographic group may prove ineffective for another group afflicted with the same phenotypic disease condition. *See* The Cystic Fibrosis Genetic Analysis Consortium, *Population Variation of Common Cystic Fibrosis Mutations*, HUMAN MUTATION 167, 167 (1994); Lap-Chee Tsui, *The Spectrum of Cystic Fibrosis Mutations*, 8 TRENDS IN GENETICS 391, 391 (1992). A genetic map based on one group may be essentially useless for identifying and depicting the genes relevant for the same disease state in another geographically distinct group. Even within geographic groups, significant variation occurs. Extensive molecular genetic studies of the Finns suggests that they are highly homogeneous, relative to other Europeans, and exhibit an exceptionally low frequency of cystic fibrosis relative to neighboring European groups. *See generally* Antti Sajantila et al., *Paternal and Maternal DNA Lineages Reveal a Bottleneck in the Founding of the Finnish Population*, 93 PROC. NAT'L ACAD. SCI. 12035 (1996). *See also* R.A. Kittles et al., *Y Chromosome Microsatellite Variation Supports a Finnish Bottleneck*, AM. J. PHYS. ANTHROPOLOGY 144 (Supp. 22 1996). In this context then, a Finn-based map of the genome would not even provide much insight into European disease-gene relationships. Clearly population history has had a major impact of the patterns of human genetic variation of biomedical importance.

[10] *See* Lander, *supra* note 2, at 536.

Americans in studies of the natural history of syphilis? Will inclusion address the concerns of the 1994 Manifesto on Genomic Studies among African Americans?[11]

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[11] In January 1994, following the November 1993 Wenner-Gren Conference where leading anthropologists critiqued the Human Genome Diversity Project at Mt. Kisco, New York, and the December 1993 World Council of Indigenous Peoples meeting in Quetzeltenango, Guatemala, where the premises and sampling strategy of the HGDP were flatly rejected by representatives of various indigenous minority groups, a consortium of African American social and biological scientists met in Washington, D.C. to formulate the Manifesto on Genomic Studies among African Americans. Six key points of this document were:

(1) African Americans expect full inclusion in any world survey of human genomic diversity. African Americans represent an amalgamation of African peoples with a unique lineage and cultural history. The inclusion of African Americans is not optional in any world survey, particularly if U.S. taxpayer monies are the funding source for such efforts;

(2) Given the high degree of genetic heterogeneity already uncovered among African Americans, no scattered, opportunistic samples can be validly extrapolated to the entire group of African Americans. It is imperative that systematic sampling, either model-based or design-based (probability) be used to identify the broad range of variability existing among African Americans and that this diversity be linked to other relevant social, cultural, historical, and ecological features of the African American existence;

(3) We are working toward the establishment of a National Review Panel for ongoing evaluations of genomic studies among African Americans. This National Review Panel will issue certification of projects that are consistent with the research aims and objectives of the African American community. The National Review Panel will also identify genetic research projects that are not consistent with the research needs of the African American community and may, in fact, be harmful to the community;

(4) As part of the certification process, acceptable genomic studies among African Americans must include representatives of the African American community in all aspects of the research process. African Americans must participate in the research design, research implementation, data collection, data analysis, data interpretation and dissemination of research results (i.e., scientific publications and policy implications of the results);

(5) A priority will be given to genomic studies that examine the linkage of African Americans to continental Africans and other Africans of the various diasporas. For too long, research dollars have been squandered on meaningless "black-white" comparisons, most of which provided few positive policy results for the African American community. The historical circumstances of African Americans has made it important to many in our community to identify the genetic connections between African Americans and Africans elsewhere. Therefore, this community priority must significantly inform prospective genomic research efforts;

(6) Genomic sampling of African Americans will be linked to improvements in the provision of health and educational services to the African American community. The largest proportion of health problems in the African American community are due to disorders that are preventable. These preventable environmental and gene-environment diseases should be addressed in conjunction with genomic studies. Indeed, the target of both disease prevention and genomic studies among African Americans must be the improved health and well being of the population and its enhanced survival into the coming centuries. Groups and individuals wishing to conduct genomic sampling among African Americans are expected to concurrently provide meaningful educational and training opportunities for African Americans.

Some insights may be gained from the on-going HGDP. The mission of the HGDP, an offshoot of the Human Genome Organization (HUGO), is to capture the genetic variation expressed in geographically remote and somewhat reproductively isolated ethnic and regional groups. A great deal of documentation has been generated by the Rural Advance Foundation International (RAFI) in response to these efforts. RAFI communications on the HGDP have expressed major reservations about the participation of the approximately 722 indigenous human communities targeted worldwide for DNA sampling by the HGDP.[12] In September 1996, a group of indigenous people and NGOs testified at a hearing of the National Academy of Sciences Committee on the HGDP opposing U.S. Government funds for the HGDP. Even if the HGDP were not being opposed by the very people it aspires to test,[13] its relevance to broadly distributed, highly biodiverse, macroethnic groups such as African Americans is highly suspect. Although the HGDP may appear to partially address the lack of variability in the HGP, it still does not respond effectively to the HGP's scientific unrepresentativeness. HGDP efforts among so-called "genetic isolates" are unlikely to generate much useful data for African Americans. Although it has been suggested that the HGDP "seeks to identify rare alleles in far-flung populations in order to reconstruct human evolution and migration,"[14] in fact, its research design, opportunistic sampling of groups adjudged as being in danger of extinction, is actually aimed at capturing highly unique alleles that occur in very low frequency, or not at all, in larger, more heterogeneous geographical groups, particularly among North Atlantic Europeans and their descendants.

II. SCIENTIFIC AND BIOMEDICAL MERITS OF REPRESENTATIVE GENETIC STUDIES

Among the most important scientific value of scientifically representative molecular genetic studies include the potential for insights into the biohistoric and phylogenetic relationships of contemporary and ancient human groups. Well-designed studies can yield a better understanding of human origins and distinguish between original (identified as "primitive") traits versus subsequent mutations (identified as "derived" traits). Anthropologically-informed molecular studies can identify the

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[12] *See Patents, Indigenous Peoples, and Human Genetic Diversity*, RAFI COMMUNIQUÉ (May 1993) <http://www.rafi.ca/communique/19932.html>.

[13] In many laboratories there has been a virtual stampede to sequence unique genes in infrequently encountered ethnic and regional groups. A few of these surreptitious opportunistic sampling efforts have begun to be challenged in the legal arena.

[14] Lander, *supra* note 2, at 537.

degree of within-group diversity and yield a better understanding of gene-gene and gene-environment interactions. Understanding the interactive foundations of disease expression is extremely important because most gene-influenced diseases, such as diabetes, hypertension, and various cancers, represent complex phenotypes and are rarely the result of single gene expression.

Poorly designed molecular genetic studies cannot be broadly extrapolated, regardless of the rigor of the bench chemistry. In DNA studies minimizing (or comparing) variation within a subspecies (even within a species) (Figure 1A), careful science must precede the selection of populations and individuals for study. This is essential because of the high degree of genetic redundancy between groups. Any variation between geographic groups will be, at best, at the microevolutionary level (that is, occurring below the species level). On the other hand, when molecular genetic studies are initiated to contrast the genomes of different genera (e.g., mouse vs. human) (Figure 1B), the contrasts are frequently macroevolutionary, that is, occurring above the species level. In comparisons between genomes, any individual mouse, or constellation of mice, can represent the mouse genome and any individual human, or constellation of humans, can represent the human genome because the magnitude of differences between the two genera are sufficient to justify the use of an extremely restricted proxy (one individual in this case) for an entire genus. The HGP is, however, targeted at the former level (Figure 1A): the project aims to reflect the normal sequence for 100,000 genes and accurately depict the ancestral and functional affinities among these genes. Such accuracy, however, is only feasible with more precise bioanthropological and biohistorical considerations going into the selection of the populations and individuals whose genes will comprise this genomic "periodic table."

The promised biomedical merits of molecular genetic testing will be determined by the responsiveness of the molecular data to at least two salient issues: (1) have the most appropriate allele or set of alleles for the ethnic or regional group in question been selected for structural and functional studies; and (2) are the proposed potential interventions (e.g., gene therapy) consistent with the explicit priorities of the tested community? The first of these issues, the importance of genetic representativeness, has already been addressed in this paper. Regarding the second issue, the case of the African Burial Ground (ABG) Project is particularly instructive.[15] What the ABG Project has reiterated is that scientific

[15] The African Burial Ground Project resulted from the accidental intrusion of government builders into an historic "Negro Burial Ground" gravesite in Lower Manhattan. *See* David W. Dunlop, *African Burial Ground Made Historic Site*, N.Y. TIMES, Feb. 26,

efforts (including genetic testing) must address the research issues of studied groups and not just the priorities of scientists. When the ABG Project was initiated, New York-based forensic anthropologists and historical archaeologists initially superimposed their own priorities on the research project. These priorities included the "racial" identification of the deceased remains from the African Burial Ground. These priorities, however, were not shared priorities among the descendent community. Instead, the descendent community and diverse community activists retaliated with their own set of research demands and, for a time, the analysis of these important and unique remains appeared stalemated.

After much effort however, the ABG Project was transferred to Dr. Michael Blakey of Howard University, in compliance with the demands of many in the descendent community. Here, the ABG Project has succeeded in charting a research course that encompasses both the priorities of the descendent community in New York and those of the scientists engaged in the project. Some of the priorities of the descendent community included the testing of hypotheses that reconstruct and evaluate the lifestyles of the individuals buried at the African Burial Ground (based upon a careful assessment of the osteological evidence) and hypotheses that seek to identify the likely ancestral homeland regions in Africa of buried individuals (based upon a thorough evaluation of extended haplotypes in the bone-derived DNA of the deceased and cultural analysis of any funereal artifacts). In African American biohistory, this is one of the very few cases where community concerns and priorities have significantly contributed to the scientific paradigm at every stage of the research. Broad African American participation in setting the research priorities, constructing hypotheses, collection and analysis of data, and the interpretation of research results has produced a higher level of accountability among the scientists engaged in the ABG Project than is usually seen in most scientific endeavors. As a consequence, the quality of the data, its utility to the targeted population, and the perceived relevance of, and hence investment in, the project among the descendent community has been remarkably high. In many respects, the ABG Project should serve as a prototype for future genomic initiatives, particularly among groups that have historically been victimized, rather than assisted, by genetic studies.

1993, at B3 (noting the efforts of African American residents to preserve the burial ground and their success with the New York Landmarks Preservation Committee); Laurie Goodstein, *N.Y. Work Halted on GSA Building*, WASH. POST, July 30, 1992, at A3 (discussing the discovery of 415 skeletons of slaves found at the construction site of a federal building); Stacy Shelton, *Burial Site Vigil Calls to Ancestors*, NEWSDAY, Aug. 10, 1992, at 2 (reporting on a vigil held by African American groups at the gravesite).

III. GENOMIC RESEARCH PRIORITIES OF AFRICAN AMERICANS

At the most basic level, African Americans want from their molecular genetic studies what other Americans want: improvements in health and health care. Specifically, African Americans are particularly concerned with frequently encountered genetic diseases and genetic diseases with high mortality. Priorities include hypertension, diabetes, various cancers, tuberculosis, and HIV infection. In conjunction with these fundamental concerns, however, the unique history of Americans of African descent in this country has mediated towards additional, attainable needs as well.

African Americans represent a recent yet highly heterogeneous, regionally diverse macroethnic group. Most anthropological genetic studies to date have tended to emphasize the admixture aspects of African American biodiversity,[16] focusing on the presence of European marker genes in African American groups. A careful review, however, of the magnitude of heterogeneity among various contemporary indigenous groups of west, central, and southwest Africa suggests that the bulk of African American heterogeneity is rooted in indigenous African variability. This African variability was subsequently elaborated upon in the American context. In the United States, the extent of gene flow between various African American communities and specific non-African groups (primarily European Americans and Native Americans) appears to be significantly correlated with the geographical region of residence, the time of contact, and the historical circumstances of contact. Socioeconomic, cultural, and biologic forces have synergistically contributed to the current biodiversity among African Americans. If this biodiversity is patterned, as the historical record predicts, it is essential that studies of molecular genetic diversity in this group be designed using sampling strategies that clearly and specifically address the magnitude and multiple origins of this variability.

The seventeenth, eighteenth, and nineteenth century African immigrants to the United States represented an assortment of indigenous ethnic groups and nation-states, mostly from the west, central, and southwest regions of the continent. The major source of Africans for the transatlantic trade was the area from modern day Senegal and Gambia to Angola, between latitudes 17° N and 17° S, including the great western bulge of the continent, eastward to longitude 5° E, north of the Bight of Biafra, and longitude 17° E south of the Bight. Additional sources in-

[16] *See, e.g.*, ADELE LOGAN ALEXANDER, AMBITIOUS LIVES: FREE WOMEN OF COLOR IN RURAL GEORGIA, 1789-1879 (1991); Ranajit Chakraborty et al., *Caucasian Genes in American Blacks: New Data*, 50 AM. J. HUM. GENETICS 145-55 (1992); Jeffrey C. Long, *The Genetic Structure of Admixed Populations*, 127 GENETICS 417-28 (1991).

cluded the coastal regions of modern day Mozambique and the western coast of Madagascar.

The great majority of contemporary African Americans are the descendants of survivors of the forced migrations of millions of people from the west African coasts, adjacent inland regions, and other areas of Africa to the western hemisphere and specifically, the United States. These migrations gained momentum around 1619 C.E., expanded during the transatlantic slave trade, and then diminished as this trade was increasingly abandoned (by 1850 C.E. in most of the Americas). The median year of arrival for Africans in the western hemisphere is estimated to be 1770 C.E.[17] Voluntary migrations of Africans to the western hemisphere much before or after this date are not thought to have significantly modified the overall African American gene pool (in contrast to the hypothesis of Van Sertima in 1976). Furthermore, significant post-emancipation migrations of continental Africans to the United States have been limited largely by restrictive U.S. immigration policies. Nevertheless, isolated instances of possible local importance have occurred, for example, the integration of twenty South African Zulu into the St. Louis, Missouri African American community after their escape from the "anthropological exhibits" of the 1904 St. Louis World's Fair.[18] Furthermore, it is important to note that African-descended individuals in the United States are the descendants of but a small proportion of the total number of Africans originally transported to the western hemisphere. Much of the human biodiversity that left Africa never made it across the Atlantic or never arrived in the United States. Once in the United States, however, these enslaved ancestral Africans may have had better opportunities for biological survival than their enslaved counterparts elsewhere in the western hemisphere.

It has been reasonably hypothesized that the genetic variability among the continental African ancestors of contemporary African Americans was initially very high as Africans of many culture groups were included in this great forced migration and because the migration extended over several centuries. This view is consistent with the observations of Gary B. Nash that among the Africans brought involuntarily into the United States, there was significant ethnic and social distinctiveness.[19]

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[17] *See generally* R. S. Cooper et al., *Patterns of Chronic Disease in Populations of the African Diaspora: United States, the Caribbean and West Africa* (May 1, 1994) (unpublished manuscript, presented at Morehouse School of Medicine Conference on African American Health and Biology).

[18] *See generally* PHILLIPS VERNER BRADFORD & HARVEY BLUME, OTA: THE PYGMY IN THE ZOO (1992).

[19] *See generally* GARY B. NASH, RED, WHITE AND BLACK: THE PEOPLES OF EARLY NORTH AMERICA (3d ed. 1992).

Nash also suggests that arriving enslaved Africans could only become communities by forging a new culture out of the elements of many old cultures combined with elements of the dominant European culture that now bounded their existence.

The historical population dynamics of African Americans from the sixteenth century through the late twentieth century has had a major impact on genetic diversity at three major stages. These are depicted in Figure 2. During Stage I, the political, economic, and social disruption preceding and concurrent with the capture and forced march of Africans to the west African coasts and the conditions of containment of those awaiting transport across the Atlantic Ocean produced largely stochastic reductions in overall genetic variability. At Stage II, the transatlantic Middle Passage and the activities associated with the slave indoctrination process further shrank genetic variability among surviving Africans, with both stochastic and directed effects.[20] At Stage III, residence in the Americas meant, for most Africans and African Americans, major alterations in the previous patterns of assortative mating, such that African ethnic groups who, within African boundaries, would have continued to practice endogamy were now captured, consolidated, contained, and redefined as "Negroes." These externally imposed conditions significantly redefined the patterns of genetic exchange.

Initially the capture of Africans for enslavement in the Americas was opportunistic.[21] As agriculture developed into a cash crop plantation system in what was to become the United States, and as Europeans and European Americans became more familiar with some of the phenotypic and sociocultural diversity among Africans, planters in North America became more particular. They began requesting from the dealers regional and ethnic groups of Africans whose physical and presumed psychological characteristics the planters felt best corresponded to specific forms of labor[22] and hence had the greatest potential to maximize profit.

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[20] *See* Olaudah Equiano, *The Interesting Narrative of the Life of Olaudah Equiano, or Gustavus Vasa, The African, in* AFRICA REMEMBERED: NARRATIVES BY WEST AFRICANS FROM THE ERA OF THE SLAVE TRADE 83 (Philip D. Curtin ed., 1967). *See generally* IV DOCUMENTS ILLUSTRATIVE OF THE HISTORY OF THE SLAVE TRADE TO AMERICA (Elizabeth Donnan ed., 1969); DANIEL P. MANNIX & MALCOLM COWLEY, BLACK CARGOES: A HISTORY OF THE ATLANTIC SLAVE TRADE 1518-1865 (1962); JOHN NEWTON, THE JOURNAL OF A SLAVE TRADER 1750-1754 (Bernard Martin & Mark Spurrel eds., 1962).

[21] *See* Venture Smith, *A Narrative of the Life and Adventures of Venture, A Native of Africa but Resident about Sixty Years in the United States of America* (New London 1978), *reprinted in* AFRO-AMERICAN HISTORY: PRIMARY SOURCES 5-10 (Thomas R. Frazier ed., 2d ed. 1988).

[22] *See generally* JOSEPH E. HOLLOWAY, AFRICANISMS IN AMERICAN CULTURE (1990); VINCENT BAKPETU THOMPSON, THE MAKING OF THE AFRICAN DIASPORA IN THE AMERICAS 1441-1900 160-64 (1987) (describing the attributes planter's typically ascribed to persons

For example, in some areas of South Carolina and much of Louisiana, planters involved in rice cultivation began requesting Africans captured from the Senegal/Gambia region, realizing that these individuals would more likely have had prior exposure to rice-based agriculture and would be more productive cultivators. Maryland and Virginian tobacco growers indicated a preference for Africans with the forest-associated broad phenotypes common on the Gold Coast, the tropical rain forest and wet savannas of modern day Ghana and Ivory Coast. In South Carolina, U.S. Navy records document that almost thirty percent of the enslaved Africans came from the region in and around modern day Angola.[23] Similar selectivity was evident in other regions of the Upper and Lower South, such that particular regions can now be linked, with varying degrees of reliability, to specific regions of residence and areas of exportation in continental Africa. For example, among contemporary African Americans of Baltimore, Maryland, the frequencies of specific βS haplotypes correspond to the proportions of enslaved Africans from the Gold Coast imported centuries earlier to nearby Virginia.[24]

Once settled in North America, Africans and their descendants maintained high degrees of local intra-African gene flow among formerly distinct African ethnic and regional groups, producing patterns of unique regional heterogeneity in the offspring. It is likely that the restructuring of traditional mating patterns among these early African migrants provided the foundation for the current high heterogeneity observed among contemporary African Americans. This African-based diversity was augmented as well by gene flow between Africans and western European groups[25] and gene flow with specific eastern Native American groups.[26]

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from various African regions); ANNE ELIZABETH YENTSCH, A CHESAPEAKE FAMILY AND THEIR SLAVES: A STUDY IN HISTORICAL ARCHAEOLOGY (1994); Ira Berlin, *Time, Space, and the Evolution of Afro-American Society on British Mainland North America*, 85 AM. HIST. REV. 44 (1980).

[23] *See* William S. Pollitzer, *Ethnicity and Human Biology*, 6 AM. J. HUM. BIOLOGY 3, 6 (1994). *See generally* AFRICA REMEMBERED, *supra* note 20; MARGARET WASHINGTON CREEL, A PECULIAR PEOPLE: SLAVE RELIGION AND COMMUNITY-CULTURE AMONG THE GULLAHS (1988).

[24] *See* Ronald L. Nagel & Helen M. Ranney, *Genetic Epidemiology of Structural Mutations of the β-Globin Gene*, 27 SEMINARS IN HEMATOLOGY 342, 349 (1990).

[25] These groups include, for example, Welsh, Irish, Anglo-Saxon, Scot, Scotch-Irish, Huguenot, Flemish, and Walloon.

[26] These groups include, for example, Seminole, Nanaticoke, Natchez, Natick, Wampanoag, Houma, Quapaw, Miccosuke, Lumbee, Cherokee, Chicahominy, and Choctaw. For a discussion of the gene flow see Michael L. Blakey, *Social Policy, Economics, and Demographic Change in Nanaticoke-Moor Ethnohistory*, 75 AM. J. PHYS. ANTHROP. 493-502 (1988) (discussing the ethnohistory of the Nanaticoke-Moors of Delaware, a group descending from Native Americans, European Americans, and Afro-Americans). *See generally* ANGIE DEBO, A HISTORY OF THE INDIANS OF THE UNITED STATES (1970); WILLIAM LOREN KATZ, BLACK INDIANS: A HIDDEN HERITAGE (1986); KENNETH WIGGINS

In certain geographical regions of importation and migration, Africans were faced with new selection pressures associated with changes in climate, diet, and disease.[27] Some of these new conditions may have stimulated alterations in the cadence of various somatic DNA/RNA processes such as transcription termination and initiation. This would have had nontransmissible but potentially biologically significant effects on individuals and regional groups of African Americans. In other geographical regions, the obligatory segregated residential patterns to which these Africans and early African Americans were subject provided the social conditions for genetic drift such as the coastal Sea Island plantations of the Carolinas and Georgia.

The extremely restrictive conditions of American slavery and hypersegregation dictated the residential patterns of the vast majority of early African Americans to such an extent that the American homeland areas of this group are still non-randomly distributed across the United States. In contemporary times, kin networks and other social, political, and economic factors have continued to maintain the distinctive residential patterns of African Americans.[28]

Many African Americans are hopeful that well-designed molecular genetic studies will shed insight into the specific recent African origins of the group. African Americans share a unique and well-documented biohistory of significance in the design and implementation of molecular genetic studies. The collective history of this recently formed macroethnic group includes initial forced migrations from selected areas of Africa to specific U.S. regions, economically mandated and geographically restricted internal migrations, and persistent non-random residential patterns. These residential patterns have influenced the direction and cadence of gene flow, the opportunities for genetic drift, and the regional variation in exposure to particular environmental selective factors. As a consequence, it is very likely that significant regional differences exist among African Americans in the frequencies of certain African and non-African marker genes, polymorphisms, and extended haplotypes. If mo-

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PORTER, THE NEGRO ON THE AMERICAN FRONTIER (1971).

[27] *See* Curtis W. Wienker, *Birth Weight in an African-American Population Living Under Moderate Ecological Stress*, 62 HUM. BIOLOGY 719, 732 (1990) (discussing a study of African American birthweight in McNary, Arizona, a location with high altitude and cold winters). *See generally* KENNETH F. KIPLE & VIRGINIA HIMMELSTEIB KING, ANOTHER DIMENSION TO THE BLACK DIASPORA: DIET, DISEASE, AND RACISM (1981).

[28] *See generally* JOYCE ASCHENBRENNER, LIFELINES: BLACK FAMILIES IN CHICAGO (1975); DANIEL M. JOHNSON & REX R. CAMPBELL, BLACK MIGRATION IN AMERICA: A SOCIAL DEMOGRAPHIC HISTORY (1981); ELMER P. MARTIN & JOANNE MITCHELL MARTIN, THE BLACK EXTENDED FAMILY (1978); CAROL B. STACK, ALL OUR KIN: STRATEGIES FOR SURVIVAL IN A BLACK COMMUNITY (1974); Morton Rubin, *Migration Patterns of Negroes from a Rural Northeast Mississippi Community*, 39 SOC. FORCES 59-66 (1960).

lecular genetic studies are combined with detailed ethnographic, historic, demographic, deep genealogic, and ecologic assessments (i.e., ethnogenetic data), it should be possible to reconstruct much of the "missing" lineage information desired by many African Americans.

Toward this end, the Genomic Models Research Group (GMRG) at the University of Maryland has developed such model-based ethnogenetic sampling strategies using African American saturation densities (i.e., intensity) and continuance densities (i.e., duration) to systematically reconstruct regional and subregional patterns of African American biological variation.[29] These sampling techniques, used as a prelude to molecular genetic studies, have already indicated significant differences in the patterns of specific regional African ancestry among African Americans originating in either the Chesapeake Bay area, the Carolina Coast area, or the Mississippi Delta areas of the United States. According to our preliminary results (Table 1), variation in ancestral African origins in each of these three regions of importation is the foundation for current biodiversity in the group. Additionally, within each region, varying degrees of gene flow have occurred between specific local African Americans, Native Americans, and European Americans (Table 2). This has further amplified the diversity within African Americans. The techniques applied in this model are appropriate for anthropological genetic studies of other U.S. ethnic groups as well.

IV. RECONCILING THE CAPABILITIES OF MOLECULAR GENETICS WITH AFRICAN AMERICAN PRIORITIES

Modern techniques in molecular biology now allow us to identify subtle distinctions within, as well as between, regional groupings of highly diverse macroethnic groups, for example U.S. Blacks, U.S. Whites, U.S. Asians, Native Americans, and Hispanics. While a great deal of research has gone into the development of sophisticated molecular tools to clarify these distinctions, much less thought has been given to either the appropriate population-level strategies necessary to identify representative subgroups or the appropriate lineages within these groups for molecular sampling. Too frequently, molecular studies of contemporary macroethnic groups have overlooked within-group biodiversity and failed to consider the salient historical and ecological factors maintaining particular patterns of variation within highly heterogeneous groups. As a

[29] *See* Fatimah Jackson et al., *Ethnogenetic Layering of the Crescent States: Using a Model-Based Strategy for Population Genetic Sampling*, 8 AM. J. HUM. BIOLOGY 118 (1996); Fatimah Jackson et al., *Regional Diversity in African Origins of African Americans Within the Crescent States*, *in* TUSKEGEE UNIVERSITY HUMAN GENOME CONFERENCE, PROGRAM ABSTRACTS (1996).

consequence, many molecular genetic studies have been designed and the collected data interpreted within the context of historically inaccurate nineteenth century folk taxonomies and static, outmoded concepts of biological race, with a blind eye to the magnitude or significance of within-group differences. African Americans want to know about this within-group diversity and how it interfaces with the complex health profile of the group. Many studies of African American biodiversity in particular have relied on scattered, opportunistic sampling and analysis of individuals whose results were inappropriate to apply to the entire population. Other studies have been cross-sectional design-based probability surveys that lacked historical depth and were extremely expensive to implement. Again, these studies usually assumed cross-regional genetic uniformity among African Americans, were often based on ethnographically weak and regionally limited personal collections of blood samples, and provided less robust assessments of evolutionary hypotheses.

As currently designed, the HGP and HGDP are not likely to generate data explicitly beneficial to African Americans and other citizens of color. If the data derived from these expensive efforts are to be useful to the majority of African Americans, the sampling strategies of the HGP and HGDP must be at least partially inclusive of the diverse African origins of African Americans. Furthermore, it is essential that ethnic communities, such as African Americans, wishing to be included in the various human genome projects be educated about the resolution power of the existing technology (its strengths and limitations) and permitted to meaningfully collaborate in the development of hypotheses, research design, the collection, analysis, and interpretation of data, and the development of subsequent policy initiatives. Recent African American biohistory is quite informative; only through full participation in the scientific process can communities of color expect to have their own concerns and priorities addressed.

Legends for Figure 1A and Figure 1B

Figure 1A Sampling sequence when comparisons are made between two or more genera. In such cases, scientific precision is more important after an individual, from a specific population, of a particular species, of the genus in question, has been selected for study. In such comparisons, the molecular assessments (D -> E) are paramount for subsequent valid reconstruction and extrapolation (E -> H).

Figure 1B Sampling sequence when comparisons are made within a specific genus and species (e.g., *Homo sapiens)*. In such cases, scientific precision must begin with the selection of a representative population (B -> C) and continue in the identification of an appropriate individual from that population (C -> D) for study. Only if this has been done following established protocols in population biology can the molecular assessments (D -> E) be validly extrapolated to higher levels of organization (E -> H).

Figure 1A

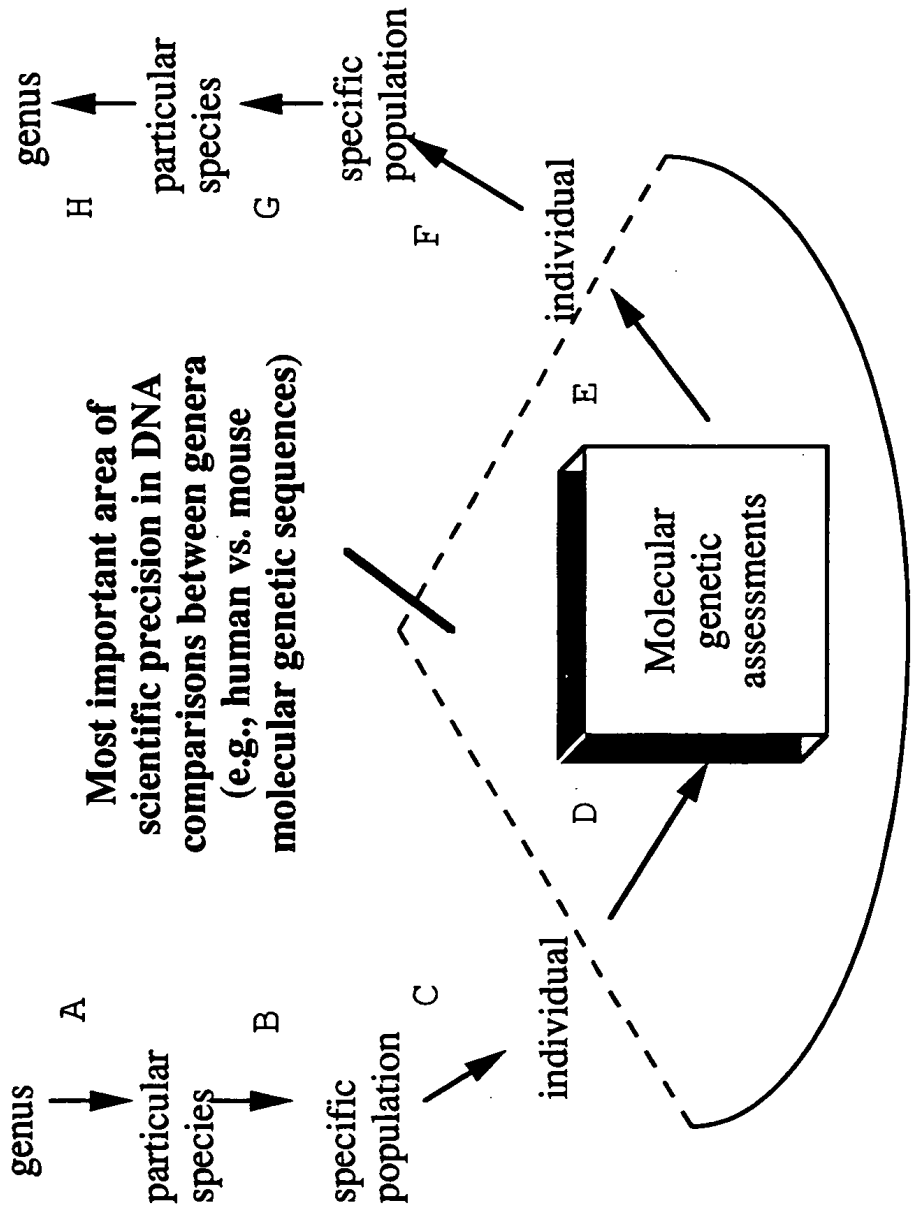
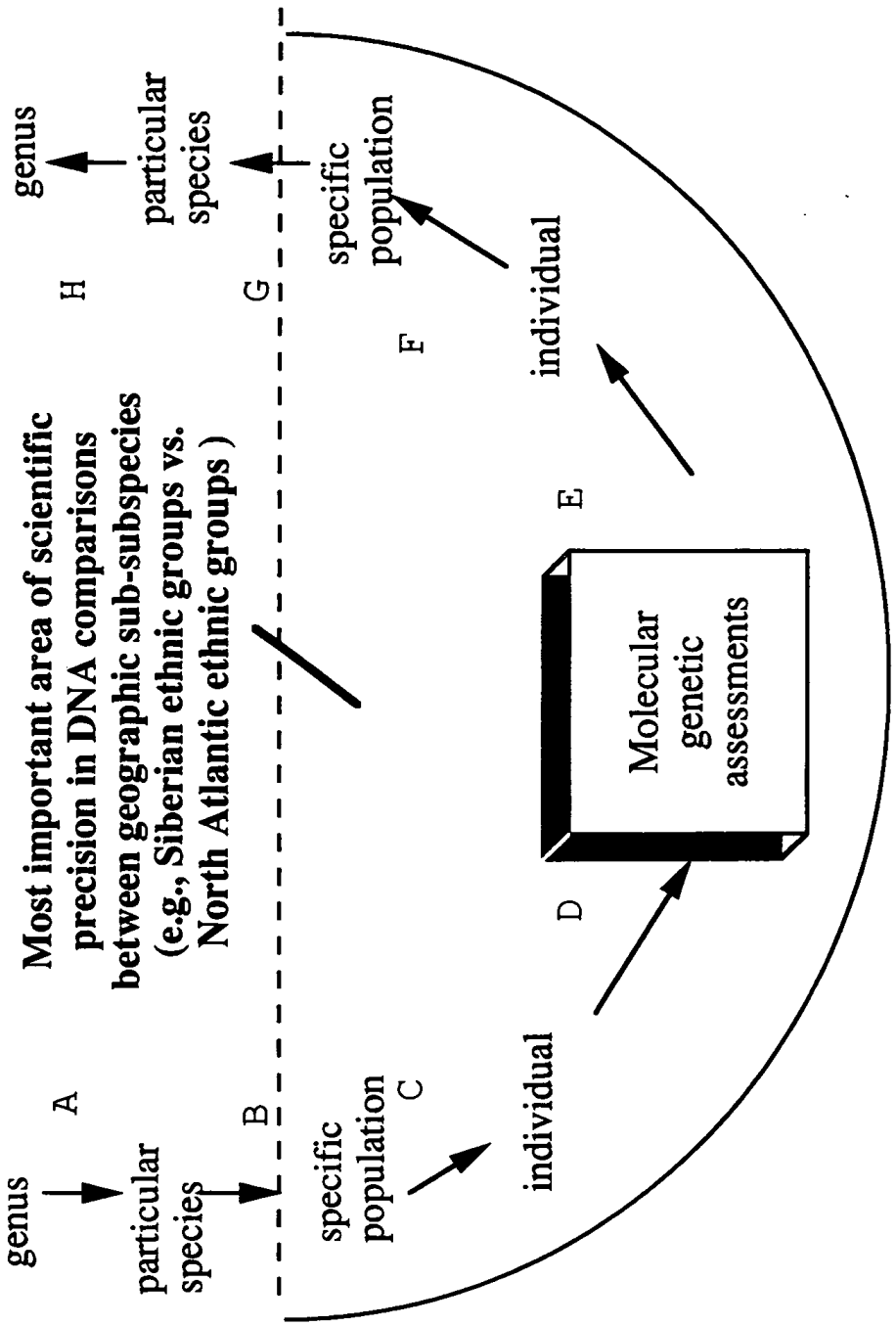
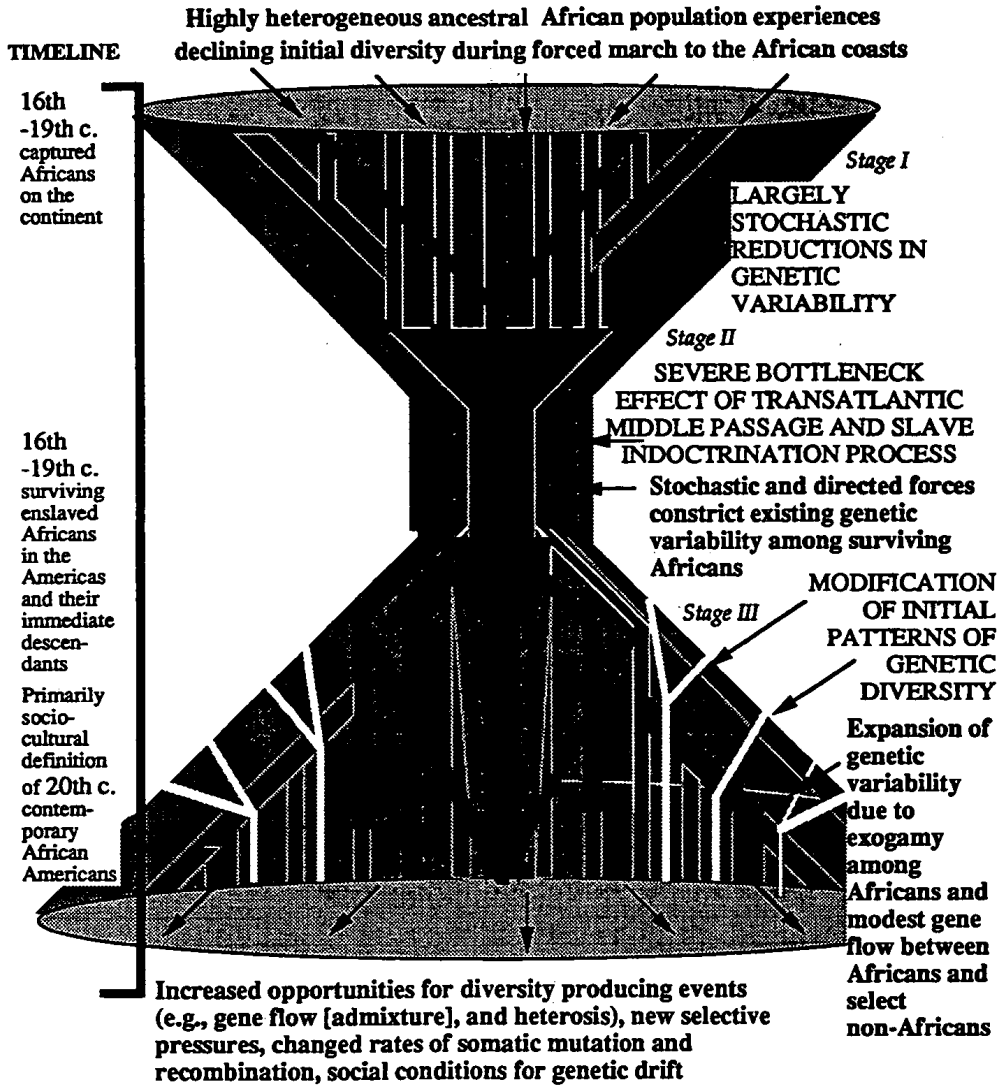

genus
A
particular species
B
specific population
C
individual
D
Molecular genetic assessments
E
individual
F
specific population
G
particular species
H
genus
Most important area of scientific precision in DNA comparisons between genera (e.g., human vs. mouse molecular genetic sequences)

Figure 1B



GENETIC VARIABILITY AMONG ANCESTRAL CONTINENTAL AFRICANS



CURRENT GENETIC VARIABILITY AMONG AFRICAN AMERICANS

Diagram from Jackson 1997

TABLE 1 **Summary of African regional origins of various local African American groups.**

US Importation Site	Location	African Regional Origins	Percentage of Site
Chesapeake Bay	ATLANTIC OCEAN INLETS IN VIRGINIA AND MARYLAND	Bight of Biafra	38%
		Central Africa	16%
		Gold Coast	16%
		Senegambia	15%
		Upper Guinea	11%
		Mozambique	4%
Carolina Coast	BAY AND LOWLAND AREAS OF NORTH AND SOUTH CAROLINA	Central Africa	40%
		Senegambia	23%
		Upper Guinea	18%
		Gold Coast	9%
		Bight of Biafra	7%
		Bight of Benin	3%
Mississippi Delta	GULF AREAS OF TEXAS, LOUISIANA, MISSISSIPPI, AND INLAND	Senegambia	32%
		Central Africa	25%
		Bight of Benin	25%
		Bight of Biafra	8%
		Upper Guinea	6%
		Gold Coast	2%
		Mozambique	2%

data derived from: Jackson et al 1996b

TABLE 2 Summary of major non-African groups historically admixing with local African Americans.

US Importation Site	Major nearby Native American groups	Major colonizing European groups
Chesapeake Bay	Delaware, Piscataway, Nahyssan, Pamunkey Nanticoke, Powhatan, Monacan, Saponi, Conoy Tutelo, Nottaway, Susquehanna, Meherrin, Choptank	Ulster English, Irish, Scots, Germans, Scots-Irish, Welsh
Carolina Coast	Nansemond, Croatan, Neusiok, Cherokee, Tuscarora, Nottaway, Pamlico, Tutelo, Neusiok, Catawba, Sewee, Waccamaw, Creek, Hitchiti, Meherrin, Muskogee	French Huguenots, Highland Scots, English Quakers, Scots-Irish, Palatinate Germans, Swiss, Spanish
Mississippi Delta	Chitimacha, Biloxi, Choctaw, Ofo, Houmas, Chickasaw, Tunica, Coushatta, Caddo, Atakapa Karankawa	Acadia French, Spanish

data revised from: Jackson et al 1996a